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## Pulse Oximetry and Oxygen Services for the Care of Acutely Unwell Children Attending Frontline Health Facilities in Lagos, Nigeria (INSPIRING-Lagos): Study Protocol for a mixed-methods evaluation.

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Pulse oximetry and oxygen for primary care

# Pulse Oximetry and Oxygen Services for the Care of Acutely Unwell Children Attending Frontline Health Facilities in Lagos, Nigeria (INSPIRING-Lagos): Study Protocol for a mixed-methods evaluation.

**Authors:** Hamish R Graham<sup>\*1,2</sup>, Omotayo E Olojede<sup>2</sup>, Ayobami A Bakare<sup>3,4</sup>, Eric D McCollum<sup>5</sup>, Agnese Iuliano<sup>6</sup>, Adamu Isah<sup>7</sup>, Adams Osebi<sup>7</sup>, Ibrahim Seriki<sup>7</sup>, Tahlil Ahmed<sup>8</sup>, <sup>8</sup>Samy Ahmar<sup>8</sup>, Christine Cassar<sup>8</sup>, Paula Valentine<sup>8</sup>, Temitayo Folorunso Olowookere<sup>9</sup>, Matt MacCalla<sup>9</sup>, Obioma Uchendu<sup>3,11</sup>, Rochelle Ann Burgess<sup>6</sup>, Tim Colbourn<sup>6</sup>, Carina King<sup>4,6</sup>, Adegoke G Falade<sup>2,12</sup> on behalf of the INSPIRING Project Consortium\*\*

## Affiliations:

<sup>1</sup> Centre for International Child Health, Murdoch Children's Research Institute, University of Melbourne, Royal Children's Hospital, Parkville, Victoria, Australia.

<sup>2</sup> Department of Paediatrics, University College Hospital, Ibadan, Nigeria.

<sup>3</sup> Department of Community Medicine, University College Hospital, Ibadan, Nigeria.

<sup>4</sup> Department of Global Public Health, Karolinska Institutet, Stockholm, Sweden.

<sup>5</sup> Eudowood Division of Pediatric Respiratory Sciences, Department of Pediatrics, School of Medicine, Johns Hopkins University, Baltimore, USA.

<sup>6</sup> Institute for Global Health, University College London, London, UK.

<sup>7</sup> Save the Children International, Abuja, Nigeria.

<sup>8</sup> Save the Children UK, London, UK.

<sup>9</sup> GlaxoSmithKline (GSK), Lagos, Nigeria.

<sup>10</sup> GlaxoSmithKline (GSK), Brentford, UK.

<sup>11</sup> Department of Community Medicine, College of Medicine, University of Ibadan, Ibadan, Nigeria.

<sup>12</sup> Department of Paediatrics, College of Medicine, University of Ibadan, Ibadan, Nigeria.

**\*Corresponding author:** Hamish Graham, Centre for International Child Health, Department of Paediatrics, University of Melbourne, Royal Children's Hospital, 50 Flemington Road, Parkville, Victoria 3052, Australia.

+61 3 93456262 [hamish.graham@rch.org.au](mailto:hamish.graham@rch.org.au)

**\*\*Full list of INSPIRING Consortium members:** Carina King (Karolinska); Tim Colbourn, Rochelle Ann Burgess, Agnese Iuliano (UCL); Hamish R Graham (Melbourne); Eric D McCollum (Johns Hopkins); Tahlil Ahmed, Samy Ahmar, Christine Cassar, Paula Valentine (Save the Children UK); Adamu Isah, Adams Osebi, Ibrahim Haruna, Abdullahi Magama (Save the Children Nigeria); Temitayo Folorunso Olowookere (GSK Nigeria); Matt MacCalla (GSK UK); Adegoke G Falade, Ayobami Adebayo Bakare, Obioma Uchendu, Julius Salako, Funmilayo Shittu, Damola Bakare, and Omotayo Olojede (University of Ibadan).

Pulse oximetry and oxygen for primary care

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Pulse oximetry and oxygen for primary care

## ABSTRACT

**Introduction:** The aim of this evaluation is to understand if introducing stabilisation rooms equipped with pulse oximetry and oxygen systems to frontline health facilities in Ikorodu, Lagos State, alongside healthcare worker (HCW) training improves the quality of care for children with pneumonia aged 0-59 months. We will explore to what extent, how, for whom, and in what contexts the intervention works.

**Methods and analysis:** Quasi-experimental time-series impact evaluation with embedded mixed-methods process and economic evaluation. Setting: 7 government primary care facilities, 7 private health facilities, 2 government secondary care facilities. Target population: Children aged 0-59 months with clinically diagnosed pneumonia, and/or suspected or confirmed COVID-19. Intervention: "stabilisation rooms" within participating primary care facilities in Ikorodu local government area, designed to allow for short-term oxygen delivery for children with hypoxaemia prior to transfer to hospital, alongside HCW training on integrated management of childhood illness (IMCI), pulse oximetry and oxygen therapy, immunisation, and nutrition. Secondary facilities will also receive training and equipment for oxygen and pulse oximetry to ensure minimum standard of care is available for referred children. Primary outcome: correct management of hypoxaemic pneumonia including administration of oxygen therapy, referral, and presentation to hospital. Secondary outcome: 14-day pneumonia case fatality rate. Evaluation period: August 2020 to September 2022.

**Ethics and dissemination:** Ethical approval from University of Ibadan, Lagos State, and University College London. Ongoing engagement with government and other key stakeholders during the project. Local dissemination events will be held with the state Ministry of Health at the end of the project (December 2022). We will publish the main impact results, process evaluation and economic evaluation results as open-access academic publications in international journals. Registration: ACTRN12621001071819.

## ARTICLE SUMMARY

### Strengths and limitations of this study

- Includes multiple government and private primary care facilities selected from a single local government area providing broad representation of primary care in Lagos
- Time-series analysis of quantitative data on pulse oximetry and oxygen practices and impact on clinical decision making and outcomes providing robust evidence of impact
- Qualitative data from healthcare workers and community members addressing perceptions and experience with pulse oximetry and oxygen therapy
- Theory-informed mixed-methods evaluation to understand whether the intervention worked, how, for whom, and in what contexts, with economic evaluation
- Flexible data collection plan to allow for COVID-19 modification

Pulse oximetry and oxygen for primary care

## INTRODUCTION

In 2019, Nigeria ranked as the country with the highest under-five mortality rate (117.2 per 1,000 live births)<sup>1</sup>. Pneumonia is the leading cause of child death in Nigeria and globally, causing approximately 134,000 and 800,000 deaths in 2017, respectively.<sup>1</sup> The under-5 mortality in Lagos state is around half the national average, at 50 per 1,000 live births, representing an urban population with lower relative poverty levels (1.1% live in severe poverty).<sup>2</sup>

From November 2018 to June 2019 we conducted a situational analysis of paediatric pneumonia in Lagos and Jigawa states of Nigeria, to inform the design of an intervention programme to reduce paediatric mortality. We found that while protective and preventive factors, such as vaccine coverage and clean cooking fuel, were high in Lagos, care-seeking and health facility service readiness were poor.<sup>3-6</sup> Therefore, taking an approach which targets improved quality of care for pneumonia diagnosis and treatment could achieve mortality impact. In the context of the emerging COVID-19 pandemic, in consultation with local stakeholders, we decided to focus on healthcare worker (HCW) capacity-building and enhancement of pulse oximetry and oxygen systems.

Pulse oximetry is a standard of care for identifying hypoxaemia (low blood oxygen levels) and guiding oxygen therapy in hospitalised patients. The World Health Organization's (WHO) Integrated Management of Childhood Illness (IMCI) guidelines also recommend pulse oximetry for identifying severely ill patients with hypoxaemia in primary care settings, requiring referral to hospital.<sup>7-9</sup> Despite their potential for reducing mortality, pulse oximeters are rarely available in frontline facilities in low- and middle-income countries.<sup>6 10-12</sup> Indeed, our survey of 58 Lagos health facilities in 2020 found pulse oximeters in none of the primary health facilities, 56% (15/27) of private health facilities, and exclusively on the paediatric ward of three secondary health facilities.<sup>13</sup>

Oxygen therapy is required for stabilisation and treatment of severely ill patients with conditions such as COVID-19, pneumonia, and sepsis, and is listed by the WHO as an Essential Medicine.<sup>14-16</sup> Effective oxygen systems require (i) reliable oxygen supply and delivery devices, (ii) rational use by skilled HCWs guided by pulse oximetry, and (iii) supportive infrastructure, management, and biomedical support (e.g. power supply, procurement and planning, skilled technicians with tools and spare parts) - **Figure 1**.<sup>17</sup> Our situational analysis revealed opportunities to improve patient access to oxygen through improved equipment selection and installation, repair and maintenance, and training and support for HCWs and technicians.<sup>6 18 19</sup> Subsequently, the COVID-19 pandemic has highlighted the importance of hospital oxygen systems and exacerbated existing deficiencies.<sup>8 20-23</sup>

The Nigerian Federal Ministry of Health (FMoH) has demonstrated its commitment to improving paediatric survival and oxygen access, with updated medicine, equipment and treatment guidelines.<sup>24-28</sup> Pulse oximetry and oxygen therapy were identified as priority areas for intervention in the context of Lagos by both local and international stakeholders.<sup>5</sup> However, there is a need for evidence on the impact and cost-effectiveness of these interventions when delivered routinely in frontline care, especially understanding the contextual mechanisms within government and private facilities, to facilitate effective adoption at scale.

This protocol outlines the mixed-methods evaluation plan for integrated HCW training, pulse oximetry and oxygen implementation in government and private health facilities in Lagos.

Pulse oximetry and oxygen for primary care

## METHODS AND ANALYSIS

### Research Questions and Study Design

The overall aim of this evaluation is to understand if introducing pulse oximetry and oxygen systems to health facilities in Lagos, alongside HCW training, improves the quality of care for children with pneumonia aged 0-59 months. We will explore to what extent, how, for whom, and in what contexts this intervention works. This aim will be addressed through specific research questions (**Table 1**) using a quasi-experimental time-series impact evaluation with embedded mixed-methods process and economic evaluation. The study period will be August 2020 – September 2022 and will be conducted in Ikorodu Local Government Area (LGA), Lagos State (**Figure 2**).

Table 1 Evaluation domains and key research questions

Domain	Research question
<b>Impact</b>	<ul style="list-style-type: none"> <li>• What is the impact of “stabilisation rooms”, enhanced with uninterrupted oxygen and pulse oximetry, alongside healthcare worker training, on the quality of care for children with hypoxaemic pneumonia aged 0-59 months attending outpatient facilities in Ikorodu LGA, Lagos state, Nigeria?</li> <li>• What is the impact of “stabilisation rooms”, on the case-fatality rate of clinical pneumonia, including suspected or confirmed COVID-19 cases, among children aged 0-59 months attending outpatient facilities in Ikorodu LGA, Lagos state, Nigeria?</li> </ul>
<b>Process</b>	<ul style="list-style-type: none"> <li>• Which attributes, mechanisms, effects (intended and unintended), and contextual factors enable, or prevent pulse oximetry and oxygen from improving case management of clinical pneumonia cases in children under-5 in Ikorodu LGA?</li> <li>• How do everyday environments of wider resource limitation in health systems affect the delivery of pulse oximetry or oxygen at health facilities?</li> <li>• What contexts shape the willingness of family members to accept the administration of oxygen and nasogastric feeding to children under-5 in Ikorodu LGA?</li> <li>• What contexts shape the willingness of practitioners to administer pulse oximetry and oxygen for clinical pneumonia and other acute infection cases in children under-5 in Ikorodu LGA?</li> <li>• How do primary and secondary care providers perceive the use of pulse oximetry, and how does it influence clinical decision making and referral recommendations for children under-5? How does this differ between government and private providers?</li> <li>• How does the use of pulse oximetry influence oxygen practices for children under-5 in different clinical contexts (public, private) in Ikorodu LGA?</li> <li>• What is the prevalence of hypoxaemia at primary care in Ikorodu LGA, amongst children with signs and symptoms of clinical pneumonia?</li> <li>• Does the type of pulse oximeter (i.e. Lifebox or Masimo Rad-G) influence their use and impact clinical care and decision making?</li> </ul>
<b>Economic</b>	<ul style="list-style-type: none"> <li>• Is this intervention package cost-effective considering opportunity costs of current and projected health spending (i.e. what is the estimated net benefit of the intervention package)?</li> <li>• If the intervention package is cost-effective is it affordable given the budget required for scale-up in Lagos state? What are the implications for other parts of Nigeria?</li> </ul>

The *impact evaluation* will estimate the intervention effect on hypoxaemic pneumonia management and 14-day mortality among children aged 0-59 months, using a time-series approach. We anticipate a baseline period lasting between 2 months and 12 months, depending on the facility, and that intervention components may be implemented at different time points (e.g. IMCI training occurring before oxygen installation).



## Pulse oximetry and oxygen for primary care

The *process evaluation* will use a theory-informed mixed-methods study design, with qualitative data from HCWs and caregivers, and quantitative monitoring and evaluation data to understand what worked, how, for whom, and in what contexts.

The *economic evaluation* will involve a time-motion study, together with analysis of administrative financial data and caregiver surveys to assess the economic cost of the intervention from the provider (Ministry of Health) and consumer (patient/caregiver) perspectives. Together with the impact evaluation data we will assess the cost-effectiveness and affordability of the intervention.

## Setting

A summary of Ikorodu LGA is presented in **Table 2**. We will be working in both government and private healthcare facilities, including 7 of the 28 government primary health centres (PHCs), 7 private health facilities, and both government secondary care facilities in Ikorodu LGA (**Figure 3**). There are no tertiary facilities in Ikorodu LGA.

Table 2 Summary characteristics of Ikorodu Local Government Area (LGA)

Characteristic	Number
Estimated population	890,000
Estimated under-5 population	160,000
Under-5 mortality ratio	50 per 1000 live births [Lagos state]
Primary government facilities	28
Primary private facilities	148
Secondary government facilities	2
Secondary private facilities	1

Source: Multiple Indicator Cluster Survey 2016-17, Survey Findings Report. Abuja, Nigeria: National Bureau of Statistics and United Nations Children's Fund., 2017. Facility number obtained from Ministry of Health in November 2019.

## Selection

We will cover the whole LGA geographically but will not include all facilities in the study. Save the Children, in collaboration with LGA leaders, purposively selected 7 government PHCs as "flagship" facilities for the program, targeting government facilities that have greatest need (Annex 1). Each PHC was then matched based on geographical location to a private health facility which had consented to take part in the programme during the formative phase and provides care for children under-five years of age.<sup>13</sup> We also included the two government secondary care facilities.

## Population

The intervention and impact evaluation will focus on children aged 0-59 months attending the outpatient areas of participating facilities for an acute illness and who are diagnosed with clinical pneumonia defined according to the 2014 WHO IMCI guidelines and/or suspected or confirmed COVID-19 (**Table 3**).<sup>29</sup> However, the intervention will be available to benefit all children and adults receiving care from participating facilities.

Pulse oximetry and oxygen for primary care

Table 3 Clinical case definitions of acute lower respiratory infections, and recommended primary care treatment according to WHO Integrated Management of Childhood Illness (IMCI) guidelines

Category	Signs and Symptoms	Treatment
<b>Pneumonia</b>	Cough and/or difficulty breathing AND Fast breathing for age AND/OR Chest indrawing	Home treatment with oral antibiotics
<b>Severe Pneumonia</b>	Cough and/or difficulty breathing AND General danger sign AND/OR Hypoxaemia	Hospital inpatient treatment with IV antibiotics (and oxygen for those with SpO <sub>2</sub> <90%)
<b>Suspected or confirmed SARS-CoV-2</b>	Clinician diagnosis AND/OR RT-PCR positive test	Not specifically addressed in IMCI. Local guidelines adapted from WHO guidelines. <sup>30</sup>

## Intervention

### *Stabilisation rooms*

The project will establish “stabilisation rooms” within the outpatient areas of participating primary facilities, designed to allow for short-term oxygen delivery for children with hypoxaemia prior to transfer to hospital (or admission to the ward). These stabilisation rooms are intended to support both short-term COVID-19 and longer-term paediatric pneumonia care needs, and will consist of the following intervention components:

1. Pulse oximeters, equipped with both paediatric and adult re-usable probes;
2. Medical oxygen supply delivered through newly installed oxygen concentrators powered from mains supply, generators and/or solar power;
3. Clinical guidelines, job aids and clinical training

Secondary health facilities that admit children will also be supported with pulse oximeters and oxygen concentrators for use on the wards to support safe care of patients referred for inpatient care.

Selection of devices was based on national and international technical guidance and experience with similar devices in Nigeria and elsewhere.<sup>21 22 25</sup> To facilitate a sub-study comparing the usability and acceptability of two oximeters, facilities will be randomly allocated, with a 1:1 ratio using a random number generator, to receive either Lifebox (Acare Technology, New Taipei City, Taiwan) or Masimo RadG (Masimo, Irvine CA, USA) oximeters.

We anticipate a 1-6 month delay in receiving both oxygen and oximetry equipment, given the global supply chain challenges during the COVID-19 pandemic; therefore, the evaluation design will need to be adaptive and flexible. The intervention will be delivered by Save the Children Nigeria, with technical support provided by private non-profit Oxygen for Life Initiative (OLI), working closely with local government.

### *Training and supervision*

The stabilisation rooms will be implemented alongside broader capacity-building activities targeting primary care HCW practices (preventive and curative). This will include training on WHO’s IMCI guidelines, pulse oximetry and oxygen therapy, immunization, and nutrition (**Table 4**).

## Pulse oximetry and oxygen for primary care

Table 4 Summary of training activities

<b>Training</b>	<b>Location &amp; Duration</b>	<b>Target</b>
Integrated Management of Childhood Illness (IMCI)	In primary facilities, 6 days.	Community Health Extension Worker, Community Health Officers, nurses,
Pulse oximetry and Oxygen therapy	In primary and secondary care facilities, 3 days.	Community Health Extension Worker, Community Health Officers, nurses, midwives, doctors, +/- technicians
Immunization “Reaching Every District”	In primary care facilities, 2-3 days.	Vaccinators, immunisation focal persons, facility officer in charge
Nutrition – Infant and Young Child Feeding (IYCF), Community Management of Acute Malnutrition (CMAM)	In training centre and primary care facilities, 3 days. Repeated after 1 year for new staff.	Community Health Extension Worker, Community Health Officers, nurses, nutrition focal person

All training activities will be coordinated by Save the Children Nigeria using the ADDIE model (A = Analysis, D = Design, D = Develop Training Materials, I = Implement/Delivery, and E = Evaluation). Save the Children Nigeria will conduct a Training Needs Assessments using their “Task Analysis” tools, assessing a health care worker’s actual skills and knowledge compared to the skills and knowledge they are meant to have based on their job descriptions. The training will be adapted from existing standard training packages to the local context with the assistance of local facilitators selected from the State Ministry of Health (SMOH) and partners (e.g. WHO, UNICEF, OLI).

