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Lin, Inês Li, McCollum, Eric D, Buckley, Eric et al. (21 more authors) (2025) The impact and cost-effectiveness of pulse oximetry and oxygen on acute lower respiratory infection outcomes in children in Malawi:a modelling study. The Lancet Global Health. e1466-e1475. ISSN: 2214-109X

https://doi.org/10.1016/S2214-109X(25)00202-5

The impact and cost-effectiveness of pulse oximetry and oxygen on acute lower respiratory infection outcomes in children in Malawi: a modelling study

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Summary

Background acute lower respiratory infections (ALRIs) are the leading global cause of post-neonatal death in children younger than 5 years. The impact, cost, and cost-effectiveness of routine pulse oximetry and oxygen on ALRI outcomes at scale remain unquantified.

Methods We evaluate the impact and cost-effectiveness of scaling up pulse oximetry and oxygen on childhood ALRI outcomes in Malawi using a new and detailed individual-based model, together with a comprehensive costing assessment for 2024 that includes both capital and operational expenditures. We model 15 scenarios ranging from no pulse oximetry or oxygen (null scenario) to high coverage (90% pulse oximetry usage and 80% oxygen availability) across the health system. Cost-effectiveness results are presented in incremental cost-effectiveness ratios (ICERs) and incremental net health benefits (INHBs) using a Malawi-specific cost-effectiveness threshold of US$80 per disability-adjusted life-year (DALY) averted.

Findings The cost-effective strategy is the full scale-up of pulse oximetry to 90% usage rate and oxygen to 80% availability. This combination results in 72% (95% CI 72–72) of hypoxaemic ALRI cases accessing oxygen, averting 71 000 (68 100–74 000) DALYs per year of implementation and 28% (27–29) of potential ALRI deaths, at an ICER of US$35 (33–36) per DALY averted and $924 (887–963) per death averted. The INHB is 40 200 (37 300–43 100) net DALYs averted.

Interpretation Pulse oximetry and oxygen are complementary cost-effective interventions in Malawi, where health expenditure is low, and should be scaled up in parallel.

Funding UK Research and Innovation, Wellcome Trust, Department for International Development, EU, Clinton Health Access Initiative, and Unitaid.

Lancet Glob Health 2025; 13: e1466–75

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Introduction

Acute lower respiratory infections (ALRIs) are the leading global cause of death in children after the neonatal period.[1] The UN Inter-agency Group for Child Mortality Estimation estimated that in 2021, globally, 725 557 deaths in children younger than 5 years are from ALRI.[2] An estimated 31% of children with WHO-classified pneumonia in low-income and middle-income countries (LMICs) have hypoxaemia (abnormally low blood oxygen levels defined as an arterial oxygen saturation <90%).[3] Pulse oximeters are non-invasive, portable devices that are more accurate for detecting hypoxaemia and more reliable for supporting oxygen treatment decisions than clinical signs alone;[4] however, availability of pulse oximeters and basic oxygen service capacity are low in most LMICs due to historical lack of investments, weak health systems, and poor governance structures.[5]

Donors and governments of high-burden countries need to be informed about the potential impact and cost-effectiveness of pulse oximetry and oxygen to consider whether these interventions represent a sound investment compared with other strategies for improving health outcomes. Previous studies in LMICs have provided estimates of the cost-effectiveness of oxygen in treating ALRIs, suggesting US$25–225 per disability-adjusted life-year (DALY) averted. However, these estimates are from localised empirical studies, which have focused mostly on concentrator-based systems[6–9] rather than national oxygen systems. National oxygen systems require capital and sustained investments and rely upon a variety of oxygen production, storage, and distribution sources beyond concentrators to reach full scale. A recent study using The Lives Saved Tool estimated that scaling up pulse oximetry and oxygen could avert 19–24% of mortality associated with ALRIs in children younger than 5 years between 2023 and 2030 in Chad, Ethiopia, and Bangladesh; however, this study did not evaluate cost-effectiveness.[10]

We aim to fill this evidence gap by modelling the impact and cost-effectiveness of scaling up routine pulse oximetry and oxygen systems on childhood ALRI outcomes in

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Research in context

Evidence before this study

Acute lower respiratory infections (ALRIs) are the leading cause of death globally in children aged 2–59 months. Oxygen therapy, guided by pulse oximetry, is required to treat severe ALRI cases with low blood oxygen levels (hypoxaemia), but it is not always available. The impact and cost-effectiveness of pulse oximetry and oxygen on ALRI outcomes at scale remain unquantified. We searched PubMed with no language restrictions for studies on the cost-effectiveness using search terms: ((cost-effective*) OR (cost-utility) OR (cost-benefit)) AND (pulse oximetry) AND (oxygen) on Aug 2, 2024 from database inception, yielding 120 results. We found four empirical studies on the cost-effectiveness of pulse oximetry and oxygen on ALRI in children, and six additional empirical studies looking at bronchiolitis, peri-operative pulse oximetry, or adults. However, there were no studies modelling the impact and cost-effectiveness of pulse oximetry and oxygen for whole countries or under different availabilities and intervention coverages.

Added value of this study

This study provides the first quantification of the impact of scaling up routine pulse oximetry and oxygen systems on ALRI mortality and cost per disability-adjusted life-year (DALY) averted in Malawi. We find that scaling up both interventions in combination is the cost-effective strategy under a range of health system conditions, including reduced quality of care and referral services. Routine pulse oximetry even under limited oxygen availability has diagnostic benefit, and oxygen-use efficiency is driven by the use of pulse oximetry. In any oxygen system, when pulse oximetry is implemented at all health system levels compared with none, access to oxygen therapy by children with ALRI and hypoxaemia doubles, and net benefit quintuples with mortality reduced by an additional 15–20 percentage points.

Implications of all the available evidence

Our study indicates that pulse oximetry and oxygen are complementary cost-effective interventions in Malawi (where health expenditure is low), and they should be scaled up concurrently to maximise impact. Additional analysis should be done in other high-burden countries, although given our findings of low cost per DALY averted across a range of scenarios and sensitivity analyses, our results suggest pulse oximetry and oxygen are likely to be cost-effective in these countries too.

Malawi, using a new individual-based model incorporating disease dynamics and health system interactions. We conducted a thorough costing assessment of scaling up oxygen systems at the national level, covering a mix of oxygen sources including pressure swing adsorption (PSA) plants, concentrators, and cylinders.

Methods

ALRI model

We developed a model of ALRI for children younger than 5 years in Malawi as a module integrated within the *Thanzi La Onse* model, which is programmed in Python language version 3.8 and used pandas data analysis library 2.[11] The model covers the natural history of ALRI disease, care seeking, and care management within the Malawian health-care system, modelled at four relevant levels: level 0 (village clinics), level 1a (health centres), level 1b (rural, community, or mission hospitals), and level 2 (central or district hospitals). The ALRI model is fully detailed in the appendix (pp 11–68). Table 1 presents the key parameters and costs for the cost-effectiveness evaluation of pulse oximetry and oxygen interventions.

For more on the ***Thanzi La Onse* model** see www.tlomodel.org

See **Online** for appendix

To map out the epidemiology, the incidence of ALRI was calculated from community health worker and health facility data from Malawi[12] as 15 cases per 100 person-years for children younger than 5 years. The proportion of ALRI cases with low oxygen saturation levels (ie, those with an SpO_2 <93%) was set at 21·9%, which is associated with disease type and pulmonary complications (appendix pp 29–35). ALRI cases present a range of signs and symptoms (appendix pp 36–39), which determine the initial contact with the health system and the care management cascade (appendix pp 47–59). A natural mortality rate (in the absence of treatment) was applied to all cases, differing by oxygen saturation, disease complications and severity of symptoms, and other comorbidities (eg, HIV and acute malnutrition). The simulation generated an ALRI cohort with a weighted average natural mortality rate of 7·47% (appendix pp 40–45).