Local facilitators who lead the training will also act as coaches, mentors and supervisors after the training has been completed and the participants have been deployed. They will visit each facility every 4-6 weeks and maintain interim contact using mobile phone-based group messaging. The Ikorodu LGA health team will also contribute to supervision through existing immunization supportive supervision arrangements.

### *Control*

The control period –before the interventions are delivered in study facilities– will consist of routine clinic operation with existing material resources.

## **Impact Evaluation**

### *Outcome*

The primary outcome is the correct management of hypoxaemic pneumonia amongst children aged 0-59 months who present to a participating health facility. ‘Correct management’ is defined as the child receiving oxygen treatment and being referred to and subsequently attending hospital (all three criteria need to be met). Clinical pneumonia is defined according to the 2014 IMCI guidelines (Table 3).<sup>9,29</sup> COVID-19 is defined as either PCR-test confirmed or based on a clinical diagnosis according to local guidelines. Oxygen treatment and referral decision will be recorded at recruitment, and hospital attendance, treatment and deaths will be confirmed by telephone interview at 2-weeks and via medical records where available. Secondary outcomes include 14-day mortality and process outcomes (see Process Evaluation).

### *Data Collection*

Study employed clinical data collectors will be responsible for recruitment and data collection in participating facilities. Each data collector will be responsible for one to two clinics, aiming to screen all children under-five who present to the clinic with an acute infection for eligibility before they have been routinely assessed by the HCW. After identifying those who meet eligibility criteria, data collectors will

## Pulse oximetry and oxygen for primary care

extract data from the HCW's clinical notes. These data will include: diagnosis, treatment and referral decision, vital signs and clinical observations. Where key data are missing, they will collect these data (e.g. oxygen saturation, or weight) and additional clinical data, including auscultation findings using standard and digital stethoscopes. Data collectors will also ask about care-seeking, intentions for onward care, vaccine status and socio-economic status. The data collector will inform the HCW if they find any signs that meet referral criteria.

Data collectors will conduct follow-up interviews 14 days after recruitment, by telephone. The follow-up interview will primarily confirm survival of the child, any onward care and oxygen received after their initial presentation, the cost of care, and treatment adherence. Where a child has died, the interview will be stopped and the study staff will attempt to conduct a verbal autopsy (VA), using the COVID-19 adapted WHO 2016 VA tool and additional social autopsy questions around care-seeking.<sup>31</sup>

Data collection will be conducted between August 2020 and September 2022 (24 months), and exact timing of baseline and intervention periods will depend on intervention implementation at different facilities.

### *Sample size*

We had originally calculated a sample size based on the case fatality rate (CFR) as a primary outcome, assuming a baseline CFR of 4% and 1920 eligible children recruited. In this scenario, we had 72% power to detect a 50% reduction in CFR<sup>32</sup> but recognised this was uncertain given the COVID-19 context and lack of baseline data. We therefore reviewed the data from August 2020 – January 2021 and found lower than expected CFR making this scenario unfeasible. We updated the sample size for the new primary outcome of “correct management of hypoxaemic pneumonia cases”, based on using a pre-post analysis. Using the following baseline assumptions, we will be able to detect a minimum 15% increase in correct management: 75 children with completed follow-up per month; 24-month data collection period; intra-cluster correlation 0.05; 10% hypoxaemic; 5% correctly managed pre-intervention. This means we should be able to detect a significant difference if the intervention results in  $\geq 20\%$  of hypoxaemic children being correctly managed.

### *Analysis*

The primary analysis will be a time-series analysis, using a change point model. In this analysis an intervention time point is not pre-specified, therefore, given the challenges we will face in defining clean “pre” and “post” intervention periods, this method allows more flexibility and fewer assumptions than interrupted time-series analysis. We will be able to assess whether: 1) changes in incidence have occurred; 2) identifies the most likely time for the change point, which we can link to the intervention and other key events.<sup>33</sup>

Sensitivity analyses will include: stratification by age-group and sex of the child; stratification by clinic type; and stratification by pneumonia severity classification. We will account for clustering of outcomes at clinic-level in analyses and explore the role of intervention dose-effects.

Secondary analyses will include: assessing impact on 14-day mortality; describing the epidemiology of hypoxaemia amongst children; predictive modelling of pneumonia mortality and hypoxaemia; analysis of changes in clinical attendance rates, referral decision making, and referral attendance over time; description of suspected COVID19 epidemiology.

## **Process Evaluation**

Process data will cover the context, intervention delivery (including fidelity and reach), and mechanisms of impact (Annex 2).<sup>34</sup>

### *Context*

## Pulse oximetry and oxygen for primary care

We will add to the contextual information from our situational analysis, with particular view on how COVID-19 alters health structures, community perceptions and care-seeking behaviours.

*Health system:* A biomedical engineer will conduct annual oxygen and pulse oximetry equipment checks, including the location, use, functionality and maintenance. A baseline assessment of existing equipment was conducted during the formative research phase (January – August 2020) and the full methods reported.<sup>13</sup>

To understand the evolving health facility context, we will periodically measure: essential medicine stock-outs of tracer drugs (e.g. AmoxDT); availability of PPE and IPC materials; staff turnover, balance of cadres, experience and gender. These data will be collected quarterly, by phone by study staff or if circumstances permit, during quarterly supervisory visits to the clinics.

*Community:* To provide an understanding of the community context in which the intervention is being implemented, we will collect data on the socio-demographic characteristics of caregivers and children, and their care-seeking patterns.

### *Intervention delivery*

Intervention delivery will be evaluated according to fidelity to the original design of the intervention, noting adaptations, reach and the change in knowledge of participants.

*Clinical practices:* The clinical data collectors will conduct case note reviews at each facility, on a quarterly basis, to determine the standard of IMCI assessment, diagnosis and treatment decision-making. The data collector will go back in time from the date of data collection in the patient registers/case notes until the pre-specified target number of cases have been identified (e.g. target for PHCs is 50 eligible children).

*Intervention fidelity:* The training delivered by Save the Children Nigeria will be independently observed by a member of the research staff, who will record whether the training was delivered as intended. On-going supervision and functioning of pulse oximeters will be recorded using routine supervision logs and work plans. Data collectors and HCWs will be asked to keep diaries to collect their everyday perceptions and experiences in relation to the intervention.<sup>35</sup>

*Reach:* Intervention reach will be assessed by tracking the coverage of trained staff and functional equipment throughout the duration of the project. These data will be routinely collected quarterly, by phone by study staff or if circumstances permit, during quarterly supervisory visits to the clinics.

### *Mechanisms of impact*

The mechanism of impact will be measured from the health provider and community perspectives.

*Health provider:* Data collected during recruitment will provide data on diagnoses made, treatments given and referral decision-making. We will extract data from a sub-set of these case notes to check for compliance to guidelines, and track this over time.

We will conduct focus group discussions (FGDs) and in-depth interviews (IDIs) with HCWs to understand their perceptions about pulse oximetry and oxygen therapy and understand changes over time (Annex 3). FGD/IDIs will be held with the healthcare providers before the intervention has been implemented, and then at select time-periods throughout the study period. IDIs will be organised around story completion activities, a method which is designed to create safe spaces for participants to reveal processes of sense-making and things about themselves that they may otherwise feel uncomfortable doing in group or public situations (such as disclosure of sensitive issues).<sup>36</sup>

*Community:* Our situational analysis, alongside studies from other contexts, have revealed considerable misconceptions about oxygen among HCWs and patients/families. We will conduct interviews and FGDs

## Pulse oximetry and oxygen for primary care

with caregivers, to understand perceptions about oxygen and behavioural responses to the intervention (Annex 4,5). We will triangulate this qualitative data with quantitative data collected in the follow-up surveys to understand changes in care-seeking behaviours following the intervention. Specific indicators include: the delay in deciding to first seek care; the location of first seeking care; the decision to attend a referral; and delay in attending a referral. In addition, data from narratives taken during verbal autopsies will be used to explore how care pathways differed between those children who survived and who died from an acute infection.<sup>37</sup>

### *Analysis*

We will report findings descriptively. Where appropriate, data will be stratified by healthcare provider cadre and facility type and differences evaluated with chi-squared and t-tests.

FGD and interview data will be analysed using a pragmatic framework approach that blends inductive and deductive analytical approaches.<sup>38</sup> Pre-defined and agreed themes based on the topic guide will guide an initial analysis, with any emerging themes coded during the analysis. All qualitative data will be coded and analysed by two researchers, and interpretation and conclusions will be shared and discussed with the core project team.

## **Economic Evaluation**

We will conduct a prospective costing of the interventions which will include financial (capital set-up and recurrent expenditures) and economic costs (time-motion studies),<sup>39-41</sup> based on the provider (Ministry of Health) perspective. We will also consider the household perspective, via surveys of financial and time (opportunity) costs to caregivers.

### *Excel budget tool*

We will use the accounts of the implementing partner to determine actual capital and recurrent expenditure on the interventions including equipment and maintenance, training, mentoring and supportive supervision, travel and allowances, and salaries of project staff, using an ingredients approach.<sup>39</sup> All costs required to replicate the intervention will be included. Cost data from the accounts will be extracted to an Excel template adapted from one used by Batura *et al* for costing complex public health interventions.<sup>39</sup>

### *Timesheet and Observation checklist*

We will conduct a time-use study of healthcare workers managing childhood pneumonia cases at primary health facilities to determine how much time is spent by healthcare workers on the use of pulse oximetry and oxygen per case. This study will be done at government PHCs as our economic evaluation is focused on the Ministry of Health provider perspective. We will collect data on time-use via a researcher observed time-motion study (if deemed safe to do so) of 30 pneumonia and 30 severe pneumonia cases (Annex 6).<sup>41</sup> For both the timesheet and observational studies we will time: communication, documentation, vital signs assessment, physical examination, use of pulse oximetry, medication given, oxygen set-up and adjustment, feeding, suctioning, medication administration. We will use time use data and the HCW cadre to estimate the healthcare provider cost of delivering pneumonia care.

### *Caregiver perspectives*

We will determine the cost to patients during the follow-up interviews with caregivers. In a random sub-sample of 100 caregivers we will administer a longer questionnaire which includes: the time taken to seek care as well as the resources spent on travel, childcare, opportunity costs of business or other activities forgone (estimated by potential lost earnings or opportunities). We will monitor the costs of essential items

Pulse oximetry and oxygen for primary care

every quarter using a basic market survey (e.g. fuel, food supplies) to monitor the wider economic impact on household costs related to changing oil-prices and COVID-19.

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Pulse oximetry and oxygen for primary care

## Data Management

We will collect data in several formats: audio; paper forms and notes; electronic data using a custom built CommCare app; teleconference recordings and text messages; paper consent forms. Data collection, storage and processing will be compliant with the European Union General Data Protection Regulations (EU GDPR). We will collect minimal personal identifiable information, including: age, date of birth, sex, education, religion, location and job title.

Personal information gathered as part of interviews and FGDs will be pseudo-anonymised with study ID numbers. Participants will be informed of the use of their data during informed consent and will be reminded that they do not have to participate. Personal identifiable information obtained during the recruitment questionnaire to enable a follow-up at 14 days will be deleted before data is stored and archived, and not be shared outside the team.

Interviews and focus group discussions will be audio recorded, using a digital voice recorder, with individual informed consent. Audio files and video files will be stored on the local researcher's computer while being processed in an encrypted folder and will be stored by the responsible investigators on university secure servers at University College London and Karolinska Institutet.

Electronic data will be collected on Android devices, using CommCare (Dimagi, Cambridge MA, USA). Each data collector will use a password protected device for data collection. Electronic data will be stored in raw instance files, and .csv and Stata .dta formats, on password protected devices, and deleted from the audio recorders and Android tablets at the end of the study period. The app includes child case logic to allow follow-up and recruitment forms to be linked with a unique and anonymised ID, and in-built cleaning rules and branching logic will be used to ensure data quality. Data checks will be done throughout the project, and major errors (e.g. eligibility and outcome) will be verified in the field. All data management and processing will be done using Stata SE14 (StataCorp, College Station TX, USA).

Completed paper consent forms will be stored in a locked filing cabinet in a guarded office compound at University College Hospital Ibadan and will be archived for 10 years, then disposed of securely by burning.

## Patient and Public Involvement

This project benefited from co-design activities from early in its genesis, including a co-design workshop in April 2019 involving representatives from civil society, local and national government, and professional organisations, together with Save the Children, GSK, and evaluation partners (Annex 7). Selection of the facilities was conducted in partnership with the Ikorodu local government. Community perspectives were sought during the situational analysis but community members were not consulted in the design of the intervention or evaluation.

## ETHICS AND DISSEMINATION

Given the rapidly changing COVID-19 situation, we have embedded adaptive methods for data collection and will continuously monitor risks. The protocol is based on the following assumptions: we will be able to collect data within health facilities; project staff will be able to move around Lagos state; the project will end in December 2022.

This study has received ethical approval from University of Ibadan (REF UI/EC/19/0551), Lagos State (REF LS/PHCB/MS/1128/VOL.V1/005), and University College London (REF 3433/005). We will seek individual written consent for FGDs/IDIs and verbal consent for other questionnaires. We will obtain facility-level approvals for equipment audits and case note reviews. All interviews, FGDs and questionnaires completed by healthcare providers will be anonymous.



## Pulse oximetry and oxygen for primary care

We do not anticipate any serious negative impacts to participants taking part in this research, and the intervention should benefit children and healthcare providers directly. The main ethical challenge presented by the impact evaluation is the management of cases with discrepant diagnoses between routine care and clinical research assessments. We decided that in cases where a child meets criteria for referral from primary to secondary-level care according to our research assessment, we will notify the responsible HCW immediately.

Due to COVID19, there may be a risk posed to study staff based in clinics while community transmission is on-going. We will ensure that staff are supplied with adequate PPE and IPC training, and we will discuss with the clinics leads how we can best support efforts to maintain hygiene and distancing practices. We will provide study staff with transport to and from clinics, and assign data collection rotas to minimise travel.

Interviews, FGDs and surveys will take between 15 and 90 minutes. To mitigate the time burden, data collection will be conducted in private locations that are convenient to the participants and we will reimburse participants for transport cost and provide a refreshment. For the recruitment questionnaires, we will monitor the duration of these interviews to ensure they do not delay a severely sick child leaving the clinic to attend hospital.

The topics of discussions, interviews and surveys may result in some participants being upset, due to recent personal experiences of a sick child, or if the discussion raises questions about their professional capacity. We will ensure that questions are asked in a neutral tone, the researchers collecting the data are sensitive to these issues, and that participants are provided with a list of currently available services relating to a range of health concerns in their local areas. In order to minimise any distress from verbal autopsies, they will be conducted no sooner than 14 days after the death (as recommended by WHO), will be done at a time and location which allows privacy for the family, and questionnaires will be pilot tested to ensure cultural sensitivity.

### *Engagement and Dissemination*

Engagement with key stakeholders, including healthcare workers, communities and SMOH officials will be done continually during the project. Local healthcare providers and caregivers will be recruited as participants, and alongside the formal data collection, will be encouraged to share thoughts and experiences around paediatric pneumonia.

The protocol was developed through round table discussions with project partners and will be shared with key stakeholders in the Ministry of Health and implementing partner Save the Children Nigeria. Local dissemination events will be held with the SMOH at the end of the project (December 2022), to share the findings and present the plans for future implementation with regular progress meetings prior.

We will publish the main impact results, process evaluation and economic evaluation results as academic publications in international journals. We will also submit abstracts to present findings at both local Nigerian conferences and international conferences on child health and pneumonia throughout the project.

Pulse oximetry and oxygen for primary care

## Acknowledgements, Competing Interests, Funding and other required statements

**Protocol version:** 2.1, 9 June 2021

**Acknowledgments:** We would like to thank representatives from the Lagos Ministry of Health and Ikorodu District Health Office for their on-going support and participation in the co-design process for this study.

**Competing interests statement:** HG, EM, CK are advisors to Lifebox Foundation on pulse oximetry. AAB, AGF, HG are board members for Oxygen for Life Initiative (OLI), a private non-profit that provides implementation services to the INSPIRING project. AI, AO, IS, TA, SA, CC, PV are employed by Save the Children UK who are part of the partnership funding the research. TFO, MM are employees of and stockholders in GSK, a multinational for-profit pharmaceutical company that produces pharmaceutical products for childhood pneumonia, including a SARS-CoV2 vaccine, and no direct financial interests in oxygen or pulse oximeter products.

**Funding:** This work was supported by the GlaxoSmithKline (GSK)-Save the Children Partnership (grant reference: 82603743). Employees of both GSK and Save the Children contributed to the design and oversight of the study as part of a co-design process. Any views or opinions presented are solely those of the authors/publisher and do not necessarily represent those of Save the Children or GSK, unless otherwise specifically stated.

**Sponsor:** University College London (UCL), contact [t.colbourn@ucl.ac.uk](mailto:t.colbourn@ucl.ac.uk).

**Author contributions:** TC, CK, RB, HG, EDM, AI, TA, SA, TFO, MM, AAB, AGF conceived of the study. HRG wrote the first manuscript draft with major input from CK, OO, TC, EDM, AGF, AAB. All authors contributed to refinement of the study protocol and approved the final manuscript. TC, CK and AGF are grant holders. HRG and OO are joint first authors. CK and AGF are joint senior authors.

**Ethics approval:** This study has received ethical approval from the Research Ethics Committee at: University of Ibadan, Nigeria (REF UI/EC/19/0551), Lagos State, Nigeria (REF LS/PHCB/MS/1128/VOL.V1/005), and University College London (REF 3433/005).

**Trial registration:** Registered on the Australian and New Zealand Clinical Trials Registry (ACTRN12621001071819)

**Data sharing statement:** Fully anonymised versions of the data will be archived at the close of the project, for sharing with other researchers within and outside of the EEA. A copy of the clean, anonymised data will be stored by UCL, University College Hospital Ibadan and Save the Children.