For the health-care provision modelling, quality of care was captured through health workers' performance in implementing Integrated Management of Childhood Illness (IMCI) guidelines, set at 75% sensitivity overall across the health system (appendix p 54–57).[13] Based on the classification given and respective care provision, treatment failure rates of oral and parenteral antibiotics were applied (appendix pp 60–67). The effect of oxygen is represented through hypoxaemic cases having higher odds (odds ratio [OR] 1·92) of parenteral antibiotic treatment failure in the absence of oxygen therapy.[6] The appendix (pp 107–108) lists the simulation outputs on fraction of cases and risk of death without treatment by case type (IMCI classification, oxygen saturation, general danger signs, abnormal chest radiography), respective effectiveness of treatment with oral antibiotics, and parental antibiotics with and without oxygen therapy.

In the absence of pulse oximetry, the identification of hypoxaemic cases relies on the IMCI classification of pneumonia (based on clinical signs and symptoms). For the provision of oxygen without routine pulse oximetry, only clinical cases classified as severe are provided with

	Value	Source and justification
ALRI epidemiology		
ALRI incidence per 100 child-years, for ages 1–11 months, 12–23 months, and 24–59 months	34·51; 18·55; 6·07	Appendix pp 20–29: describes the estimation of pathogen-attributed incidence, pneumonia or other ALRI disease type incidence, and ALRI incidence by age group
Proportion of ALRI with low oxygen saturation levels (SpO_2 <93%)	0·219	Appendix pp 29–35: describes the modelling of disease progression, and the estimated parameter value based on Malawi studies; nearly half (48·7%[12]) are SpO_2 <90%
Overall ALRI mortality without treatment; mortality without treatment by SpO_2 (≥93%, 90–92%, <90%)	0·07472; 0·0340; 0·1473; 0·2976	Simulation output values. Appendix (pp 40–45): describes the mortality model, including the increased risk of death by SpO_2
Overall treatment failure of 3-day oral antibiotic for fast-breathing pneumonia; overall treatment failure of 5-day oral antibiotic for chest-indrawing pneumonia; overall treatment failure of first-line parenteral antibiotics; overall treatment failure of second-line parenteral antibiotics	0·101; 0·108; 0·193; 0·196	Appendix pp 60–67: the risk of treatment failure differs by case type: oxygen saturation, severe symptoms, abnormal chest radiography, malnutrition, HIV not on ART
Odds ratio of parenteral treatment failure in hypoxaemic cases without oxygen therapy compared with those with oxygen therapy	1·92 (95% CI 1·43–2·56)	Used the inverse of OR=0·52 (95% CI 0·39–0·70)[6]
Proportion of initial care seeking by facility level (0: village clinics; 1a: health centre; 1b: rural hospital; 2: district hospital)	0·094; 0·596; 0·155; 0·155	Appendix pp 48–50: describes data sources and assumptions; symptom severity increases care seeking at hospitals
Pulse oximetry and oxygen costs		
Equivalent annual cost of pulse oximeter (1 device)	$248·51	Appendix p 80: describes the capital and operational costs for first year of implementation and the estimation of equivalent annual cost
Pulse oximeter, cost per patient at: hospital (levels 2 and 1b); health centre (level 1a); village clinics (level 0)	$0·167; $0·096; $0·063	Appendix pp 80–81: describes the estimation of the unit cost based on the equivalent annual cost and outpatient department visits by facility level
Equivalent annual cost of PSA plants (existing PSA system; +planned PSA system)	$1 343 489; $2 907 718	Appendix pp 81–85: describes the capital and operational costs for first year of implementation and the estimation of equivalent annual cost