Pulse oximetry and oxygen for primary care

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Pulse oximetry and oxygen for primary care

## Figures

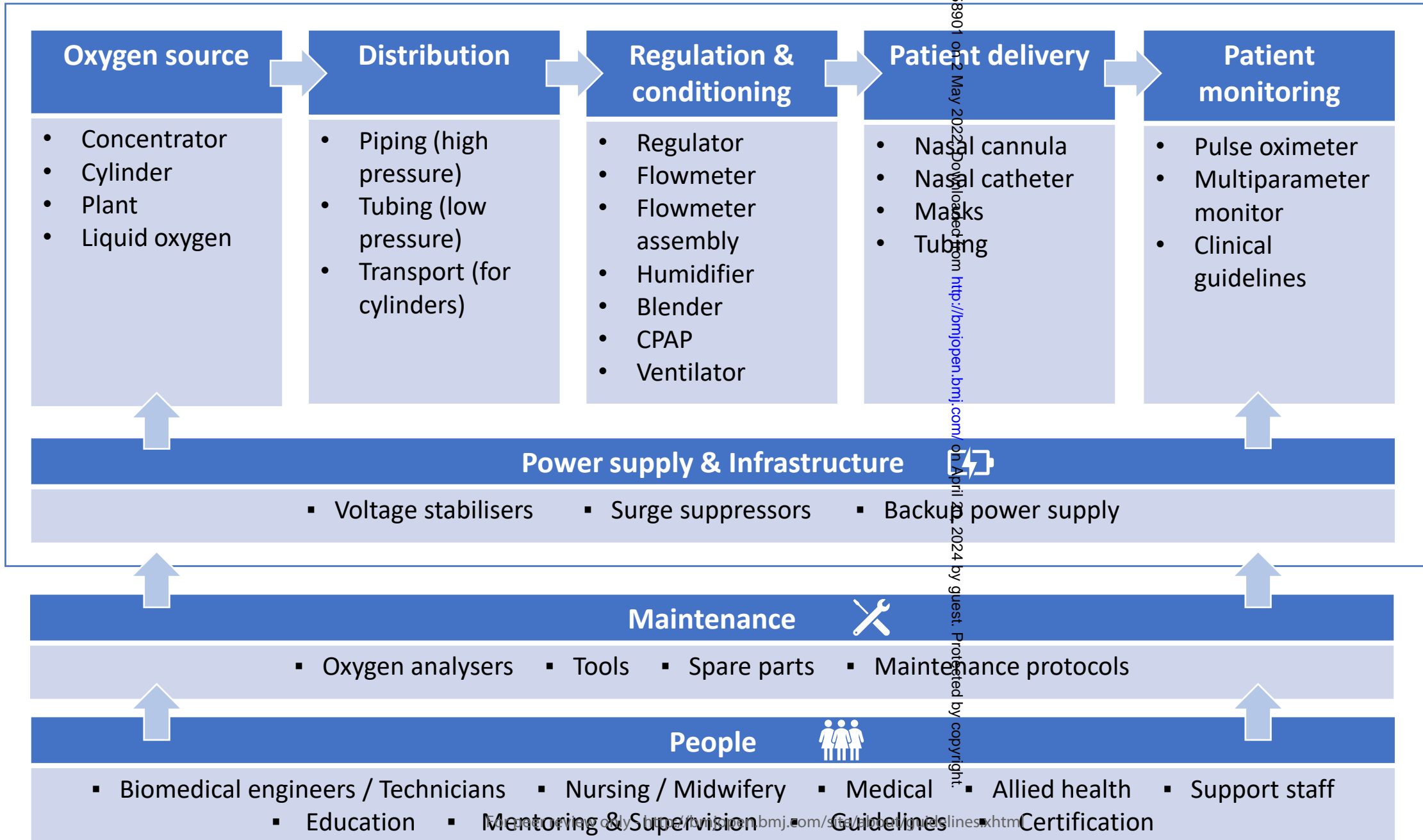
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**Figure 1 Hospital oxygen systems require a range of medical devices and other equipment and supplies (Adapted from WHO-UNICEF Technical Specifications and Guidance for Oxygen Therapy Devices)**

**Figure 2 Overall INSPIRING Lagos evaluation design**

**Figure 3 Map of Nigeria, Lagos state, and Ikorodu local government area (LGA)**

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**Formative Phase**

Device selection

Equipment audit

Community perceptions

Process Evaluation

Economic Evaluation

Baseline

Pulse oximetry and training

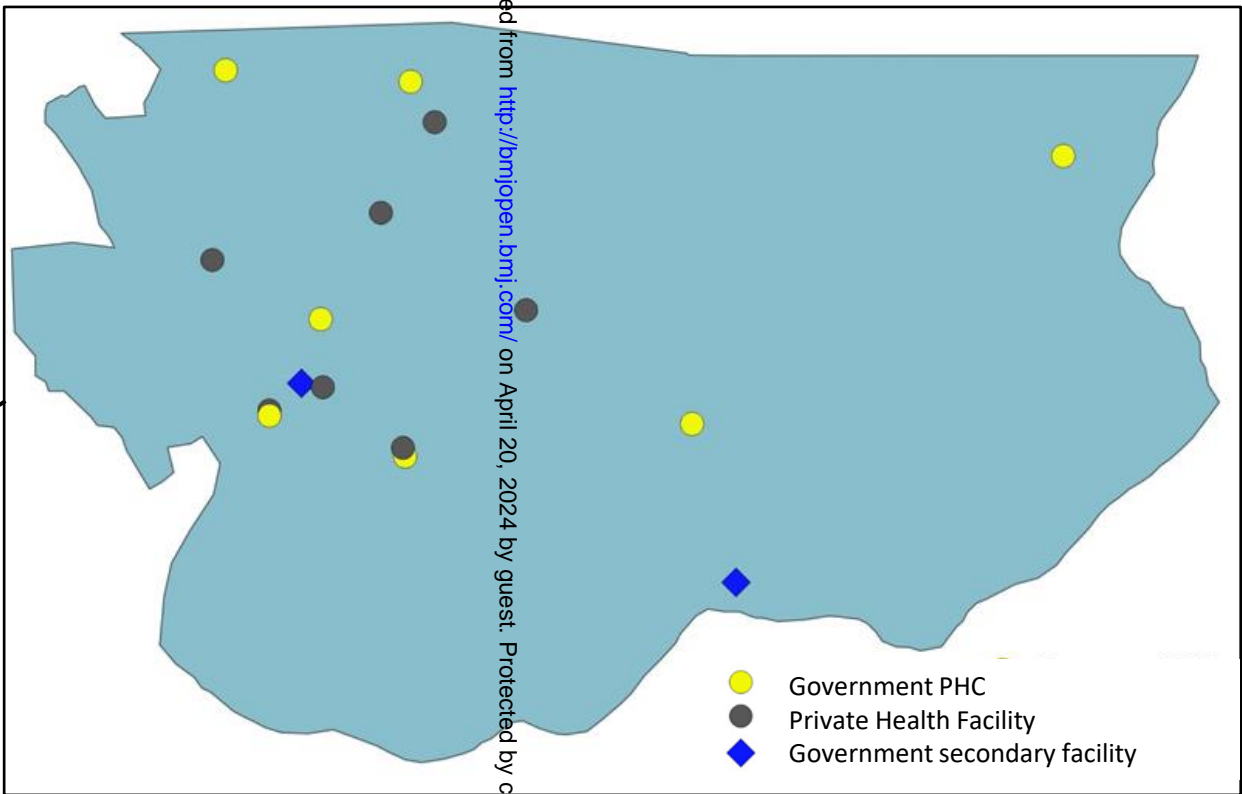
Oxygen implementation

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### Ikorodu LGA



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Supplemental file to:

*Pulse Oximetry and Oxygen Services for the Care of Acutely Unwell Children Attending Frontline Health Facilities in Lagos, Nigeria (INSPIRING-Lagos): Study Protocol for a mixed-methods evaluation.*

## Supplemental file

- Annex 1: Description of intervention facilities
- Annex 2: Secondary outcomes, process and economic indicators
- Annex 3: Healthcare worker in depth interview (IDI) and focus group discussion (FGD)
- Annex 4: Caregiver focus group discussions (FGDs)
- Annex 5: Caregiver in depth interview (IDI)
- Annex 6: Time use study tool
- Annex 7: Program management

### Annex 1: Description of intervention facilities

	Admission duration	Admit neonates	Power supply/day	Tech support	Ward (beds)	Oxygen	Pulse oximeter
<b>Government “flagship” primary health centres (PHCs)</b>							
PHC1	Overnight, 1-2 days	No	24hrs	No	General (18)	Cylinder: maternity Concentrator: not functional	No
PHC2	6 hrs	No	6hrs	No	General (2)	Cylinder: maternity, clinic Concentrator: storage	No
PHC3	5 hrs	No	24 hrs	No	General (1)	Cylinder: maternity Concentrator: not functional	No
PHC4	2-3 hours	No	24 hrs	No	General (2)	Cylinder: none Concentrator: not functional	No
PHC5	2-3 hours	Yes	3-8 hrs	No	General (2)	Cylinder: not functional Concentrator: not functional	No
PHC6	6 hours	No	8hrs	No	General (1)	Cylinder: maternity Concentrator: none	No
PHC7	2-4 hours	No	variable	No	General (2)	Cylinder: maternity Concentrator: maternity	No
<b>Private health facilities</b>							
PRV1	Overnight, no limit	Yes	24 hrs	No	General (12)	Cylinder: emergency Concentrator: not functional	No
PRV2	Overnight, no limit	Yes	15-20 hours	Yes	Paediatric (3)	Cylinder: emergency Concentrator: not functional	Yes
PRV3	Overnight, no limit	Yes	24 hours	No	Paediatric (6) Neonatal (5)	Cylinder: none Concentrator: not functional	Yes
PRV4	Overnight, no limit	Yes	24 hours	No	Paediatric (6)	Cylinder: emergency Concentrator: not functional	Yes
PRV5	Overnight, no limit	Yes	24 hours	Yes	Paediatric (10)	Cylinder: paediatric ward Concentrator: not functional	Yes
PRV6	10 hours	No	10 hours daily	No	General (10)	Cylinder: operating theatre Concentrator: not functional	No
PRV7	Overnight, no limit	No	15-18 hours	No	General (10)	Cylinder: emergency, operating theatre Concentrator: emergency	No
<b>Government secondary health facilities</b>							
H1	Overnight, no limit	Yes	24 hours	Yes	Paediatric (6) General (33)	Cylinder: piped to wards Concentrator: not functional	Yes
H2	Overnight, no limit	Yes	24 hours	Yes	Paediatric (6) Neonatal (6) Postnatal (20) Adult (265)	Cylinder: all wards Concentrator: not functional	Yes

## Annex 2: Secondary outcomes, process and economic indicators

Process Evaluation	Indicator	Frequency of data collection	Person collecting	Source of data	Tools required	Data type
Intervention delivery						
	Training fidelity	Once	Lagos UCH manager	Observation	Checklist	Quantitative/Qual
	Pre/Post testing	Once	STC trainer	Participant self-completed	Questionnaire	Quantitative
	Supervision reports	Monthly	STC supervisor	Observation	Checklist	Text
	Supervision visits conducted	Monthly	STC supervisor	Work plans	-	Quantitative
	Device breakages / presence	Bi-weekly	UCH data collectors	Observation	Checklist	Quantitative
	Training coverage over time	TBD	STC trainer	Observation	Checklist	Quantitative
	Oxygen system functionality	Bi-annual	UCH data collectors	Equipment testing and interviews	Questionnaire	Quantitative
	Oximeter functionality	Bi-annual	UCH data collectors	Equipment testing and interviews	Questionnaire	Quantitative
	Availability of PPE	Monthly	UCH data collectors	Observation	Checklist	Quantitative
	Availability of soap/alcohol gel	Monthly	UCH data collectors	Observation	Checklist	Quantitative
	Trainer/supervisor perceptions	Midline/endline	UCH data collectors	Interviews	Topic guide	Qualitative
	Provider perceptions	Midline/endline	UCH data collectors	Group discussions	Topic guide	Qualitative
Clinical indicators						
	14-day mortality	Daily	UCH data collectors	Clinical assessment and case notes	Questionnaire and checklist	Quantitative
	Correct IMCI assessment	Daily	UCH data collectors	Clinical assessment and case notes	Questionnaire and checklist	Quantitative
	Correct IMCI diagnosis	Daily	UCH data collectors	Clinical assessment and case notes	Questionnaire and checklist	Quantitative
	Correct treatment decision	Daily	UCH data collectors	Clinical assessment and case notes	Questionnaire and checklist	Quantitative
	Correct referral decision	Daily	UCH data collectors	Clinical assessment and case notes	Questionnaire and checklist	Quantitative

	Appropriate oxygen treatment	Daily	UCH data collectors	Clinical assessment and case notes	Questionnaire and checklist	Quantitative
	Referral attendance	Daily	UCH data collectors	Caregiver follow-up interviews	Questionnaire	Quantitative
	Drug stock audits	Three monthly	STC supervisor	Observation	Questionnaire	Quantitative
<b>Community</b>						
	Caregiver perceptions	Base/mid/endline	UCH data collectors	Interviews and discussions	Topic guide	Qualitative
	Delay in first seeking care	Daily	UCH data collectors	Caregiver recruitment interview	Questionnaire	Quantitative
	Location of first seeking care	Daily	UCH data collectors	Caregiver recruitment interview	Questionnaire	Quantitative
	Delay in attending referral	Daily	UCH data collectors	Caregiver follow-up interviews	Questionnaire	Quantitative
	Cost of care episode	Daily	UCH data collectors	Caregiver follow-up interviews	Questionnaire	Quantitative

<b>Economic Evaluation</b>	<b>Indicator</b>	<b>Frequency of data collection</b>	<b>Person collecting</b>	<b>Source of data</b>	<b>Tools required</b>	<b>Data type</b>
<b>Provider side</b>						
	Training	Endline	STC administration	STC accounts	Budget tool	Quantitative
	Supervision	Endline	STC administration	STC accounts	Budget tool	Quantitative
	Equipment	Endline	UCL/UCH administration	UCL/UCH accounts	Budget tool	Quantitative
	PPE costs	Endline	STC administration	STC accounts	Budget tool	Quantitative
	Salaries	Endline	STC administration	STC accounts	Budget tool	Quantitative
	Maintenance	Quarterly	STC administration	Supervision reports	Checklist	Quantitative
	Discrete choice experiment	Baseline	UCH data collector	Questionnaire	Questionnaire	Quantitative
	Time use	Base/mid/endline	UCH data collector	Observation	Checklist	Quantitative
<b>Patient side</b>						
	Cost to patient	Daily	UCH data collector	Caregiver follow-up interviews	Questionnaire	Quantitative
	Caregiver motivations	Base/mid/endline	UCH data collector	Group discussion	Topic guide	Qualitative
	Time taken to seek care	Base/mid/endline	UCH data collector	Economic interviews	Questionnaire	Quantitative

### Annex 3: Healthcare worker in depth interview (IDI) and focus group discussion (FGD)

We will be conducting interviews and focus groups with healthcare providers who work on paediatric wards, which can provide oxygen and nasogastric feeding for children.

#### 1. Clinical context

- Can you tell me about a typical day in your setting?
  - o Probe: What sort of duties do you have on the ward? How many children do you see?
- Can you describe a typical case of pneumonia in your setting?
  - o How long are they admitted for? What sort of treatments do they get?
- How do you decide if it is a severe or non-severe case of pneumonia?

#### 2. Oxygen

- Can you tell me about the last time you provided oxygen to a child?
  - o What was the child's illness? Duration of oxygen? Did she/he recover?
- How often do you provide oxygen?
- How do you decide who to give oxygen?
- Do you encounter any challenges in giving oxygen?
  - o For example, do you have children who you cannot give it to? Or who refuse? Or cannot afford to have oxygen?

#### 3. Nasogastric feeding

- Can you tell me about the last time you inserted a nasogastric tube for feeding in a child?
  - o What was the child's illness? Duration of NG feeds? Did she/he recover?
- How often do you provide nasogastric feeding?
- How do you decide who to give a nasogastric tube?
- Do you encounter any challenges in giving nasogastric feeding?
  - o For example, do you have children who you cannot give it to? Or who refuse? Or cannot afford it?

#### 4. Community perceptions

- How do caregivers react when you say their child needs oxygen?
- How do caregivers react when you say their child needs a nasogastric tube for feeding?
- Do caregivers refuse these treatments? If yes, why?

#### 5. Recommendations

- What do you think is going right in your efforts to provide care for severely sick children? What are the main enablers of these efforts?
- What are the main barriers you face in providing care for severely sick children?
- What could be done in the communities to improve the health of children and prevent pneumonia?
- What could be done within your setting to improve the diagnosis and management of paediatric pneumonia?

#### Annex 4: Caregiver focus group discussion (FGD)

Pneumonia is a serious illness in children, which affects the lungs. This makes it difficult for children to breath, and can cause them to be very sick, and if it is not treated properly, can sometimes lead to children dying.

- Have you heard of pneumonia before?
- Do you know anyone who has had pneumonia, or a child with pneumonia?
- How is this different from other common infections and illnesses in children?

One of the treatments for pneumonia is to give them oxygen. We are going to tell you a story about a child who fell sick with pneumonia and was referred for oxygen treatment. We will pause in the story to ask you about your thoughts on ways their journey story could have been made better. Is that ok?

##### *Narrative on the referral to hospital for treatment*

- In this case, what challenges might the family face in going to the hospital?
- What factors would influence the decision to go?
- What would you do in this situation? Why?

##### *Narrative on the recommendation for oxygen treatment at hospital*

- Are you familiar with oxygen? What do you understand about this treatment?
- In this case, what challenges might the family face in accepting oxygen treatment?
- What factors would influence the decision to accept or not accept the treatment?
- What would you do in this situation? Why?

##### *Narrative on the recommendation for nasogastric feeding at hospital*

- Are you familiar with feeding through a tube? What do you understand about this treatment?
- In this case, what challenges might the family face in accepting tube feeding treatment?
- What factors would influence the decision to accept or not accept the treatment?
- What would you do in this situation? Why?

##### *Narrative including a conversation in a community about misconceptions about feeding, force feeding and oxygen treatments*

- Are you familiar with conversations such as these in your community?
- Why do you think people might think these things?
- Are you familiar with force feeding practices? What are these? When or why do they happen?

## Annex 5: Caregiver in depth interview (IDI)

Thanks for agreeing to talk to me today. The point of the interview is to understand your experiences of your child's recent illness. First, I want to get to know a bit more about you and your typical family life. Can you tell me what an average day is like? What do you do? (Ice breaking question- also gives wider context)

### 1. Tell me a little bit about yourself and family.

- How many children do you have?
- What is your relationship with the father/mother of your children? (What kind of marriage?)
- Who lives in your household?
- Where were you born? Are you from here?

### 2. Care-seeking

Tell me the story of your child's recent pneumonia illness, including the care you received from any providers and the decisions you/your family/a healthcare provider made.

- Can you tell me about how you recognised that your child was ill and decided to seek care?
- What made you think your child was sick? What symptoms did you recognize?
- Did you know it was pneumonia? What do you understand of pneumonia?
- After you decided your child was sick, where and when was the decision to seek care made? Does anything about the child change this decision (e.g. gender/age)?
- Who made the decision to seek care, you, your partner, other family members? Together? How do you usually make decisions about seeking health care in your family?
- Did your communities cultural beliefs or religion influence your decision? If yes, how?
- Do your own cultural beliefs or religion influence where you decided to seek care? If yes, how?

### 3. Facility care

- Which facility did you attend first? Why did you decide to go there? Was this your first choice?
- How did you travel there, how long did it take and cost?
- What happened when you got to the facility?
- Was your child referred to hospital for review or admission? Did you take your child to hospital? If yes, what type of hospital was it (e.g. private/mission)? Why did you choose to go to this facility?
- At hospital, what care did your child receive? How many nights admitted?
- How much did this care cost? How long was your child admitted for?

### 4. Oxygen treatment

- Was your child recommended for oxygen treatment?
- How long did your child receive oxygen for? Was this the recommended time, or shorter/longer?
- How did you decide for your child to receive this treatment? Were you hesitant? Why?
- Did the healthcare provide explain this treatment to you?
- Did you pay for this treatment? Were you willing to pay? How much?
- Had you heard about oxygen treatment before you came here? What did you know about it?

### 5. Feeding

- Was your child recommended for tube feeding?
- How long did your child receive NG feeding? Was this the recommended time, or shorter/longer?
- How did you decide for your child to receive this treatment? Were you hesitant? Why?
- Did the healthcare provide explain this treatment to you?
- Did you pay for this treatment? Were you willing to pay? How much?
- Had you heard about tube feeding before you came here? What did you know about it?
- Did your child receive any other food or drink while they had this tube? Why was that given?

## Annex 6: Time use study tool

**Instructions:** This tool aims to estimate the proportion of the clinicians' and nurses' time spent on Pneumonia patients. For this purpose, this tool tracks the various activities and time between clinician or nurse and patient. The time spent on activities will then be compared to the service providers' total time at work and her/his base salary. Thus an estimate of the monetary value of staff time in Pneumonia treatment will be created.

It is necessary to keep this tracking sheet for the same patient for the duration of hospitalization. To make sure the tool stays with the same patient, please fill in the patient information in the box below. In order to relate the time spent for Pneumonia patients to the workload due to other patients, it is also necessary to indicate the working hours of the respective service providers. This information stays within the project and is not shared to anyone outside of the project. Please do not exaggerate the working hours or the time spent with the patients, since both will bias the result of this study.

Please use the code of activities on the next page to describe the activity being observed. If you find the activity is not on the list, please use the code 88 and give some additional information. This coding is used to assess the time spent on Pneumonia patients in terms of the corresponding activities.

The first step to start the tracking should be to note the sequential number (1 for the first questionnaire, and so on) of this specific questionnaire as soon as the patient is assessed. We aim to have a sample of 30 severe and 30 very severe cases.

**Questionnaire number:** \_\_\_\_\_ of 30 pneumonia  
 \_\_\_\_\_ of 30 severe pneumonia

Health Facility:

Date of admission:

Time of admission:

Date of discharge:

Time of discharge:

Patient Name:

Address:

Age (months):

Sex (M/F):

Classification (pneumonia/severe pneumonia):

### Codes

Activity	Code
<b>Outpatient / Admission assessment and documentation</b> , including clinical assessment, documentation, admission checklist etc.	1
<b>Clinical handover</b> about patients with pneumonia, including nursing and medical handover at beginning and end of each shift.	2
<b>Ward round and other clinical discussions</b> about patient management, including ward rounds, interdisciplinary discussions, etc.	3
<b>Patient counselling and discussion</b> , including providing advice, answering questions, giving emotional support, discussing health, etc.	4
<b>Vital signs</b> , including documentation, getting equipment, measurement, and documentation (e.g. heart rate, respiratory rate, blood pressure, weight, height, SpO <sub>2</sub> )	5
<b>Administration of IV or IM drugs</b> , including documentation, drawing up, checking, and giving (e.g. benzylpenicillin, ceftriaxone, gentamicin, chloramphenicol)	6
<b>Administration of ORAL drugs</b> , including documentation, dispensing, checking, and giving (e.g. amoxicillin, paracetamol, ibuprofen)	7
<b>Administration of INHALED drugs</b> , including documentation, drawing up, checking, and giving (e.g. salbutamol)	8
<b>Starting Oxygen therapy</b> , including getting oxygen source, and setting up oxygen equipment and delivery devices, documentation, etc.	9
<b>Monitoring and adjusting oxygen therapy</b> , including pulse oximetry checks, adjusting flow rates, cleaning/adjusting prongs, suctioning, documentation, etc.	10
<b>Administration of IV or NG (nasogastric) fluids</b> , including documentation, drawing up, checking, setting up equipment, and giving (e.g. 0.9% saline, blood).	11
<b>Administration of ORAL fluids</b> , including documentation, dispensing, checking, and giving (e.g. ORS).	12
<b>Chest Xray</b> , including requesting, performing, reviewing results.	13
<b>Other radiology/imaging</b> , including requesting, performing, reviewing results (e.g. lung ultrasound).	14
<b>Blood test</b> , including requesting, taking sample, sending to lab, receiving results, reviewing results (e.g. Hb, HIV test, malaria film/RDT).	15
<b>Other pathology/lab test</b> , including requesting, taking sample, sending to lab, receiving results, reviewing results (e.g. wound swab, sputum sample, etc.).	16
<b>Discharge planning and discharge</b> , including talking to family, arranging follow up, giving discharge instructions, etc.	17
<b>Other administrative tasks for patient:</b> (please specify)	18
<b>Other:</b> (please specify)	88





## Annex 7: Program management

Table 5 INSPIRING collaboration partners and roles

Institution	Role
Save the Children UK, London, UK	Funder, Implementer
Save the Children Nigeria, Abuja, UK	Implementer
GlaxoSmithKline (GSK), Brentford, UK	Funder
GlaxoSmithKline (GSK) Nigeria, Lagos, Nigeria	Funding partner
Lagos State Ministry of Health, Lagos, Nigeria	Implementation partner
Ikorodu Local Government Area Office, Lagos, Nigeria	Implementation partner
University College London (UCL), London, UK	Lead Evaluation partner
Karolinska Institutet (KI), Solna, Sweden	Evaluation partner
University of Ibadan (UI) / University College Hospital (UCH), Ibadan, Nigeria	Lead Nigerian Evaluation partner
Murdoch Children's Research Institute (MCRI) / University of Melbourne (UoM)	Evaluation partner
Johns Hopkins University (JHU)	Evaluation partner

# Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

## Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRIT reporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin J, Dickersin K, Hróbjartsson A, Schulz KF, Parulekar WR, Krleža-Jerić K, Laupacis A, Moher D. SPIRIT 2013 Explanation and Elaboration: Guidance for protocols of clinical trials. *BMJ*. 2013;346:e7586

		Page
	Reporting Item	Number
<b>Administrative information</b>		
Title	<a href="#">#1</a> Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1

1	Trial registration	<a href="#">#2a</a>	Trial identifier and registry name. If not yet registered,	15
2			name of intended registry	
3				
4				
5				
6	Trial registration:	<a href="#">#2b</a>	All items from the World Health Organization Trial	15
7				
8	data set		Registration Data Set	
9				
10				
11				
12	Protocol version	<a href="#">#3</a>	Date and version identifier	15
13				
14				
15	Funding	<a href="#">#4</a>	Sources and types of financial, material, and other	15
16			support	
17				
18				
19				
20	Roles and	<a href="#">#5a</a>	Names, affiliations, and roles of protocol contributors	15
21				
22	responsibilities:			
23				
24	contributorship			
25				
26				
27				
28	Roles and	<a href="#">#5b</a>	Name and contact information for the trial sponsor	15
29				
30	responsibilities:			
31				
32	sponsor contact			
33				
34	information			
35				
36				
37				
38	Roles and	<a href="#">#5c</a>	Role of study sponsor and funders, if any, in study	15
39			design; collection, management, analysis, and	
40	responsibilities:		interpretation of data; writing of the report; and the	
41			decision to submit the report for publication, including	
42	sponsor and funder		whether they will have ultimate authority over any of	
43			these activities	
44				
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52	Roles and	<a href="#">#5d</a>	Composition, roles, and responsibilities of the	15
53			coordinating centre, steering committee, endpoint	
54	responsibilities:		adjudication committee, data management team, and	
55				
56	committees			
57				
58				
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other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)

## Introduction

Background and rationale	<a href="#">#6a</a>	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4
Background and rationale: choice of comparators	<a href="#">#6b</a>	Explanation for choice of comparators	4
Objectives	<a href="#">#7</a>	Specific objectives or hypotheses	4
Trial design	<a href="#">#8</a>	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	4
<b>Methods:</b>			
Participants, interventions, and outcomes			
Study setting	<a href="#">#9</a>	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	6

1	Eligibility criteria	<a href="#">#10</a>	Inclusion and exclusion criteria for participants. If	6
2			applicable, eligibility criteria for study centres and	
3			individuals who will perform the interventions (eg,	
4			surgeons, psychotherapists)	
5				
6				
7				
8				
9				
10				
11	Interventions:	<a href="#">#11a</a>	Interventions for each group with sufficient detail to allow	7
12			replication, including how and when they will be	
13	description		administered	
14				
15				
16				
17				
18				
19	Interventions:	<a href="#">#11b</a>	Criteria for discontinuing or modifying allocated	7
20			interventions for a given trial participant (eg, drug dose	
21	modifications		change in response to harms, participant request, or	
22			improving / worsening disease)	
23				
24				
25				
26				
27				
28				
29	Interventions:	<a href="#">#11c</a>	Strategies to improve adherence to intervention protocols,	7
30			and any procedures for monitoring adherence (eg, drug	
31	adherence		tablet return; laboratory tests)	
32				
33				
34				
35				
36	Interventions:	<a href="#">#11d</a>	Relevant concomitant care and interventions that are	7
37			permitted or prohibited during the trial	
38	concomitant care			
39				
40				
41				
42	Outcomes	<a href="#">#12</a>	Primary, secondary, and other outcomes, including the	8
43			specific measurement variable (eg, systolic blood	
44			pressure), analysis metric (eg, change from baseline, final	
45			value, time to event), method of aggregation (eg, median,	
46			proportion), and time point for each outcome. Explanation	
47			of the clinical relevance of chosen efficacy and harm	
48			outcomes is strongly recommended	
49				
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1	Participant timeline	<a href="#">#13</a>	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Fig 2
2				
3				
4				
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10				
11	Sample size	<a href="#">#14</a>	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	9
12				
13				
14				
15				
16				
17				
18				
19				
20				
21	Recruitment	<a href="#">#15</a>	Strategies for achieving adequate participant enrolment to reach target sample size	9
22				
23				
24				
25				
26	<b>Methods:</b>			
27				
28	<b>Assignment of</b>			
29	<b>interventions (for</b>			
30	<b>controlled trials)</b>			
31				
32				
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36	Allocation: sequence generation	<a href="#">#16a</a>	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	NA
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53	Allocation concealment mechanism	<a href="#">#16b</a>	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque,	NA
54				
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1		sealed envelopes), describing any steps to conceal the	
2		sequence until interventions are assigned	
3			
4			
5			
6	Allocation:	<a href="#">#16c</a> Who will generate the allocation sequence, who will enrol	NA
7			
8	implementation	participants, and who will assign participants to	
9		interventions	
10			
11			
12			
13	Blinding (masking)	<a href="#">#17a</a> Who will be blinded after assignment to interventions (eg,	NA
14		trial participants, care providers, outcome assessors, data	
15		analysts), and how	
16			
17			
18			
19			
20			
21	Blinding (masking):	<a href="#">#17b</a> If blinded, circumstances under which unblinding is	NA
22		permissible, and procedure for revealing a participant's	
23	emergency	allocated intervention during the trial	
24			
25	unblinding		
26			
27			
28			
29	<b>Methods: Data</b>		
30			
31	<b>collection,</b>		
32			
33	<b>management, and</b>		
34			
35	<b>analysis</b>		
36			
37			
38	Data collection plan	<a href="#">#18a</a> Plans for assessment and collection of outcome,	13
39		baseline, and other trial data, including any related	
40		processes to promote data quality (eg, duplicate	
41		measurements, training of assessors) and a description	
42		of study instruments (eg, questionnaires, laboratory tests)	
43		along with their reliability and validity, if known. Reference	
44		to where data collection forms can be found, if not in the	
45		protocol	
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1	Data collection plan:	<a href="#">#18b</a>	Plans to promote participant retention and complete	13
2				
3	retention		follow-up, including list of any outcome data to be	
4			collected for participants who discontinue or deviate from	
5			intervention protocols	
6				
7				
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10				
11	Data management	<a href="#">#19</a>	Plans for data entry, coding, security, and storage,	13
12			including any related processes to promote data quality	
13			(eg, double data entry; range checks for data values).	
14			Reference to where details of data management	
15			procedures can be found, if not in the protocol	
16				
17				
18	Statistics: outcomes	<a href="#">#20a</a>	Statistical methods for analysing primary and secondary	7
19			outcomes. Reference to where other details of the	
20			statistical analysis plan can be found, if not in the protocol	
21				
22				
23	Statistics: additional	<a href="#">#20b</a>	Methods for any additional analyses (eg, subgroup and	7
24	analyses		adjusted analyses)	
25				
26				
27	Statistics: analysis	<a href="#">#20c</a>	Definition of analysis population relating to protocol non-	7
28	population and		adherence (eg, as randomised analysis), and any	
29	missing data		statistical methods to handle missing data (eg, multiple	
30			imputation)	
31				
32				
33				
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46	<b>Methods: Monitoring</b>			
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48				
49	Data monitoring:	<a href="#">#21a</a>	Composition of data monitoring committee (DMC);	NA
50	formal committee		summary of its role and reporting structure; statement of	
51			whether it is independent from the sponsor and	
52			competing interests; and reference to where further	
53				
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1 details about its charter can be found, if not in the  
 2 protocol. Alternatively, an explanation of why a DMC is  
 3  
 4 not needed  
 5  
 6  
 7

8	Data monitoring:	<a href="#">#21b</a>	Description of any interim analyses and stopping	NA
9	interim analysis		guidelines, including who will have access to these	
10			interim results and make the final decision to terminate	
11			the trial	
12				
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14				
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18	Harms	<a href="#">#22</a>	Plans for collecting, assessing, reporting, and managing	9
19			solicited and spontaneously reported adverse events and	
20			other unintended effects of trial interventions or trial	
21			conduct	
22				
23				
24				
25				
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27				
28	Auditing	<a href="#">#23</a>	Frequency and procedures for auditing trial conduct, if	NA
29			any, and whether the process will be independent from	
30			investigators and the sponsor	
31				
32				
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35	<b>Ethics and</b>			
36	<b>dissemination</b>			
37				
38				
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41	Research ethics	<a href="#">#24</a>	Plans for seeking research ethics committee / institutional	13
42	approval		review board (REC / IRB) approval	
43				
44				
45				
46	Protocol	<a href="#">#25</a>	Plans for communicating important protocol modifications	NA
47	amendments		(eg, changes to eligibility criteria, outcomes, analyses) to	
48			relevant parties (eg, investigators, REC / IRBs, trial	
49			participants, trial registries, journals, regulators)	
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1	Consent or assent	<a href="#">#26a</a>	Who will obtain informed consent or assent from potential	NA
2			trial participants or authorised surrogates, and how (see	
3			Item 32)	
4				
5				
6				
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8				
9	Consent or assent:	<a href="#">#26b</a>	Additional consent provisions for collection and use of	NA
10	ancillary studies		participant data and biological specimens in ancillary	
11			studies, if applicable	
12				
13				
14				
15				
16	Confidentiality	<a href="#">#27</a>	How personal information about potential and enrolled	13
17			participants will be collected, shared, and maintained in	
18			order to protect confidentiality before, during, and after	
19			the trial	
20				
21				
22				
23				
24				
25				
26	Declaration of	<a href="#">#28</a>	Financial and other competing interests for principal	15
27	interests		investigators for the overall trial and each study site	
28				
29				
30				
31				
32	Data access	<a href="#">#29</a>	Statement of who will have access to the final trial	15
33			dataset, and disclosure of contractual agreements that	
34			limit such access for investigators	
35				
36				
37				
38				
39	Ancillary and post	<a href="#">#30</a>	Provisions, if any, for ancillary and post-trial care, and for	NA
40	trial care		compensation to those who suffer harm from trial	
41			participation	
42				
43				
44				
45				
46				
47	Dissemination policy:	<a href="#">#31a</a>	Plans for investigators and sponsor to communicate trial	14
48	trial results		results to participants, healthcare professionals, the	
49			public, and other relevant groups (eg, via publication,	
50			reporting in results databases, or other data sharing	
51			arrangements), including any publication restrictions	
52				
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1	Dissemination policy: <a href="#">#31b</a>	Authorship eligibility guidelines and any intended use of	14
2		professional writers	
3	authorship		
4			
5			
6	Dissemination policy: <a href="#">#31c</a>	Plans, if any, for granting public access to the full	14
7		reproducible	
8		protocol, participant-level dataset, and statistical code	
9			
10			
11	research		
12			
13			
14	<b>Appendices</b>		
15			
16			
17	Informed consent	<a href="#">#32</a> Model consent form and other related documentation	NA
18			
19	materials	given to participants and authorised surrogates	
20			
21			
22			
23	Biological specimens	<a href="#">#33</a> Plans for collection, laboratory evaluation, and storage of	NA
24		biological specimens for genetic or molecular analysis in	
25		the current trial and for future use in ancillary studies, if	
26		applicable	
27			
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# BMJ Open

## Pulse Oximetry and Oxygen Services for the Care of Children with Pneumonia Attending Frontline Health Facilities in Lagos, Nigeria (INSPIRING-Lagos): Study Protocol for a mixed-methods evaluation

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Pulse oximetry and oxygen for primary care

# Pulse Oximetry and Oxygen Services for the Care of Children with Pneumonia Attending Frontline Health Facilities in Lagos, Nigeria (INSPIRING-Lagos): Study Protocol for a mixed-methods evaluation.