Equivalent annual cost of delivery trucks (existing PSA system; +planned PSA system)	$98 463; $236 312	Appendix pp 87–88: describes the capital and operational costs for first year of implementation and the estimation of equivalent annual cost
Equivalent annual cost of cylinders plus fuel for distribution (existing PSA system; +planned PSA system)	$234 326; $316 752	Appendix pp 86, 88–90: describes the capital and operational costs for first year of implementation and the estimation of equivalent annual cost
Equivalent annual cost of concentrators (existing PSA system; +planned PSA system)	$562 244; $838 925	Appendix pp 86, 90–91: describes the capital and operational costs for first year of implementation and the estimation of equivalent annual cost
Equivalent annual cost of pulse oximeters for monitoring oxygen administration (existing PSA system; +planned PSA system)	$216 878; $391 447	Appendix pp 86, 91–92: describes the capital and operational costs for first year of implementation and the estimation of equivalent annual cost
Equivalent annual cost of ventilators (existing PSA system; +planned PSA system)	$262 557; $525 114	Appendix pp 86, 93: describes the capital and operational costs for first year of implementation and the estimation of equivalent annual cost
Equivalent annual cost of patient monitors (existing PSA system; +planned PSA system)	$162 698; $324 971	Appendix pp 86, 94: describes the capital and operational costs for first year of implementation and the estimation of equivalent annual cost
Equivalent annual cost of resuscitation sets (existing PSA system; +planned PSA system)	$15 617; $32 887	Appendix pp 86, 95: describes the capital and operational costs for first year of implementation and the estimation of equivalent annual cost
Equivalent annual cost of suction devices (existing PSA system; +planned PSA system)	$155 522; $310 810	Appendix pp 86, 96: describes the capital and operational costs for first year of implementation and the estimation of equivalent annual cost
Total equivalent annual cost of oxygen system (existing PSA system; +planned PSA system)	$3 051 794; $5 884 936	The sum of the annual equivalent costs of each component of the oxygen system
Outpatient consultation cost: district hospital (level 2); rural hospital (level 1b); health centre (level 1a); village clinic (level 0)	$2·58; $2·47; $2·17; $1·76	Appendix pp 99–100: WHO-CHOICE estimates plus inflation to 2024
Inpatient bed days cost: district hospital (levels 2); rural hospital (level 1b)	$7·94; $6·89	Appendix pp 99–100: WHO-CHOICE estimates plus inflation to 2024
Antibiotics unit cost (amoxicillin 250 mg tablet; ampicillin 500 mg vial; gentamicin 10 mg/mL ampoule; ceftriaxone 1 g vial)	$0·02734; $0·25752; $0·15037; $0·6801	Appendix pp 98–99: MSH 2015 estimates plus inflation to 2024
Oxygen service availability		
Overall oxygen availability of existing PSA plants system; oxygen availability of existing PSA system by facility level: district hospital (level 2); rural hospital (level 1b); health centre (level 1a)	40·0%; 51·6%; 33·3%; 31·3%	Appendix pp 74–79: describes the estimation of oxygen availability by facility level. The distribution of oxygen was assumed to be proportional to the demand of each facility level. At the health centre (level 1a), oxygen serves for patient stabilisation; full provision requires referral to higher-level facilities (level 1b or 2)
Overall oxygen availability of +planned PSA plants system; oxygen availability of +planned PSA system by facility level: district hospital (level 2); rural hospital (level 1b); health centre (level 1a)	80·0%; 88·1%; 75·4%; 73·9%	Appendix pp 74–79: describes the estimation of oxygen availability by facility level. The distribution of oxygen was assumed to be proportional to the demand of each facility level. At the health centre (level 1a), oxygen serves for patient stabilisation; full provision requires referral to higher-level facilities (level 1b or 2)