**Authors:** Hamish R Graham\*<sup>1,2</sup>, Omotayo E Olojede<sup>2</sup>, Ayobami A Bakare<sup>3,4</sup>, Eric D McCollum<sup>5</sup>, Agnese Iuliano<sup>6</sup>, Adamu Isah<sup>7</sup>, Adams Osebi<sup>7</sup>, Ibrahim Seriki<sup>7</sup>, Tahlil Ahmed<sup>8</sup>, <sup>8</sup>Samy Ahmar<sup>8</sup>, Christine Cassar<sup>8</sup>, Paula Valentine<sup>8</sup>, Temitayo Folorunso Olowookere<sup>9</sup>, Matt MacCalla<sup>10</sup>, Obioma Uchendu<sup>3,11</sup>, Rochelle Ann Burgess<sup>6</sup>, Tim Colbourn<sup>6</sup>, Carina King<sup>4,6</sup>, Adegoke G Falade<sup>2,12</sup> on behalf of the INSPIRING Project Consortium\*\*

## Affiliations:

<sup>1</sup> Centre for International Child Health, Murdoch Children's Research Institute, University of Melbourne, Royal Children's Hospital, Parkville, Victoria, Australia.

<sup>2</sup> Department of Paediatrics, University College Hospital, Ibadan, Nigeria.

<sup>3</sup> Department of Community Medicine, University College Hospital, Ibadan, Nigeria.

<sup>4</sup> Department of Global Public Health, Karolinska Institutet, Stockholm, Sweden.

<sup>5</sup> Eudowood Division of Pediatric Respiratory Sciences, Department of Pediatrics, School of Medicine, Johns Hopkins University, Baltimore, USA.

<sup>6</sup> Institute for Global Health, University College London, London, UK.

<sup>7</sup> Save the Children International, Abuja, Nigeria.

<sup>8</sup> Save the Children UK, London, UK.

<sup>9</sup> GlaxoSmithKline (GSK), Lagos, Nigeria.

<sup>10</sup> GlaxoSmithKline (GSK), Brentford, UK.

<sup>11</sup> Department of Community Medicine, College of Medicine, University of Ibadan, Ibadan, Nigeria.

<sup>12</sup> Department of Paediatrics, College of Medicine, University of Ibadan, Ibadan, Nigeria.

**\*Corresponding author:** Hamish Graham, Centre for International Child Health, Department of Paediatrics, University of Melbourne, Royal Children's Hospital, 50 Flemington Road, Parkville, Victoria 3052, Australia.

+61 3 93456262 [hamish.graham@rch.org.au](mailto:hamish.graham@rch.org.au)

**\*\*Full list of INSPIRING Consortium members:** Carina King (Karolinska); Tim Colbourn, Rochelle Ann Burgess, Agnese Iuliano (UCL); Hamish R Graham (Melbourne); Eric D McCollum (Johns Hopkins); Tahlil Ahmed, Samy Ahmar, Christine Cassar, Paula Valentine (Save the Children UK); Adamu Isah, Adams Osebi, Ibrahim Haruna, Abdullahi Magama (Save the Children Nigeria); Temitayo Folorunso Olowookere (GSK Nigeria); Matt MacCalla (GSK UK); Adegoke G Falade, Ayobami Adebayo Bakare, Obioma Uchendu, Julius Salako, Funmilayo Shittu, Damola Bakare, and Omotayo Olojede (University of Ibadan).

Pulse oximetry and oxygen for primary care

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**Keywords:** Paediatric pneumonia, healthcare providers, management, Integrated Management of Childhood Illness, pulse oximetry, oxygen therapy

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Pulse oximetry and oxygen for primary care

## ABSTRACT

**Introduction:** The aim of this evaluation is to understand if introducing stabilisation rooms equipped with pulse oximetry and oxygen systems to frontline health facilities in Ikorodu, Lagos State, alongside healthcare worker (HCW) training improves the quality of care for children with pneumonia aged 0-59 months. We will explore to what extent, how, for whom, and in what contexts the intervention works.

**Methods and analysis:** Quasi-experimental time-series impact evaluation with embedded mixed-methods process and economic evaluation. Setting: 7 government primary care facilities, 7 private health facilities, 2 government secondary care facilities. Target population: Children aged 0-59 months with clinically diagnosed pneumonia, and/or suspected or confirmed COVID-19. Intervention: “stabilisation rooms” within participating primary care facilities in Ikorodu local government area, designed to allow for short-term oxygen delivery for children with hypoxaemia prior to transfer to hospital, alongside HCW training on integrated management of childhood illness (IMCI), pulse oximetry and oxygen therapy, immunisation, and nutrition. Secondary facilities will also receive training and equipment for oxygen and pulse oximetry to ensure minimum standard of care is available for referred children. Primary outcome: correct management of hypoxaemic pneumonia including administration of oxygen therapy, referral, and presentation to hospital. Secondary outcome: 14-day pneumonia case fatality rate. Evaluation period: August 2020 to September 2022.

**Ethics and dissemination:** Ethical approval from University of Ibadan, Lagos State, and University College London. Ongoing engagement with government and other key stakeholders during the project. Local dissemination events will be held with the State Ministry of Health at the end of the project (December 2022). We will publish the main impact results, process evaluation and economic evaluation results as open-access academic publications in international journals. Registration: ACTRN12621001071819.

## ARTICLE SUMMARY

### Strengths and limitations of this study

- INSPIRING-Lagos is a multi-site study involving a range of public and private primary care facilities in urban Nigeria that will provide robust data on the impact of introducing pulse oximetry and oxygen-equipped stabilisation rooms to primary care settings.
- The impact evaluation will involve time-series analysis of quantitative data on pulse oximetry and oxygen practices, providing robust evidence of impact.
- We use qualitative data from healthcare workers and community members to understand perceptions and experience with pulse oximetry and oxygen therapy
- We will also conduct a theory-informed mixed-methods process evaluation to understand how the intervention worked, for whom, and in what contexts, and an economic evaluation to estimate cost-effectiveness in the urban Nigerian context.
- The main limitation is on the strength of our impact data due to lack of randomly selected controls and unpredictable influence of the COVID-19 pandemic on sample size and participant characteristics.

Pulse oximetry and oxygen for primary care

## INTRODUCTION

In 2019, Nigeria ranked as the country with the highest under-five mortality rate (117.2 per 1,000 live births)<sup>1</sup>. Pneumonia is the leading cause of child death in Nigeria and globally, causing approximately 134,000 and 800,000 deaths in 2017, respectively.<sup>1</sup> The under-5 mortality in Lagos state is around half the national average, at 50 per 1,000 live births, representing an urban population with lower relative poverty levels (1.1% live in severe poverty).<sup>2</sup>

From November 2018 to June 2019 we conducted a situational analysis of paediatric pneumonia in Lagos and Jigawa states of Nigeria, to inform the design of an intervention programme to reduce paediatric mortality. We found that while protective and preventive factors, such as vaccine coverage and clean cooking fuel, were high in Lagos, care-seeking and health facility service readiness were poor.<sup>3-6</sup> Therefore, taking an approach which targets improved quality of care for pneumonia diagnosis and treatment could achieve mortality impact. In the context of the emerging COVID-19 pandemic, in consultation with local stakeholders, we decided to focus on healthcare worker (HCW) capacity-building and enhancement of pulse oximetry and oxygen systems.

Pulse oximetry is a standard of care for identifying hypoxaemia (low blood oxygen levels) and guiding oxygen therapy in hospitalised patients. The World Health Organization's (WHO) Integrated Management of Childhood Illness (IMCI) guidelines also recommend pulse oximetry for identifying severely ill patients with hypoxaemia in primary care settings, requiring referral to hospital.<sup>7-9</sup> Despite their potential for reducing mortality, pulse oximeters are rarely available in frontline facilities in low- and middle-income countries.<sup>6 10-12</sup> Indeed, our survey of 58 Lagos health facilities in 2020 found pulse oximeters in none of the primary health facilities, 56% (15/27) of private health facilities, and exclusively on the paediatric ward of three secondary health facilities.<sup>13</sup>

Oxygen therapy is required for stabilisation and treatment of severely ill patients with conditions such as COVID-19, pneumonia, and sepsis, and is listed by the WHO as an Essential Medicine.<sup>14-16</sup> Effective oxygen systems require (i) reliable oxygen supply and delivery devices, (ii) rational use by skilled HCWs guided by pulse oximetry, and (iii) supportive infrastructure, management, and biomedical support (e.g. power supply, procurement and planning, skilled technicians with tools and spare parts) - **Figure 1**.<sup>17</sup> Our situational analysis revealed opportunities to improve patient access to oxygen through improved equipment selection and installation, repair and maintenance, and training and support for HCWs and technicians.<sup>6 18 19</sup> Subsequently, the COVID-19 pandemic has highlighted the importance of hospital oxygen systems and exacerbated existing deficiencies.<sup>8 20-23</sup>

The Nigerian Federal Ministry of Health (FMoH) has demonstrated its commitment to improving paediatric survival and oxygen access, with updated medicine, equipment and treatment guidelines.<sup>24-28</sup> Pulse oximetry and oxygen therapy were identified as priority areas for intervention in the context of Lagos by both local and international stakeholders.<sup>5</sup> However, there is a need for evidence on the impact and cost-effectiveness of these interventions when delivered routinely in frontline care, especially understanding the contextual mechanisms within government and private facilities, to facilitate effective adoption at scale.

This protocol outlines the mixed-methods evaluation plan for integrated HCW training, pulse oximetry and oxygen implementation in government and private health facilities in Lagos.

Pulse oximetry and oxygen for primary care

## METHODS AND ANALYSIS

### Research Questions and Study Design

The overall aim of this evaluation is to understand if introducing pulse oximetry and oxygen systems to health facilities in Lagos, alongside HCW training, improves the quality of care for children with pneumonia aged 0-59 months. We will explore to what extent, how, for whom, and in what contexts this intervention package works. This aim will be addressed through specific research questions (**Table 1**) using a quasi-experimental time-series impact evaluation with embedded mixed-methods process and economic evaluation. The study period will be August 2020 – September 2022 and will be conducted in Ikorodu Local Government Area (LGA), Lagos State (**Figure 2**).

Table 1 Evaluation domains and key research questions

Domain	Research question
<b>Impact</b>	<ul style="list-style-type: none"> <li>• What is the impact of “stabilisation rooms”, enhanced with uninterrupted oxygen and pulse oximetry, alongside healthcare worker training, on the quality of care for children with hypoxaemic pneumonia aged 0-59 months attending outpatient facilities in Ikorodu LGA, Lagos state, Nigeria?</li> <li>• What is the impact of “stabilisation rooms”, on the case-fatality rate of clinical pneumonia, including suspected or confirmed COVID-19 cases, among children aged 0-59 months attending outpatient facilities in Ikorodu LGA, Lagos state, Nigeria?</li> </ul>
<b>Process</b>	<ul style="list-style-type: none"> <li>• Which attributes, mechanisms, effects (intended and unintended), and contextual factors enable, or prevent pulse oximetry and oxygen from improving case management of clinical pneumonia cases in children under-5 in Ikorodu LGA?</li> <li>• How do everyday environments of wider resource limitation in health systems affect the delivery of pulse oximetry or oxygen at health facilities?</li> <li>• What contexts shape the willingness of family members to accept the administration of (i) oxygen and (ii) nasogastric feeding to children under-5 in Ikorodu LGA?</li> <li>• What contexts shape the willingness of practitioners to administer pulse oximetry and oxygen for clinical pneumonia and other acute infection cases in children under-5 in Ikorodu LGA?</li> <li>• How do primary and secondary care providers perceive the use of pulse oximetry, and how does it influence clinical decision making and referral recommendations for children under-5? How does this differ between government and private providers?</li> <li>• How does the use of pulse oximetry influence oxygen practices for children under-5 in different clinical contexts (public, private) in Ikorodu LGA?</li> <li>• What is the prevalence of hypoxaemia at primary care in Ikorodu LGA, amongst children with signs and symptoms of clinical pneumonia?</li> <li>• Does the type of pulse oximeter (i.e. Lifebox or Masimo Rad-G) influence their use and impact clinical care and decision making?</li> </ul>
<b>Economic</b>	<ul style="list-style-type: none"> <li>• Is this intervention package cost-effective considering opportunity costs of current and projected health spending (i.e. what is the estimated net benefit of the intervention package)?</li> <li>• If the intervention package is cost-effective is it affordable given the budget required for scale-up in Lagos state? What are the implications for other parts of Nigeria?</li> </ul>

The *impact evaluation* will estimate the intervention effect on hypoxaemic pneumonia management and 14-day mortality among children aged 0-59 months, using a time-series approach. We anticipate a baseline period lasting between 2 months and 12 months, depending on the facility, and that intervention components may be implemented at different time points (e.g. IMCI training occurring before oxygen installation).

## Pulse oximetry and oxygen for primary care

The *process evaluation* will use a theory-informed mixed-methods study design, with qualitative data from HCWs and caregivers, and quantitative monitoring and evaluation data to understand what worked, how, for whom, and in what contexts.

The *economic evaluation* will involve a time-motion study, together with analysis of administrative financial data and caregiver surveys to assess the economic cost of the intervention from the provider (Ministry of Health) and consumer (patient/caregiver) perspectives. Together with the impact evaluation data we will assess the cost-effectiveness and affordability of the intervention.

## Setting

A summary of Ikorodu LGA is presented in **Table 2**. We will be working in both government and private healthcare facilities, including 7 of the 28 government primary health centres (PHCs), 7 private health facilities, and both government secondary care facilities in Ikorodu LGA (**Figure 3**). There are no tertiary facilities in Ikorodu LGA.

Table 2 Summary characteristics of Ikorodu Local Government Area (LGA)

Characteristic	Number
Estimated population	890,000
Estimated under-5 population	160,000
Under-5 mortality ratio	50 per 1000 live births [Lagos state]
Government primary care facilities	28
Private primary care facilities	148
Government secondary facilities	2
Private secondary facilities	1

Source: Multiple Indicator Cluster Survey 2016-17, Survey Findings Report. Abuja, Nigeria: National Bureau of Statistics and United Nations Children's Fund., 2017. Facility number obtained from Ministry of Health in November 2019.

## Selection

We will cover the whole LGA geographically but will not include all facilities in the study. Save the Children, in collaboration with LGA leaders, purposively selected 7 government PHCs as "flagship" facilities for the program, targeting government facilities that have greatest need (Annex 1). Each PHC was then matched based on geographical location to a private health facility which had consented to take part in the programme during the formative phase and provides care for children under-five years of age.<sup>13</sup> We also included the two government secondary care facilities.

## Population

The intervention and impact evaluation will focus on children aged 0-59 months attending the outpatient areas of participating facilities for an acute illness and who are diagnosed with clinical pneumonia defined according to the 2014 WHO IMCI guidelines and/or suspected or confirmed COVID-19 (**Table 3**).<sup>29</sup> However, the intervention will be available to benefit all children and adults receiving care from participating facilities.

Pulse oximetry and oxygen for primary care

Table 3 Clinical case definitions of acute lower respiratory infections, and recommended primary care treatment according to WHO Integrated Management of Childhood Illness (IMCI) guidelines

Category	Signs and Symptoms	Treatment
<b>Pneumonia</b>	Cough and/or difficulty breathing AND Fast breathing for age AND/OR Chest indrawing	Home treatment with oral antibiotics
<b>Severe Pneumonia</b>	Cough and/or difficulty breathing AND General danger sign AND/OR Hypoxaemia	Hospital inpatient treatment with IV antibiotics (and oxygen for those with SpO <sub>2</sub> <90%)
<b>Suspected or confirmed SARS-CoV-2</b>	Clinician diagnosis AND/OR RT-PCR positive test	Not specifically addressed in IMCI. Local guidelines adapted from WHO guidelines. <sup>30</sup>

## Intervention

### *Stabilisation rooms*

The project will establish “stabilisation rooms” within the outpatient areas of participating primary facilities, designed to allow for short-term oxygen delivery for children with hypoxaemia prior to transfer to hospital (or admission to the ward). These stabilisation rooms are intended to support both short-term COVID-19 and longer-term paediatric pneumonia care needs, and will consist of the following intervention components:

1. Pulse oximeters, equipped with both paediatric and adult re-usable probes;
2. Medical oxygen supply delivered through newly installed oxygen concentrators powered from mains supply, generators and/or solar power;
3. Clinical guidelines, job aids and clinical training

Secondary health facilities that admit children will also be supported with pulse oximeters and oxygen concentrators for use on the wards to support safe care of patients referred for inpatient care. The intervention does not include portable oxygen for transport or direct referral support.

Selection of devices was based on national and international technical guidance and experience with similar devices in Nigeria and elsewhere.<sup>21 22 25</sup> To facilitate a sub-study comparing the usability and acceptability of two oximeters, facilities will be randomly allocated, with a 1:1 ratio using a random number generator, to receive either Lifebox (Acare Technology, New Taipei City, Taiwan) or Masimo RadG (Masimo, Irvine CA, USA) oximeters.

We anticipate a 1-6 month delay in receiving both oxygen and oximetry equipment, given the global supply chain challenges during the COVID-19 pandemic; therefore, the evaluation design will need to be adaptive and flexible. The intervention will be delivered by Save the Children Nigeria, with technical support provided by private non-profit Oxygen for Life Initiative (OLI), working closely with local government.

### *Training and supervision*

The stabilisation rooms will be implemented alongside broader capacity-building activities targeting primary care HCW practices (preventive and curative). This will include training on WHO’s IMCI guidelines, pulse oximetry and oxygen therapy, immunization, and nutrition (**Table 4**). This includes guidance to conduct pulse oximetry on all acutely unwell children, provide oxygen using nasal prongs to those with low

Pulse oximetry and oxygen for primary care

blood oxygen levels ( $SpO_2 < 90\%$ ), prescribe appropriate antibiotics, and arrange transfer to an admission facility for those requiring inpatient care (typically by private vehicle) as per WHO IMCI guidelines.

Table 4 Summary of training activities

Training	Location & Duration	Target
Integrated Management of Childhood Illness (IMCI)	In primary facilities, 6 days.	Community Health Extension Worker, Community Health Officers, nurses,
Pulse oximetry and Oxygen therapy	In primary and secondary care facilities, 3 days.	Community Health Extension Worker, Community Health Officers, nurses, midwives, doctors, +/- technicians
Immunization "Reaching Every District"	In primary care facilities, 2-3 days.	Vaccinators, immunisation focal persons, facility officer in charge
Nutrition – Infant and Young Child Feeding (IYCF), Community Management of Acute Malnutrition (CMAM)	In training centre and primary care facilities, 3 days. Repeated after 1 year for new staff.	Community Health Extension Worker, Community Health Officers, nurses, nutrition focal person

All training activities will be coordinated by Save the Children Nigeria using the ADDIE model (A = Analysis, D = Design, D = Develop Training Materials, I = Implement/Delivery, and E = Evaluation). Save the Children Nigeria will conduct a Training Needs Assessments using their "Task Analysis" tools, assessing a health care worker's actual skills and knowledge compared to the skills and knowledge they are meant to have based on their job descriptions. The training will be adapted from existing standard training packages to the local context with the assistance of local facilitators selected from the State Ministry of Health (SMOH) and partners (e.g. WHO, UNICEF, OLI).

Local facilitators who lead the training will also act as coaches, mentors and supervisors after the training has been completed and the participants have been deployed. They will visit each facility every 4-6 weeks and maintain interim contact using mobile phone-based group messaging. The Ikorodu LGA health team will also contribute to supervision through existing immunization supportive supervision arrangements.

#### Control

The control period –before the interventions are delivered in study facilities– will consist of routine clinic operation with existing material resources.

### Impact Evaluation

#### Outcome

The primary outcome is the correct management of hypoxaemic pneumonia amongst children aged 0-59 months who present to a participating health facility. 'Correct management' is defined as the child receiving oxygen treatment and being referred to and subsequently attending hospital (all three criteria need to be met). Clinical pneumonia is defined according to the 2014 IMCI guidelines (Table 3).<sup>9,29</sup> COVID-19 is defined as either PCR-test confirmed or based on a clinical diagnosis according to local guidelines. At the time of developing this protocol we knew little about the epidemiology or clinical features of COVID-19 in children and, while many presented with signs of respiratory infection, there had been reports of 'silent/happy hypoxia'. Therefore, we elected to include any children with suspected COVID-19 infection irrespective of respiratory signs. Oxygen treatment and referral decision will be recorded at recruitment, and hospital attendance, treatment and deaths will be confirmed by telephone interview at 2-weeks and

1 Pulse oximetry and oxygen for primary care

2 via medical records where available. Secondary outcomes include 14-day mortality and process outcomes  
3 (see Process Evaluation).  
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#### 5 *Data Collection*

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7 Study employed clinical data collectors will be responsible for recruitment and data collection in  
8 participating facilities. Each data collector will be responsible for one to two clinics, visiting each clinic at  
9 scheduled times each week according to a monthly roster that ensures we recruit at different times and  
10 days in each facility to maximise representativeness of data. During scheduled clinic visits, data collectors  
11 will screen all children under-five who present to the clinic with an acute infection for eligibility before they  
12 have been routinely assessed by the HCW. This assessment involves a directed history and physical  
13 examination to identify clinical features of pneumonia and COVID-19, including pulse oximetry and  
14 auscultation (using standard and digital stethoscopes). After identifying those who meet eligibility criteria,  
15 data collectors will obtain consent, complete an additional medical and socio-economic questionnaire, and  
16 arrange for phone follow-up. Following the HCW consultation, data collectors will enquire about caregiver  
17 intentions for onward care and extract routine clinical data from the HCW's clinical notes (including  
18 diagnosis, treatment and referral decision, vital signs and clinical observations). The data collector will  
19 inform the HCW if they find any signs that meet referral criteria and document whether this results in any  
20 change in patient management.  
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24 Data collectors will conduct follow-up interviews 14 days after recruitment, by telephone. The follow-up  
25 interview will confirm survival of the child, and record details of any onward care and oxygen received after  
26 their initial presentation, the cost of care, and treatment adherence. Where a child has died, the interview  
27 will be stopped and the study staff will attempt to conduct a verbal autopsy (VA), using the COVID-19  
28 adapted WHO 2016 VA tool and additional social autopsy questions around care-seeking.<sup>31</sup>  
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31 Data collection will be conducted between August 2020 and September 2022 (24 months), and exact timing  
32 of baseline and intervention periods will depend on intervention implementation at different facilities.  
33

#### 34 *Sample size*

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36 We had originally calculated a sample size based on the case fatality rate (CFR) as a primary outcome,  
37 assuming a baseline CFR of 4% and 1920 eligible children recruited. In this scenario, we had 72% power to  
38 detect a 50% reduction in CFR<sup>32</sup> but recognised this was uncertain given the COVID-19 context and lack of  
39 baseline data. We therefore reviewed the data from August 2020 – January 2021 and found lower than  
40 expected CFR making this scenario unfeasible. We used this data to update the sample size for the new  
41 primary outcome of “correct management of hypoxaemic pneumonia cases”, based on using a pre-post  
42 analysis. Using the following numbers extracted from the 6-month baseline data, we will be able to detect a  
43 minimum 15% increase in correct management: 75 children with completed follow-up per month; 24-  
44 month data collection period; intra-cluster correlation 0.05; 10% hypoxaemic; 5% correctly managed pre-  
45 intervention. This means we should be able to detect a significant difference if the intervention results in  
46  $\geq 20\%$  of hypoxaemic children being correctly managed.  
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#### 50 *Analysis*

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52 The primary analysis will be a time-series analysis, using a change point model. In this analysis an  
53 intervention time point is not pre-specified, therefore, given the challenges we will face in defining clean  
54 “pre” and “post” intervention periods, this method allows more flexibility and fewer assumptions than  
55 interrupted time-series analysis. We will be able to assess whether care has improved and identify the most  
56 likely time for the change point, which we can link to the intervention and other key events.<sup>33</sup>  
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Pulse oximetry and oxygen for primary care

Sensitivity analyses will include: stratification by age-group and sex of the child; stratification by clinic type; and stratification by pneumonia severity classification. We will account for clustering of outcomes at clinic-level in analyses and explore the role of intervention dose-effects.

Secondary analyses will include: assessing impact on 14-day mortality; describing the epidemiology of hypoxaemia amongst children; predictive modelling of pneumonia mortality and hypoxaemia; analysis of changes in clinical attendance rates, referral decision making, and referral attendance over time; description of suspected COVID19 epidemiology.

## Process Evaluation

Process data will cover the context, intervention delivery (including fidelity and reach), and mechanisms of impact (Annex 2).<sup>34</sup>

### *Context*

We will add to the contextual information from our situational analysis, with particular view on how COVID-19 alters health structures, community perceptions and care-seeking behaviours.

*Health system:* A biomedical engineer will conduct annual oxygen and pulse oximetry equipment checks, including the location, use, functionality and maintenance. A baseline assessment of existing equipment was conducted during the formative research phase (January – August 2020) and the full methods reported.<sup>13</sup>

To understand the evolving health facility context, we will periodically measure: essential medicine stock-outs of tracer drugs (e.g. AmoxDT); availability of PPE and IPC materials; staff turnover, balance of cadres, experience and gender. These data will be collected quarterly, by phone by study staff or if circumstances permit, during quarterly supervisory visits to the clinics.

*Community:* To provide an understanding of the community context in which the intervention is being implemented, we will collect data on the socio-demographic characteristics of caregivers and children, and their care-seeking patterns.

### *Intervention delivery*

Intervention delivery will be evaluated according to fidelity to the original design of the intervention, noting adaptations, reach and the change in knowledge of participants.

*Clinical practices:* The clinical data collectors will conduct case note reviews at each facility, on a quarterly basis, to determine the standard of IMCI assessment, diagnosis and treatment decision-making. The data collector will go back in time from the date of data collection in the patient registers/case notes until the pre-specified target number of cases have been identified (e.g. target for PHCs is 50 eligible children).

*Intervention fidelity:* The training delivered by Save the Children Nigeria will be independently observed by a member of the research staff, who will record whether the training was delivered as intended. On-going supervision and functioning of pulse oximeters will be recorded using routine supervision logs and work plans. Data collectors and HCWs will be asked to keep diaries to collect their everyday perceptions and experiences in relation to the intervention.<sup>35</sup>

*Reach:* Intervention reach will be assessed by tracking the coverage of trained staff and functional equipment throughout the duration of the project. These data will be routinely collected quarterly, by phone by study staff or if circumstances permit, during quarterly supervisory visits to the clinics.

### *Mechanisms of impact*

The mechanism of impact will be measured from the health provider and community perspectives.



Pulse oximetry and oxygen for primary care

*Health provider:* Data collected during recruitment will provide data on diagnoses made, treatments given and referral decision-making. We will extract data from a sub-set of these case notes to check for compliance to guidelines, and track this over time.

We will conduct focus group discussions (FGDs) and in-depth interviews (IDIs) with HCWs to understand their perceptions about pulse oximetry and oxygen therapy and understand changes over time (Annex 3). FGD/IDIs will be held with the healthcare providers before the intervention has been implemented, and then at select time-periods throughout the study period. IDIs will be organised around story completion activities, a method which is designed to create safe spaces for participants to reveal processes of sense-making and things about themselves that they may otherwise feel uncomfortable doing in group or public situations (such as disclosure of sensitive issues).<sup>36</sup>

*Community:* Our situational analysis, alongside studies from other contexts, have revealed considerable misconceptions about oxygen among HCWs and patients/families. We will conduct interviews and FGDs with caregivers, to understand perceptions about oxygen and behavioural responses to the intervention (Annex 4,5). We will triangulate this qualitative data with quantitative data collected in the follow-up surveys to understand changes in care-seeking behaviours following the intervention. Specific indicators include: the delay in deciding to first seek care; the location of first seeking care; the decision to attend a referral; and delay in attending a referral. In addition, data from narratives taken during verbal autopsies will be used to explore how care pathways differed between those children who survived and who died from an acute infection.<sup>37</sup>

#### *Analysis*

We will report findings descriptively. Where appropriate, data will be stratified by healthcare provider cadre and facility type and differences evaluated with chi-squared and t-tests.

FGD and interview data will be analysed using a pragmatic framework approach that blends inductive and deductive analytical approaches.<sup>38</sup> Pre-defined and agreed themes based on the topic guide will guide an initial analysis, with any emerging themes coded during the analysis. All qualitative data will be coded and analysed by two researchers, and interpretation and conclusions will be shared and discussed with the core project team.

### **Economic Evaluation**

We will conduct a prospective costing of the interventions which will include financial (capital set-up and recurrent expenditures) and economic costs (time-motion studies),<sup>39-41</sup> based on the provider (Ministry of Health) perspective. We will also consider the household perspective, via surveys of financial and time (opportunity) costs to caregivers.

#### *Excel budget tool*

We will use the accounts of the implementing partner to determine actual capital and recurrent expenditure on the interventions including equipment and maintenance, training, mentoring and supportive supervision, travel and allowances, and salaries of project staff, using an ingredients approach.<sup>39</sup> All costs required to replicate the intervention will be included. Cost data from the accounts will be extracted to an Excel template adapted from one used by Batura *et al* for costing complex public health interventions.<sup>39</sup>

#### *Timesheet and Observation checklist*

We will conduct a time-use study of healthcare workers managing childhood pneumonia cases at primary health facilities to determine how much time is spent by healthcare workers on the use of pulse oximetry and oxygen per case. This study will be done at government PHCs as our economic evaluation is focused on

### Pulse oximetry and oxygen for primary care

the Ministry of Health provider perspective. We will collect data on time-use via a researcher observed time-motion study (if deemed safe to do so) of 30 pneumonia and 30 severe pneumonia cases (Annex 6).<sup>41</sup> For both the timesheet and observational studies we will time: communication, documentation, vital signs assessment, physical examination, use of pulse oximetry, medication given, oxygen set-up and adjustment, feeding, suctioning, medication administration. We will use time use data and the HCW cadre to estimate the healthcare provider cost of delivering pneumonia care.

### *Caregiver perspectives*

We will determine the cost to patients during the follow-up interviews with caregivers. In a random sub-sample of 100 caregivers we will administer a longer questionnaire which includes: the time taken to seek care as well as the resources spent on travel, childcare, opportunity costs of business or other activities forgone (estimated by potential lost earnings or opportunities). We will monitor the costs of essential items every quarter using a basic market survey (e.g. fuel, food supplies) to monitor the wider economic impact on household costs related to changing oil-prices and COVID-19.

Pulse oximetry and oxygen for primary care

## Data Management

We will collect data in several formats: audio; paper forms and notes; electronic data using a custom-built CommCare app; teleconference recordings and text messages; paper consent forms. Data collection, storage and processing will be compliant with the European Union General Data Protection Regulations (EU GDPR). We will collect minimal personal identifiable information, including: age, date of birth, sex, education, religion, location and job title.

Personal information gathered as part of interviews and FGDs will be pseudo-anonymised with study ID numbers. Participants will be informed of the use of their data during informed consent and will be reminded that they do not have to participate. Personal identifiable information obtained during the recruitment questionnaire to enable a follow-up at 14 days will be deleted before data is stored and archived, and not be shared outside the team.

Interviews and focus group discussions will be audio-recorded, using a digital voice recorder, with individual informed consent. Audio files and video files will be stored on the local researcher's computer while being processed in an encrypted folder and will be stored by the responsible investigators on university secure servers at University College London and Karolinska Institutet.

Electronic data will be collected on Android devices, using CommCare (Dimagi, Cambridge MA, USA). Each data collector will use a password protected device for data collection. Electronic data will be stored in raw instance files, and .csv and Stata .dta formats, on password protected devices, and deleted from the audio recorders and Android tablets at the end of the study period. The app includes child case logic to allow follow-up and recruitment forms to be linked with a unique and anonymised ID, and in-built cleaning rules and branching logic will be used to ensure data quality. Data checks will be done throughout the project, and major errors (e.g. eligibility and outcome) will be verified in the field. All data management and processing will be done using Stata SE14 (StataCorp, College Station TX, USA).

Completed paper consent forms will be stored in a locked filing cabinet in a guarded office compound at University College Hospital Ibadan and will be archived for 10 years, then disposed of securely by burning.

## Patient and Public Involvement

This project benefited from co-design activities from early in its genesis, including a co-design workshop in April 2019 involving representatives from civil society, local and national government, and professional organisations, together with Save the Children, GSK, and evaluation partners (Annex 7). Selection of the facilities was conducted in partnership with the Ikorodu Local Government. Community perspectives were sought during the situational analysis but community members were not consulted in the design of the intervention or evaluation.

## ETHICS AND DISSEMINATION

Given the rapidly changing COVID-19 situation, we have embedded adaptive methods for data collection and will continuously monitor risks. The protocol is based on the following assumptions: we will be able to collect data within health facilities; project staff will be able to move around Lagos state; the project will end in December 2022.

This study has received ethical approval from the University of Ibadan (REF UI/EC/19/0551), Lagos State (REF LS/PHCB/MS/1128/VOL.V1/005), and University College London (REF 3433/005). We will seek individual written consent for FGDs/IDIs and verbal consent for other questionnaires. We will obtain facility-level approvals for equipment audits and case note reviews. All interviews, FGDs and questionnaires completed by healthcare providers will be anonymous.

## Pulse oximetry and oxygen for primary care

We do not anticipate any serious negative impacts to participants taking part in this research, and the intervention should benefit children and healthcare providers directly. The main ethical challenge presented by the impact evaluation is the management of cases with discrepant diagnoses between routine care and clinical research assessments. We decided that in cases where a child meets the criteria for referral from primary to secondary-level care according to our research assessment, we will notify the responsible HCW immediately.

Due to COVID19, there may be a risk posed to study staff based in clinics while community transmission is on-going. We will ensure that staff are supplied with adequate PPE and IPC training, and we will discuss with the clinics leads how we can best support efforts to maintain hygiene and distancing practices. We will provide study staff with transport to and from clinics, and assign data collection rotas to minimise travel.

Interviews, FGDs and surveys will take between 15 and 90 minutes. To mitigate the time burden, data collection will be conducted in private locations that are convenient to the participants and we will reimburse participants for transport cost and provide a refreshment. For the recruitment questionnaires, we will monitor the duration of these interviews to ensure they do not delay a severely sick child leaving the clinic to attend hospital.

The topics of discussions, interviews and surveys may result in some participants being upset, due to recent personal experiences of a sick child, or if the discussion raises questions about their professional capacity. We will ensure that questions are asked in a neutral tone, the researchers collecting the data are sensitive to these issues, and that participants are provided with a list of currently available services relating to a range of health concerns in their local areas. In order to minimise any distress from verbal autopsies, they will be conducted no sooner than 14 days after the death (as recommended by WHO), will be done at a time and location which allows privacy for the family, and questionnaires will be pilot tested to ensure cultural sensitivity.

### *Engagement and Dissemination*

Engagement with key stakeholders, including healthcare workers, communities and SMOH officials will be done continuously during the project. Local healthcare providers and caregivers will be recruited as participants, and alongside the formal data collection, will be encouraged to share thoughts and experiences around paediatric pneumonia.

The protocol was developed through round table discussions with project partners and will be shared with key stakeholders in the Ministry of Health and implementing partner Save the Children Nigeria. Local dissemination events will be held with the SMOH at the end of the project (December 2022), to share the findings and present the plans for future implementation with regular progress meetings prior.

We will publish the main impact results, process evaluation and economic evaluation results as academic publications in international journals. We will also submit abstracts to present findings at both local Nigerian conferences and international conferences on child health and pneumonia throughout the project.

Pulse oximetry and oxygen for primary care

## Acknowledgements, Competing Interests, Funding and other required statements

**Protocol version:** 2.1, 9 June 2021

**Acknowledgments:** We would like to thank representatives from the Lagos Ministry of Health and Ikorodu District Health Office for their on-going support and participation in the co-design process for this study.

**Competing interests statement:** HG, EM, CK are advisors to Lifebox Foundation on pulse oximetry. AAB, AGF, HG are board members for Oxygen for Life Initiative (OLI), a private non-profit that provides implementation services to the INSPIRING project. AI, AO, IS, TA, SA, CC, PV are employed by Save the Children UK who are part of the partnership funding the research. TFO, MM are employees of and stockholders in GSK, a multinational for-profit pharmaceutical company that produces pharmaceutical products for childhood pneumonia, including a SARS-CoV2 vaccine, and no direct financial interests in oxygen or pulse oximeter products.

**Funding:** This work was supported by the GlaxoSmithKline (GSK)-Save the Children Partnership (grant reference: 82603743). Employees of both GSK and Save the Children contributed to the design and oversight of the study as part of a co-design process. Any views or opinions presented are solely those of the authors/publisher and do not necessarily represent those of Save the Children or GSK, unless otherwise specifically stated.

**Sponsor:** University College London (UCL), contact [t.colbourn@ucl.ac.uk](mailto:t.colbourn@ucl.ac.uk).

**Author contributions:** TC, CK, RAB, HRG, EDM, AI, TA, SA, TFO, MM, AAB, AGF conceived of the study. HRG wrote the first manuscript draft with major input from CK, OO, TC, EDM, AGF, AAB. HRG, OEO, AAB, EDM, AI, AI, AO, IS, TA, SA, CC, PV, TFO, MM, OU, RAB, TC, CK, AGF contributed to refinement of the study protocol and approved the final manuscript. TC, CK and AGF are grant holders. HRG and OO are joint first authors. CK and AGF are joint senior authors. INSPIRING Project Consortium members all contributed to development of this protocol.