All costs are in 2024 US dollars. Equivalent annual costs: capital costs were depreciated over the useful lifespan of the equipment, plus operational cost for year 1. ALRI=acute lower respiratory infection. ART=antiretroviral therapy. MSH= Management Sciences for Health. OR=odds ratio. PSA=pressure swing absorption.

Table 1: **Key parameters for ALRI epidemiology and pulse oximetry and oxygen cost components of the model**

oxygen if SpO_2 is lower than 90% (monitoring pulse oximeters are included in the oxygen system). Therefore, hypoxaemic cases not classified as severe are not identified as needing oxygen therapy. In the presence of pulse oximetry, both severe and non-severe classifications with SpO_2 lower than 90% are identified as needing oxygen support.

The *Thanzi La Onse* project received ethical approval from the College of Medicine Malawi Research Ethics Committee (P.10/19/2820) in Malawi. Only anonymised secondary data are used in the *Thanzi La Onse* model, including in the ALRI model used in this paper; therefore, individual informed consent was not required.

Costing of pulse oximetry and oxygen

Two oxygen systems were costed for analysis: the current system of oxygen provision, here referred to as existing PSA system (low oxygen availability), and the scale-up in these provisions, referred to as +planned PSA system (high oxygen availability), as described in the Malawi National Medical Oxygen Ecosystem Roadmap 2021–26.[14] Both systems comprise a mix of oxygen sources, including pressure swing adsorption plants, which provide the bulk of the oxygen supply; oxygen concentrators to address gaps in distribution; and cylinders for oxygen delivery to the patient, storage, and distribution. Other components included in the systems costs were delivery trucks for cylinder distribution (as a proxy to address the cost of logistical structure challenges), pulse oximeters for monitoring safe administration of oxygen to patients, ventilators, patient monitors, and resuscitation and suction devices. The total cost of the oxygen system components (capital plus operating costs) in the first year of implementation was budgeted, and capital costs of equipment were annualised over their useful life[15] (eg, PSA costs spread over 15 years) to get the equivalent annual costs for year 1 (ie, 2024). All costs are reported in 2024 US dollars (appendix pp 80–96).

Assuming a daily oxygen production rate of 6·0 to 8·5 effective h, we estimate the existing PSA system would meet 40% of oxygen demand in Malawi and the +planned PSA system would meet 80% of oxygen demand (appendix pp 74–79).

The cost incurred for the treatment of children with hypoxaemic ALRI was estimated to be around 25·9% of the total oxygen system, based on the total litres required for oxygen therapy of the ALRI cohort in the simulation compared with the national volume demand.[14] Therefore, ALRI can be said to account for $789 050 of the existing PSA system costs and $1 521 566 of the +planned PSA system annually. The cost per child treated with oxygen (for an average of 3 days) was estimated to be $23 for infants younger than 2 months and $46 for children aged 2–59 months, from our estimated unit cost per L of $0·0053 (appendix p 97), which is consistent with the estimates reported in *The Lancet Global Health* Commission on Medical Oxygen Security.[5]

We assumed routine pulse oximetry coverage required one device per health worker at the outpatient department, with each pulse oximeter estimated to cost $250 per year. This equivalent annual cost includes all capital expenses for an expected lifespan of 5 years, plus yearly maintenance. The unit cost is then based on the number of patients seen at the outpatient department in each health facility level.[13] Additional costs to the health system resulting from increased demand for services and consumables with the implementation of the interventions include antibiotics, outpatient consultation and hospitalisation bed days (table 1).

Scenarios and model simulation settings

The scenarios start with no oxygen and no pulse oximetry (the null scenario), and are then grouped into three blocks, the first without any oxygen service availability, the second with oxygen availability at 40% (existing PSA system), and the third with oxygen availability at 80% (+planned PSA system). Each block has scenarios sequentially scaling up pulse oximetry to: central or district hospitals (level 2); rural, community, or mission hospitals (levels 2 and 1b); health centres (levels 2, 1b, and 1a); and village clinics (levels 2, 1b, 1a, and 0; appendix pp 69–73). We created a representative mix of ALRI cases by running the natural history model on a population of 150 000 children younger than 5 years. When we applied the age-specific pathogen-attributed incidences, it yielded 20 752 symptomatic infections. For each incident case we considered 20 replicates, each time re-applying the disease characteristics (symptoms, severity, and death), to represent the total ALRI cases (n=415 040) in the population of 3 000 000 children younger than 5 years in Malawi in 2024. The effect of health-care system interventions were applied to each ALRI case who sought care. We re-ran the model for each of the 15 scenarios, using the same seed (equal random number generation) so the result differences were due to scenario parameters and not random variation.

Across all scenarios, health system settings and conditions are constant: 100% antibiotics availability, health worker diagnostic accuracy at 75%, referral rate of 85% for severe cases seen at levels 0 and 1a to facility levels 1b and 2, 90% pulse oximetry usage rate if available, and 60% seek follow-up care with oral treatment failure.