**Ethics approval:** This study has received ethical approval from the Research Ethics Committee at: University of Ibadan, Nigeria (REF UI/EC/19/0551), Lagos State, Nigeria (REF LS/PHCB/MS/1128/VOL.V1/005), and University College London (REF 3433/005).

**Trial registration:** Registered on the Australian and New Zealand Clinical Trials Registry (ACTRN12621001071819)

**Data sharing statement:** Fully anonymised versions of the data will be archived at the close of the project, for sharing with other researchers within and outside of the EEA. A copy of the clean, anonymised data will be stored by UCL, University College Hospital Ibadan and Save the Children.

Pulse oximetry and oxygen for primary care

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Pulse oximetry and oxygen for primary care

## Figures

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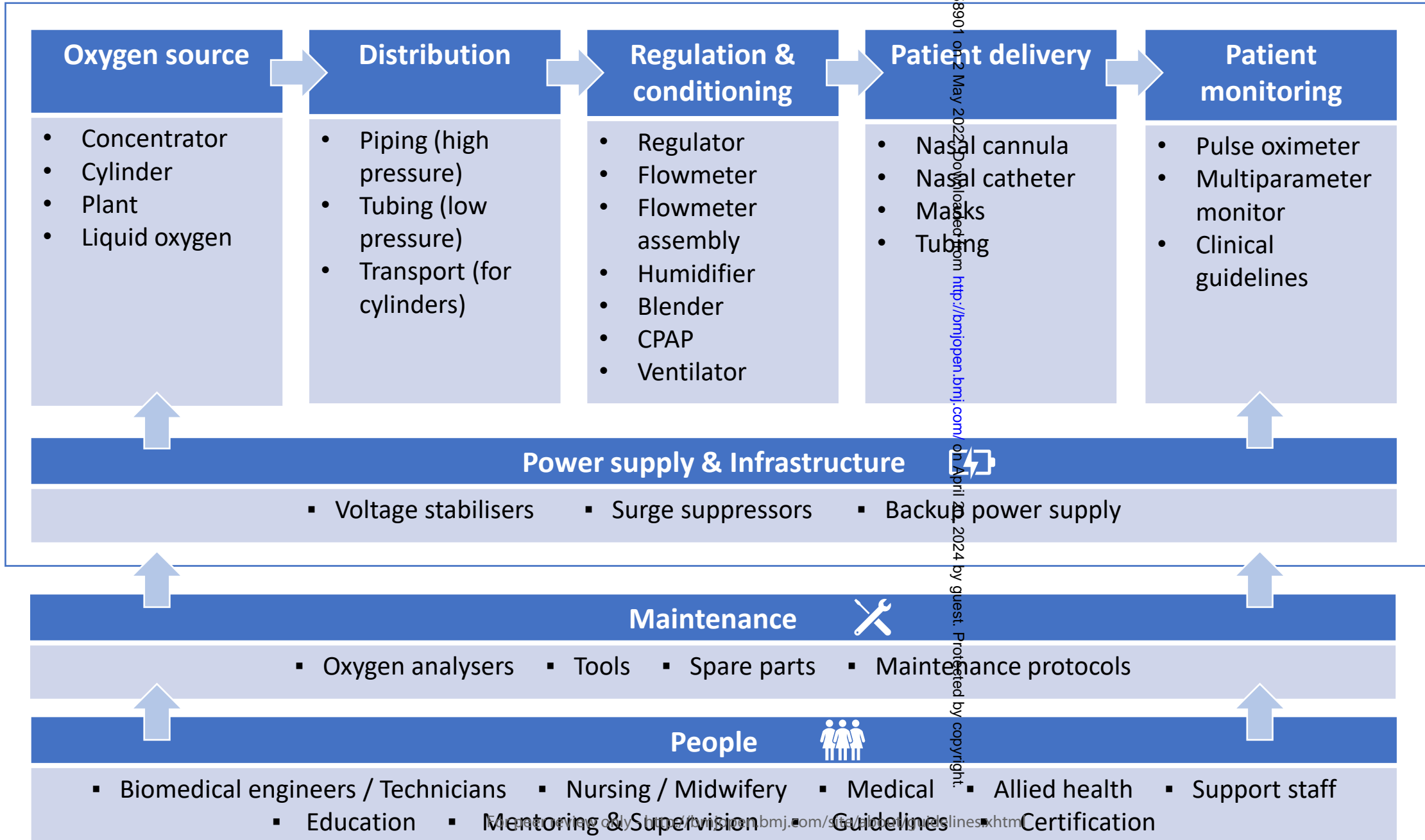
**Figure 1 Hospital oxygen systems require a range of medical devices and other equipment and supplies (Adapted from WHO-UNICEF Technical Specifications and Guidance for Oxygen Therapy Devices)**

**Figure 2 Overall INSPIRING Lagos evaluation design**

**Figure 3 Map of Nigeria, Lagos state, and Ikorodu local government area (LGA)**

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**Formative Phase**

Device selection

Equipment audit

Community perceptions

Process Evaluation

Economic Evaluation

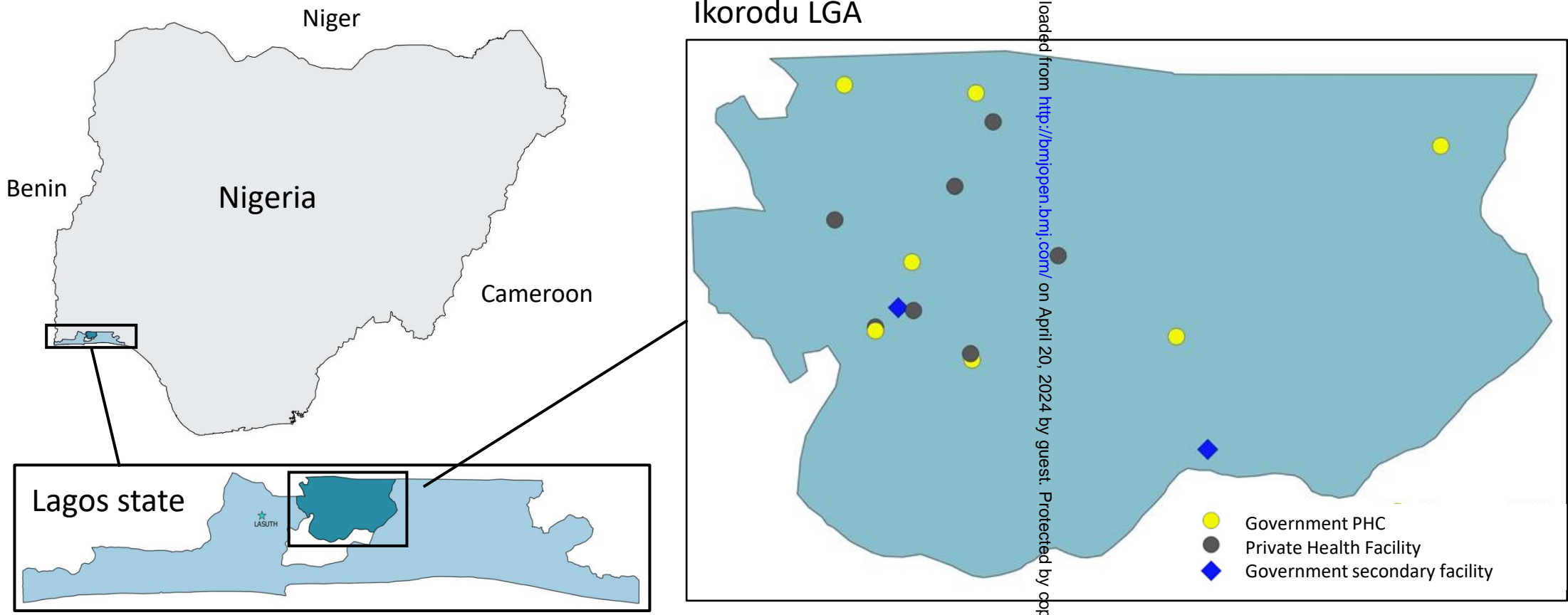
Baseline

Pulse oximetry and training

Oxygen implementation

Sep 19 – Jul 20      Aug 2020 – Jul 2021      Aug 2021 – Sep 2022

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Supplemental file to:

*Pulse Oximetry and Oxygen Services for the Care of Acutely Unwell Children Attending Frontline Health Facilities in Lagos, Nigeria (INSPIRING-Lagos): Study Protocol for a mixed-methods evaluation.*

## Supplemental file

- Annex 1: Description of intervention facilities
- Annex 2: Secondary outcomes, process and economic indicators
- Annex 3: Healthcare worker in depth interview (IDI) and focus group discussion (FGD)
- Annex 4: Caregiver focus group discussions (FGDs)
- Annex 5: Caregiver in depth interview (IDI)
- Annex 6: Time use study tool
- Annex 7: Program management

### Annex 1: Description of intervention facilities

	Admission duration	Admit neonates	Power supply/day	Tech support	Ward (beds)	Oxygen	Pulse oximeter
<b>Government “flagship” primary health centres (PHCs)</b>							
PHC1	Overnight, 1-2 days	No	24hrs	No	General (18)	Cylinder: maternity Concentrator: not functional	No
PHC2	6 hrs	No	6hrs	No	General (2)	Cylinder: maternity, clinic Concentrator: storage	No
PHC3	5 hrs	No	24 hrs	No	General (1)	Cylinder: maternity Concentrator: not functional	No
PHC4	2-3 hours	No	24 hrs	No	General (2)	Cylinder: none Concentrator: not functional	No
PHC5	2-3 hours	Yes	3-8 hrs	No	General (2)	Cylinder: not functional Concentrator: not functional	No
PHC6	6 hours	No	8hrs	No	General (1)	Cylinder: maternity Concentrator: none	No
PHC7	2-4 hours	No	variable	No	General (2)	Cylinder: maternity Concentrator: maternity	No
<b>Private health facilities</b>							
PRV1	Overnight, no limit	Yes	24 hrs	No	General (12)	Cylinder: emergency Concentrator: not functional	No
PRV2	Overnight, no limit	Yes	15-20 hours	Yes	Paediatric (3)	Cylinder: emergency Concentrator: not functional	Yes
PRV3	Overnight, no limit	Yes	24 hours	No	Paediatric (6) Neonatal (5)	Cylinder: none Concentrator: not functional	Yes
PRV4	Overnight, no limit	Yes	24 hours	No	Paediatric (6)	Cylinder: emergency Concentrator: not functional	Yes
PRV5	Overnight, no limit	Yes	24 hours	Yes	Paediatric (10)	Cylinder: paediatric ward Concentrator: not functional	Yes
PRV6	10 hours	No	10 hours daily	No	General (10)	Cylinder: operating theatre Concentrator: not functional	No
PRV7	Overnight, no limit	No	15-18 hours	No	General (10)	Cylinder: emergency, operating theatre Concentrator: emergency	No
<b>Government secondary health facilities</b>							
H1	Overnight, no limit	Yes	24 hours	Yes	Paediatric (6) General (33)	Cylinder: piped to wards Concentrator: not functional	Yes
H2	Overnight, no limit	Yes	24 hours	Yes	Paediatric (6) Neonatal (6) Postnatal (20) Adult (265)	Cylinder: all wards Concentrator: not functional	Yes

## Annex 2: Secondary outcomes, process and economic indicators

Process Evaluation	Indicator	Frequency of data collection	Person collecting	Source of data	Tools required	Data type
Intervention delivery						
	Training fidelity	Once	Lagos UCH manager	Observation	Checklist	Quantitative/Qual
	Pre/Post testing	Once	STC trainer	Participant self-completed	Questionnaire	Quantitative
	Supervision reports	Monthly	STC supervisor	Observation	Checklist	Text
	Supervision visits conducted	Monthly	STC supervisor	Work plans	-	Quantitative
	Device breakages / presence	Bi-weekly	UCH data collectors	Observation	Checklist	Quantitative
	Training coverage over time	TBD	STC trainer	Observation	Checklist	Quantitative
	Oxygen system functionality	Bi-annual	UCH data collectors	Equipment testing and interviews	Questionnaire	Quantitative
	Oximeter functionality	Bi-annual	UCH data collectors	Equipment testing and interviews	Questionnaire	Quantitative
	Availability of PPE	Monthly	UCH data collectors	Observation	Checklist	Quantitative
	Availability of soap/alcohol gel	Monthly	UCH data collectors	Observation	Checklist	Quantitative
	Trainer/supervisor perceptions	Midline/endline	UCH data collectors	Interviews	Topic guide	Qualitative
	Provider perceptions	Midline/endline	UCH data collectors	Group discussions	Topic guide	Qualitative
Clinical indicators						
	14-day mortality	Daily	UCH data collectors	Clinical assessment and case notes	Questionnaire and checklist	Quantitative
	Correct IMCI assessment	Daily	UCH data collectors	Clinical assessment and case notes	Questionnaire and checklist	Quantitative
	Correct IMCI diagnosis	Daily	UCH data collectors	Clinical assessment and case notes	Questionnaire and checklist	Quantitative
	Correct treatment decision	Daily	UCH data collectors	Clinical assessment and case notes	Questionnaire and checklist	Quantitative
	Correct referral decision	Daily	UCH data collectors	Clinical assessment and case notes	Questionnaire and checklist	Quantitative

	Appropriate oxygen treatment	Daily	UCH data collectors	Clinical assessment and case notes	Questionnaire and checklist	Quantitative
	Referral attendance	Daily	UCH data collectors	Caregiver follow-up interviews	Questionnaire	Quantitative
	Drug stock audits	Three monthly	STC supervisor	Observation	Questionnaire	Quantitative
<b>Community</b>						
	Caregiver perceptions	Base/mid/endline	UCH data collectors	Interviews and discussions	Topic guide	Qualitative
	Delay in first seeking care	Daily	UCH data collectors	Caregiver recruitment interview	Questionnaire	Quantitative
	Location of first seeking care	Daily	UCH data collectors	Caregiver recruitment interview	Questionnaire	Quantitative
	Delay in attending referral	Daily	UCH data collectors	Caregiver follow-up interviews	Questionnaire	Quantitative
	Cost of care episode	Daily	UCH data collectors	Caregiver follow-up interviews	Questionnaire	Quantitative

<b>Economic Evaluation</b>	<b>Indicator</b>	<b>Frequency of data collection</b>	<b>Person collecting</b>	<b>Source of data</b>	<b>Tools required</b>	<b>Data type</b>
<b>Provider side</b>						
	Training	Endline	STC administration	STC accounts	Budget tool	Quantitative
	Supervision	Endline	STC administration	STC accounts	Budget tool	Quantitative
	Equipment	Endline	UCL/UCH administration	UCL/UCH accounts	Budget tool	Quantitative
	PPE costs	Endline	STC administration	STC accounts	Budget tool	Quantitative
	Salaries	Endline	STC administration	STC accounts	Budget tool	Quantitative
	Maintenance	Quarterly	STC administration	Supervision reports	Checklist	Quantitative
	Discrete choice experiment	Baseline	UCH data collector	Questionnaire	Questionnaire	Quantitative
	Time use	Base/mid/endline	UCH data collector	Observation	Checklist	Quantitative
<b>Patient side</b>						
	Cost to patient	Daily	UCH data collector	Caregiver follow-up interviews	Questionnaire	Quantitative
	Caregiver motivations	Base/mid/endline	UCH data collector	Group discussion	Topic guide	Qualitative
	Time taken to seek care	Base/mid/endline	UCH data collector	Economic interviews	Questionnaire	Quantitative

### Annex 3: Healthcare worker in depth interview (IDI) and focus group discussion (FGD)

We will be conducting interviews and focus groups with healthcare providers who work on paediatric wards, which can provide oxygen and nasogastric feeding for children.

#### 1. Clinical context

- Can you tell me about a typical day in your setting?
  - o Probe: What sort of duties do you have on the ward? How many children do you see?
- Can you describe a typical case of pneumonia in your setting?
  - o How long are they admitted for? What sort of treatments do they get?
- How do you decide if it is a severe or non-severe case of pneumonia?

#### 2. Oxygen

- Can you tell me about the last time you provided oxygen to a child?
  - o What was the child's illness? Duration of oxygen? Did she/he recover?
- How often do you provide oxygen?
- How do you decide who to give oxygen?
- Do you encounter any challenges in giving oxygen?
  - o For example, do you have children who you cannot give it to? Or who refuse? Or cannot afford to have oxygen?

#### 3. Nasogastric feeding

- Can you tell me about the last time you inserted a nasogastric tube for feeding in a child?
  - o What was the child's illness? Duration of NG feeds? Did she/he recover?
- How often do you provide nasogastric feeding?
- How do you decide who to give a nasogastric tube?
- Do you encounter any challenges in giving nasogastric feeding?
  - o For example, do you have children who you cannot give it to? Or who refuse? Or cannot afford it?

#### 4. Community perceptions

- How do caregivers react when you say their child needs oxygen?
- How do caregivers react when you say their child needs a nasogastric tube for feeding?
- Do caregivers refuse these treatments? If yes, why?

#### 5. Recommendations

- What do you think is going right in your efforts to provide care for severely sick children? What are the main enablers of these efforts?
- What are the main barriers you face in providing care for severely sick children?
- What could be done in the communities to improve the health of children and prevent pneumonia?
- What could be done within your setting to improve the diagnosis and management of paediatric pneumonia?

#### Annex 4: Caregiver focus group discussion (FGD)

Pneumonia is a serious illness in children, which affects the lungs. This makes it difficult for children to breath, and can cause them to be very sick, and if it is not treated properly, can sometimes lead to children dying.

- Have you heard of pneumonia before?
- Do you know anyone who has had pneumonia, or a child with pneumonia?
- How is this different from other common infections and illnesses in children?

One of the treatments for pneumonia is to give them oxygen. We are going to tell you a story about a child who fell sick with pneumonia and was referred for oxygen treatment. We will pause in the story to ask you about your thoughts on ways their journey story could have been made better. Is that ok?

##### *Narrative on the referral to hospital for treatment*

- In this case, what challenges might the family face in going to the hospital?
- What factors would influence the decision to go?
- What would you do in this situation? Why?

##### *Narrative on the recommendation for oxygen treatment at hospital*

- Are you familiar with oxygen? What do you understand about this treatment?
- In this case, what challenges might the family face in accepting oxygen treatment?
- What factors would influence the decision to accept or not accept the treatment?
- What would you do in this situation? Why?

##### *Narrative on the recommendation for nasogastric feeding at hospital*

- Are you familiar with feeding through a tube? What do you understand about this treatment?
- In this case, what challenges might the family face in accepting tube feeding treatment?
- What factors would influence the decision to accept or not accept the treatment?
- What would you do in this situation? Why?

##### *Narrative including a conversation in a community about misconceptions about feeding, force feeding and oxygen treatments*

- Are you familiar with conversations such as these in your community?
- Why do you think people might think these things?
- Are you familiar with force feeding practices? What are these? When or why do they happen?



## Annex 5: Caregiver in depth interview (IDI)

Thanks for agreeing to talk to me today. The point of the interview is to understand your experiences of your child's recent illness. First, I want to get to know a bit more about you and your typical family life. Can you tell me what an average day is like? What do you do? (Ice breaking question- also gives wider context)

### 1. Tell me a little bit about yourself and family.

- How many children do you have?
- What is your relationship with the father/mother of your children? (What kind of marriage?)
- Who lives in your household?
- Where were you born? Are you from here?

### 2. Care-seeking

Tell me the story of your child's recent pneumonia illness, including the care you received from any providers and the decisions you/your family/a healthcare provider made.

- Can you tell me about how you recognised that your child was ill and decided to seek care?
- What made you think your child was sick? What symptoms did you recognize?
- Did you know it was pneumonia? What do you understand of pneumonia?
- After you decided your child was sick, where and when was the decision to seek care made? Does anything about the child change this decision (e.g. gender/age)?
- Who made the decision to seek care, you, your partner, other family members? Together? How do you usually make decisions about seeking health care in your family?
- Did your communities cultural beliefs or religion influence your decision? If yes, how?
- Do your own cultural beliefs or religion influence where you decided to seek care? If yes, how?

### 3. Facility care

- Which facility did you attend first? Why did you decide to go there? Was this your first choice?
- How did you travel there, how long did it take and cost?
- What happened when you got to the facility?
- Was your child referred to hospital for review or admission? Did you take your child to hospital? If yes, what type of hospital was it (e.g. private/mission)? Why did you choose to go to this facility?
- At hospital, what care did your child receive? How many nights admitted?
- How much did this care cost? How long was your child admitted for?

### 4. Oxygen treatment

- Was your child recommended for oxygen treatment?
- How long did your child receive oxygen for? Was this the recommended time, or shorter/longer?
- How did you decide for your child to receive this treatment? Were you hesitant? Why?
- Did the healthcare provide explain this treatment to you?
- Did you pay for this treatment? Were you willing to pay? How much?
- Had you heard about oxygen treatment before you came here? What did you know about it?

### 5. Feeding

- Was your child recommended for tube feeding?
- How long did your child receive NG feeding? Was this the recommended time, or shorter/longer?
- How did you decide for your child to receive this treatment? Were you hesitant? Why?
- Did the healthcare provide explain this treatment to you?
- Did you pay for this treatment? Were you willing to pay? How much?
- Had you heard about tube feeding before you came here? What did you know about it?
- Did your child receive any other food or drink while they had this tube? Why was that given?

## Annex 6: Time use study tool

**Instructions:** This tool aims to estimate the proportion of the clinicians' and nurses' time spent on Pneumonia patients. For this purpose, this tool tracks the various activities and time between clinician or nurse and patient. The time spent on activities will then be compared to the service providers' total time at work and her/his base salary. Thus an estimate of the monetary value of staff time in Pneumonia treatment will be created.

It is necessary to keep this tracking sheet for the same patient for the duration of hospitalization. To make sure the tool stays with the same patient, please fill in the patient information in the box below. In order to relate the time spent for Pneumonia patients to the workload due to other patients, it is also necessary to indicate the working hours of the respective service providers. This information stays within the project and is not shared to anyone outside of the project. Please do not exaggerate the working hours or the time spent with the patients, since both will bias the result of this study.

Please use the code of activities on the next page to describe the activity being observed. If you find the activity is not on the list, please use the code 88 and give some additional information. This coding is used to assess the time spent on Pneumonia patients in terms of the corresponding activities.

The first step to start the tracking should be to note the sequential number (1 for the first questionnaire, and so on) of this specific questionnaire as soon as the patient is assessed. We aim to have a sample of 30 severe and 30 very severe cases.

**Questionnaire number:** \_\_\_\_\_ of 30 pneumonia  
 \_\_\_\_\_ of 30 severe pneumonia

Health Facility:

Date of admission:

Time of admission:

Date of discharge:

Time of discharge:

Patient Name:

Address:

Age (months):

Sex (M/F):

Classification (pneumonia/severe pneumonia):

### Codes

Activity	Code
<b>Outpatient / Admission assessment and documentation</b> , including clinical assessment, documentation, admission checklist etc.	1
<b>Clinical handover</b> about patients with pneumonia, including nursing and medical handover at beginning and end of each shift.	2
<b>Ward round and other clinical discussions</b> about patient management, including ward rounds, interdisciplinary discussions, etc.	3
<b>Patient counselling and discussion</b> , including providing advice, answering questions, giving emotional support, discussing health, etc.	4
<b>Vital signs</b> , including documentation, getting equipment, measurement, and documentation (e.g. heart rate, respiratory rate, blood pressure, weight, height, SpO <sub>2</sub> )	5
<b>Administration of IV or IM drugs</b> , including documentation, drawing up, checking, and giving (e.g. benzylpenicillin, ceftriaxone, gentamicin, chloramphenicol)	6
<b>Administration of ORAL drugs</b> , including documentation, dispensing, checking, and giving (e.g. amoxicillin, paracetamol, ibuprofen)	7
<b>Administration of INHALED drugs</b> , including documentation, drawing up, checking, and giving (e.g. salbutamol)	8
<b>Starting Oxygen therapy</b> , including getting oxygen source, and setting up oxygen equipment and delivery devices, documentation, etc.	9
<b>Monitoring and adjusting oxygen therapy</b> , including pulse oximetry checks, adjusting flow rates, cleaning/adjusting prongs, suctioning, documentation, etc.	10
<b>Administration of IV or NG (nasogastric) fluids</b> , including documentation, drawing up, checking, setting up equipment, and giving (e.g. 0.9% saline, blood).	11
<b>Administration of ORAL fluids</b> , including documentation, dispensing, checking, and giving (e.g. ORS).	12
<b>Chest Xray</b> , including requesting, performing, reviewing results.	13
<b>Other radiology/imaging</b> , including requesting, performing, reviewing results (e.g. lung ultrasound).	14
<b>Blood test</b> , including requesting, taking sample, sending to lab, receiving results, reviewing results (e.g. Hb, HIV test, malaria film/RDT).	15
<b>Other pathology/lab test</b> , including requesting, taking sample, sending to lab, receiving results, reviewing results (e.g. wound swab, sputum sample, etc.).	16
<b>Discharge planning and discharge</b> , including talking to family, arranging follow up, giving discharge instructions, etc.	17
<b>Other administrative tasks for patient:</b> (please specify)	18
<b>Other:</b> (please specify)	88



## Annex 7: Program management

Table 5 INSPIRING collaboration partners and roles

Institution	Role
Save the Children UK, London, UK	Funder, Implementer
Save the Children Nigeria, Abuja, UK	Implementer
GlaxoSmithKline (GSK), Brentford, UK	Funder
GlaxoSmithKline (GSK) Nigeria, Lagos, Nigeria	Funding partner
Lagos State Ministry of Health, Lagos, Nigeria	Implementation partner
Ikorodu Local Government Area Office, Lagos, Nigeria	Implementation partner
University College London (UCL), London, UK	Lead Evaluation partner
Karolinska Institutet (KI), Solna, Sweden	Evaluation partner
University of Ibadan (UI) / University College Hospital (UCH), Ibadan, Nigeria	Lead Nigerian Evaluation partner
Murdoch Children's Research Institute (MCRI) / University of Melbourne (UoM)	Evaluation partner
Johns Hopkins University (JHU)	Evaluation partner

# Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

## Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRIT reporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin J, Dickersin K, Hróbjartsson A, Schulz KF, Parulekar WR, Krleža-Jerić K, Laupacis A, Moher D. SPIRIT 2013 Explanation and Elaboration: Guidance for protocols of clinical trials. *BMJ*. 2013;346:e7586

		Page
	Reporting Item	Number
<b>Administrative information</b>		
Title	<a href="#">#1</a> Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1

1	Trial registration	<a href="#">#2a</a>	Trial identifier and registry name. If not yet registered,	15
2			name of intended registry	
3				
4				
5				
6	Trial registration:	<a href="#">#2b</a>	All items from the World Health Organization Trial	15
7				
8	data set		Registration Data Set	
9				
10				
11				
12	Protocol version	<a href="#">#3</a>	Date and version identifier	15
13				
14				
15	Funding	<a href="#">#4</a>	Sources and types of financial, material, and other	15
16			support	
17				
18				
19				
20	Roles and	<a href="#">#5a</a>	Names, affiliations, and roles of protocol contributors	15
21				
22	responsibilities:			
23				
24	contributorship			
25				
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27				
28	Roles and	<a href="#">#5b</a>	Name and contact information for the trial sponsor	15
29				
30	responsibilities:			
31				
32	sponsor contact			
33				
34	information			
35				
36				
37				
38	Roles and	<a href="#">#5c</a>	Role of study sponsor and funders, if any, in study	15
39			design; collection, management, analysis, and	
40	responsibilities:		interpretation of data; writing of the report; and the	
41			decision to submit the report for publication, including	
42	sponsor and funder		whether they will have ultimate authority over any of	
43			these activities	
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52	Roles and	<a href="#">#5d</a>	Composition, roles, and responsibilities of the	15
53			coordinating centre, steering committee, endpoint	
54	responsibilities:		adjudication committee, data management team, and	
55				
56	committees			
57				
58				
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other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)

## Introduction

Background and rationale	<a href="#">#6a</a>	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4
Background and rationale: choice of comparators	<a href="#">#6b</a>	Explanation for choice of comparators	4
Objectives	<a href="#">#7</a>	Specific objectives or hypotheses	4
Trial design	<a href="#">#8</a>	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	4
<b>Methods:</b>			
Participants, interventions, and outcomes			
Study setting	<a href="#">#9</a>	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	6



1	Eligibility criteria	<a href="#">#10</a>	Inclusion and exclusion criteria for participants. If	6
2			applicable, eligibility criteria for study centres and	
3			individuals who will perform the interventions (eg,	
4			surgeons, psychotherapists)	
5				
6				
7				
8				
9				
10				
11	Interventions:	<a href="#">#11a</a>	Interventions for each group with sufficient detail to allow	7
12			replication, including how and when they will be	
13	description		administered	
14				
15				
16				
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18				
19	Interventions:	<a href="#">#11b</a>	Criteria for discontinuing or modifying allocated	7
20			interventions for a given trial participant (eg, drug dose	
21	modifications		change in response to harms, participant request, or	
22			improving / worsening disease)	
23				
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28				
29	Interventions:	<a href="#">#11c</a>	Strategies to improve adherence to intervention protocols,	7
30			and any procedures for monitoring adherence (eg, drug	
31	adherence		tablet return; laboratory tests)	
32				
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35				
36	Interventions:	<a href="#">#11d</a>	Relevant concomitant care and interventions that are	7
37			permitted or prohibited during the trial	
38	concomitant care			
39				
40				
41				
42	Outcomes	<a href="#">#12</a>	Primary, secondary, and other outcomes, including the	8
43			specific measurement variable (eg, systolic blood	
44			pressure), analysis metric (eg, change from baseline, final	
45			value, time to event), method of aggregation (eg, median,	
46			proportion), and time point for each outcome. Explanation	
47			of the clinical relevance of chosen efficacy and harm	
48			outcomes is strongly recommended	
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1	Participant timeline	<a href="#">#13</a>	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Fig 2
2				
3				
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10				
11	Sample size	<a href="#">#14</a>	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	9
12				
13				
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19				
20				
21	Recruitment	<a href="#">#15</a>	Strategies for achieving adequate participant enrolment to reach target sample size	9
22				
23				
24				
25				
26	<b>Methods:</b>			
27				
28	<b>Assignment of</b>			
29	<b>interventions (for</b>			
30	<b>controlled trials)</b>			
31				
32				
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36	Allocation: sequence generation	<a href="#">#16a</a>	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	NA
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53	Allocation concealment mechanism	<a href="#">#16b</a>	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque,	NA
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1		sealed envelopes), describing any steps to conceal the	
2		sequence until interventions are assigned	
3			
4			
5			
6	Allocation:	<a href="#">#16c</a> Who will generate the allocation sequence, who will enrol	NA
7			
8	implementation	participants, and who will assign participants to	
9			
10		interventions	
11			
12			
13	Blinding (masking)	<a href="#">#17a</a> Who will be blinded after assignment to interventions (eg,	NA
14			
15		trial participants, care providers, outcome assessors, data	
16			
17		analysts), and how	
18			
19			
20			
21	Blinding (masking):	<a href="#">#17b</a> If blinded, circumstances under which unblinding is	NA
22			
23	emergency	permissible, and procedure for revealing a participant's	
24			
25	unblinding	allocated intervention during the trial	
26			
27			
28			
29	<b>Methods: Data</b>		
30			
31	<b>collection,</b>		
32			
33	<b>management, and</b>		
34			
35	<b>analysis</b>		
36			
37			
38	Data collection plan	<a href="#">#18a</a> Plans for assessment and collection of outcome,	13
39			
40		baseline, and other trial data, including any related	
41			
42		processes to promote data quality (eg, duplicate	
43			
44		measurements, training of assessors) and a description	
45			
46		of study instruments (eg, questionnaires, laboratory tests)	
47			
48		along with their reliability and validity, if known. Reference	
49			
50		to where data collection forms can be found, if not in the	
51			
52		protocol	
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1	Data collection plan:	<a href="#">#18b</a>	Plans to promote participant retention and complete	13
2				
3	retention		follow-up, including list of any outcome data to be	
4			collected for participants who discontinue or deviate from	
5			intervention protocols	
6				
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11	Data management	<a href="#">#19</a>	Plans for data entry, coding, security, and storage,	13
12			including any related processes to promote data quality	
13			(eg, double data entry; range checks for data values).	
14			Reference to where details of data management	
15			procedures can be found, if not in the protocol	
16				
17				
18	Statistics: outcomes	<a href="#">#20a</a>	Statistical methods for analysing primary and secondary	7
19			outcomes. Reference to where other details of the	
20			statistical analysis plan can be found, if not in the protocol	
21				
22				
23	Statistics: additional	<a href="#">#20b</a>	Methods for any additional analyses (eg, subgroup and	7
24	analyses		adjusted analyses)	
25				
26				
27	Statistics: analysis	<a href="#">#20c</a>	Definition of analysis population relating to protocol non-	7
28	population and		adherence (eg, as randomised analysis), and any	
29	missing data		statistical methods to handle missing data (eg, multiple	
30			imputation)	
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46	<b>Methods: Monitoring</b>			
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49	Data monitoring:	<a href="#">#21a</a>	Composition of data monitoring committee (DMC);	NA
50	formal committee		summary of its role and reporting structure; statement of	
51			whether it is independent from the sponsor and	
52			competing interests; and reference to where further	
53				
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1 details about its charter can be found, if not in the  
 2 protocol. Alternatively, an explanation of why a DMC is  
 3  
 4 not needed  
 5  
 6  
 7

8	Data monitoring:	<a href="#">#21b</a>	Description of any interim analyses and stopping	NA
9	interim analysis		guidelines, including who will have access to these	
10			interim results and make the final decision to terminate	
11			the trial	
12				
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18	Harms	<a href="#">#22</a>	Plans for collecting, assessing, reporting, and managing	9
19			solicited and spontaneously reported adverse events and	
20			other unintended effects of trial interventions or trial	
21			conduct	
22				
23				
24				
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27				
28	Auditing	<a href="#">#23</a>	Frequency and procedures for auditing trial conduct, if	NA
29			any, and whether the process will be independent from	
30			investigators and the sponsor	
31				
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35	<b>Ethics and</b>			
36	<b>dissemination</b>			
37				
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41	Research ethics	<a href="#">#24</a>	Plans for seeking research ethics committee / institutional	13
42	approval		review board (REC / IRB) approval	
43				
44				
45				
46	Protocol	<a href="#">#25</a>	Plans for communicating important protocol modifications	NA
47	amendments		(eg, changes to eligibility criteria, outcomes, analyses) to	
48			relevant parties (eg, investigators, REC / IRBs, trial	
49			participants, trial registries, journals, regulators)	
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1	Consent or assent	<a href="#">#26a</a>	Who will obtain informed consent or assent from potential	NA
2			trial participants or authorised surrogates, and how (see	
3			Item 32)	
4				
5				
6				
7				
8	Consent or assent:	<a href="#">#26b</a>	Additional consent provisions for collection and use of	NA
9	ancillary studies		participant data and biological specimens in ancillary	
10			studies, if applicable	
11				
12				
13				
14				
15	Confidentiality	<a href="#">#27</a>	How personal information about potential and enrolled	13
16			participants will be collected, shared, and maintained in	
17			order to protect confidentiality before, during, and after	
18			the trial	
19				
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25				
26	Declaration of	<a href="#">#28</a>	Financial and other competing interests for principal	15
27	interests		investigators for the overall trial and each study site	
28				
29				
30				
31	Data access	<a href="#">#29</a>	Statement of who will have access to the final trial	15
32			dataset, and disclosure of contractual agreements that	
33			limit such access for investigators	
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39	Ancillary and post	<a href="#">#30</a>	Provisions, if any, for ancillary and post-trial care, and for	NA
40	trial care		compensation to those who suffer harm from trial	
41			participation	
42				
43				
44				
45				
46				
47	Dissemination policy:	<a href="#">#31a</a>	Plans for investigators and sponsor to communicate trial	14
48	trial results		results to participants, healthcare professionals, the	
49			public, and other relevant groups (eg, via publication,	
50			reporting in results databases, or other data sharing	
51			arrangements), including any publication restrictions	
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1	Dissemination policy: <a href="#">#31b</a>	Authorship eligibility guidelines and any intended use of	14
2		professional writers	
3	authorship		
4			
5			
6	Dissemination policy: <a href="#">#31c</a>	Plans, if any, for granting public access to the full	14
7		reproducible	
8		protocol, participant-level dataset, and statistical code	
9			
10			
11	research		
12			
13			
14	<b>Appendices</b>		
15			
16			
17	Informed consent	<a href="#">#32</a> Model consent form and other related documentation	NA
18			
19	materials	given to participants and authorised surrogates	
20			
21			
22			
23	Biological specimens	<a href="#">#33</a> Plans for collection, laboratory evaluation, and storage of	NA
24		biological specimens for genetic or molecular analysis in	
25		the current trial and for future use in ancillary studies, if	
26		applicable	
27			
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 35 [Penelope.ai](#)  
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