Analyses

For this economic evaluation, we took the health-care provider perspective, as the health system is mostly government-funded and donor-funded. The cost-effectiveness analysis was conducted for a single year cohort (2024), capturing health outcomes in DALYs due to premature death and health-care costs incurred in this period—eg, outpatient consultation, inpatient bed days, antibiotics, pulse oximetry, and oxygen therapy.

DALYs were computed for each death in the cohort, which equals the health-adjusted life expectancy in

Malawi (2021 WHO estimates[16]) at the age of death, and discounted at 3% per year as recommended by the International Decision Support Initiative reference case.[17] For an average age of 1·45 years in the cohort, one death is equivalent to 26·6 DALYs.

For each intervention scenario, we calculated the number of deaths averted (lives saved) and DALYs averted relative to the null scenario. We also calculated the incremental cost effectiveness ratios (ICERs), noting which strategies were dominated by less costly and more effective scenarios, and which strategies were extendedly dominated (ie, had an ICER greater than that of the next, more effective alternative). We then plotted each scenario on the cost-effectiveness plane as DALYs averted against incremental costs, and determined the cost-effectiveness frontier as the scenarios averting the most DALYs for the least incremental cost. We used a very stringent cost-effectiveness threshold (CET) of $80 per DALY averted, equivalent to the CET of $65 used to select interventions to be prioritised for funding Malawi's national Health Sector Strategic Plan III 2023–30,[18,19] inflated to 2024 US$ value.[20] Notably, a CET of $80 is only 16% of Malawi's per capita GDP. Using this CET, we calculated the incremental net health benefits (INHBs) for each scenario as incremental net DALYs averted. This metric represents the DALYs averted by the intervention strategy, adjusted for the DALY value of the difference in costs, using the CET of $80.

To quantify the uncertainty in the outcome estimates due to stochastic processes in the model, we performed a non-parametric bootstrap analysis with 1000 resamples of the paired individual-level outcomes between the null scenario and intervention scenarios. Within each iteration, the model outputted differences in cost, deaths averted, DALYs averted, and the resulting ICERs and incremental net benefits. We report the mean estimate and 2·5 and 97·5 percentiles of the bootstrap distribution in the Results.

To assess the effect of individual parameters on model outcomes, we conducted deterministic one-way sensitivity analyses by varying input values of key parameters, whereby ALRI accounted for 50% of the total oxygen need in Malawi (rather than the default 25·9%); pulse oximetry costs were doubled, to conservatively account for device wear and tear; outpatient and inpatient costs were twice as much as default; the referral rate of severe cases diagnosed at facility levels 1a and 0 was reduced to 60%; health worker diagnostic performance were 100% or 50%; health system conditions were perfect (defined as 100% health worker diagnostic performance, 100% referral rate of severe cases diagnosed, and 100% pulse oximetry usage rate); the relationship between oxygen production capacity and service availability followed a saturation curve, whereby additional planned PSAs covered 70% of the national demand (rather than default of 80%); the incidence of ALRI was reduced by half; the baseline odds of death was reduced by half; and the effect of oxygen was reduced by decreasing the OR of parenteral treatment failure in hypoxaemic cases without oxygen therapy compared with those with oxygen therapy to 1·43 (the inverse of OR=0·7).[6] Bootstrap methods were also applied to each sensitivity analysis, with results reported as mean and 95% CIs.

Descriptive statistical analyses informing some parameter values were performed in Stata and costing assessments were completed in Excel. The analysis scripts for simulation outputs, bootstrap iterations for uncertainty quantification, and cost-effectiveness analysis were programmed and executed in Python version 3.8.

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

In total, 415 040 cases of children with ALRI were simulated for 2024; baseline characteristics of the cohort can be found in the appendix (pp 104–106). Implementation of routine pulse oximetry at all hospitals of varying capacity, without oxygen (no oxygen availability and pulse oximetry at levels 2 and 1b) and the scale-up of oxygen systems to 80% service availability along with

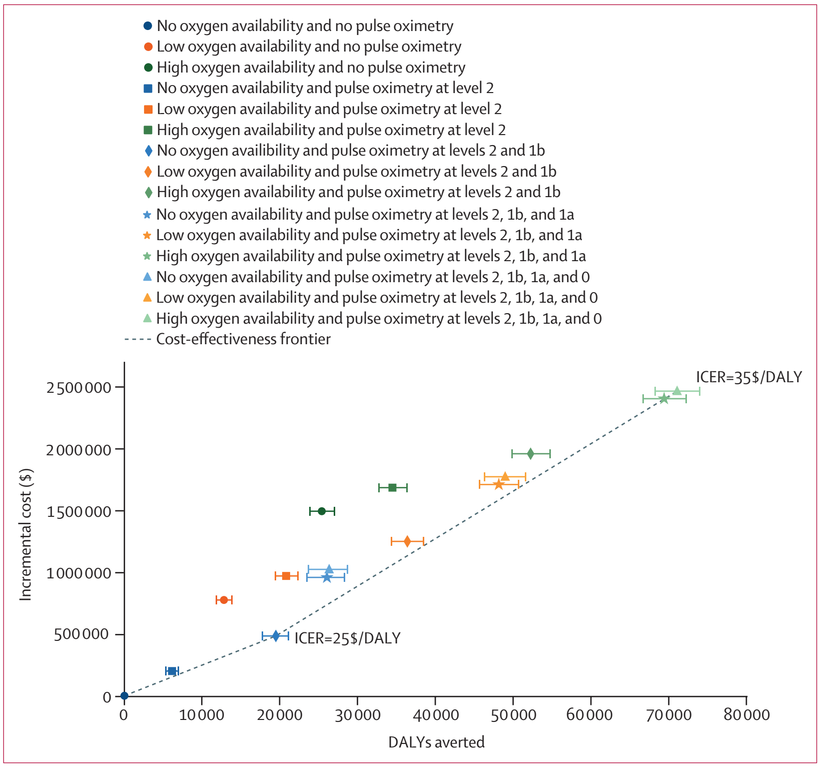

***Figure:* Pulse oximetry and oxygen scale-up scenarios on the cost-effectiveness plane: incremental effectiveness in DALYs averted of intervention scenarios against the incremental cost, relative to the null scenario**
DALY=disability-adjusted life-year. ICER=incremental cost-effectiveness ratio.

	Simulation output		Bootstrap results reporting the mean estimate (95% CI)				
	Total deaths	Total cost (US$)*	Access to oxygen†	Mortality reduction	DALYs averted	ICER ($/DALY averted)	Incremental net health benefit (DALYS averted)
No oxygen availability and no pulse oximetry (null scenario)	9485	5 127 777	0	NA	NA	NA	NA
No oxygen availability and pulse oximetry at level 2	9255	5 327 670	0	2·4% (2·1–2·8)	6100 (5200–7000)	Extendedly dominated	3600 (2700–4600)
No oxygen availability and pulse oximetry at levels 2 and 1b	8754	5 611 671	0	7·7% (7·0–8·4)	19 500 (17 600–21 100)	25 (23–27)	13 400 (11 600–15 100)
No oxygen availability and pulse oximetry at levels 2, 1b, and 1a	8509	6 085 817	0	10·3% (9·3–11·2)	26 000 (23 400–28 300)	Extendedly dominated	14 000 (11 400–16 400)
No oxygen availability and pulse oximetry at levels 2, 1b, 1a, and 0	8498	6 150 698	0	10·4% (9·4–11·3)	26 300 (23 600–28 700)	Extendedly dominated	13 500 (10 800–15 900)
Low oxygen availability and no pulse oximetry	9005	5 902 980	18·2% (17·8–18·5)	5·1% (4·6–5·5)	12 800 (11 700–13 900)	Dominated	3100 (2000–4200)
Low oxygen availability and pulse oximetry at level 2	8704	6 097 465	22·4% (22·0–22·7)	8·2% (7·7–8·8)	20 800 (19 300–22 400)	Dominated	8700 (7200–10 200)
Low oxygen availability and pulse oximetry at levels 2 and 1b	8119	6 377 019	27·1% (26·7–27·5)	14·4% (13·6–15·2)	36 400 (34 200–38 500)	Extendedly dominated	20 700 (18 700–22 800)
Low oxygen availability and pulse oximetry at levels 2, 1b, and 1a	7678	6 837 542	35·6% (35·1–36·0)	19·1% (18·2–20·0)	48 100 (45 500–50 700)	Extendedly dominated	26 700 (24 200–29 400)
Low oxygen availability and pulse oximetry at levels 2, 1b, 1a, and 0	7647	6 900 486	36·7% (36·3–37·2)	19·4% (18·4–20·3)	48 900 (46 200–51 600)	Extendedly dominated	26 800 (24 100–29 400)
High oxygen availability and no pulse oximetry	8533	6 621 392	34·7% (34·3–35·1)	10·0% (9·4–10·7)	25 400 (23 800–27 100)	Dominated	6700 (5100–8300)
High oxygen availability and pulse oximetry at level 2	8191	6 812 152	41·9% (41·5–42·4)	13·6% (13·0–14·4)	34 400 (32 600–36 400)	Dominated	13 400 (11 600–15 300)
High oxygen availability and pulse oximetry at levels 2 and 1b	7524	7 086 551	52·5% (52·0–52·9)	20·7% (19·8–21·6)	52 200 (49 700–54 800)	Extendedly dominated	27 700 (25 200–30 200)
High oxygen availability and pulse oximetry at levels 2, 1b, and 1a	6879	7 532 457	69·5% (69·1–70·0)	27·5% (26·5–28·5)	69 300 (66 500–72 300)	Extendedly dominated	39 300 (36 500–42 200)
High oxygen availability and pulse oximetry at levels 2, 1b, 1a, and 0	6816	7 593 675	71·9% (71·5–72·4)	28·1% (27·1–29·2)	71 000 (68 100–74 000)	35 (33–36)	40 200 (37 300–43 100)

Low oxygen availability refers to 40% overall oxygen service availability of the existing PSA system. High oxygen availability refers to 80% overall oxygen service availability of the +planned PSA system. Level 2 refers to central or district hospitals, level 1b refers to rural, community, or mission hospitals, level 1a refers to health centres, and level 0 refers to village clinics. Dominated refers to more costly and less effective, extendedly dominated refers to dominated by a linear combination of two or more other alternatives. ALRI=acute lower respiratory infections. DALY=disability-adjusted life-year. ICER=incremental cost-effectiveness ratio. NA=not applicable. *Cost includes antibiotics, outpatient consultation, inpatient bed days, pulse oximetry, and oxygen incurred for ALRI children (full breakdown of costs in the appendix p 114).†Proportion of hypoxaemic cases who receive oxygen therapy.

Table 2: **Cost-effectiveness results for each scenario of pulse oximetry and oxygen scale-up for ALRI in children younger than 5 years in Malawi**

pulse oximetry across all levels of the health system (high oxygen availability and pulse oximetry at levels 2, 1b, 1a, and 0) are on the cost-effectiveness frontier, whereas all other scenarios were dominated or extendedly dominated (figure). The full scale-up scenario was the cost-effective strategy, averting 71 000 (95% CI 68 100–74 000) DALYs at an ICER of $35 (33–36) per DALY averted, with an INHB of 40 200 (37 300–43 100) net DALYs averted on population burden of disease (table 2). This strategy achieved a 28% reduction in ALRI mortality compared with the null scenario, at an incremental cost of $924 (887–963) per death averted. As illustrated in the cost-effectiveness plane, within each oxygen availability block, the progressive implementation of pulse oximetry across the four health system levels moved the strategy towards the cost-effectiveness frontier, showing complementarity between pulse oximetry and delivery of oxygen.

The implementation of routine pulse oximetry results in DALYs being averted even when oxygen therapy is not available. The resulting benefit arises from identifying cases with SpO_2 below 90% that would otherwise be under-classified as non-severe and managed as outpatients. The addition of the diagnostic tool can correct health workers' assessment accuracy and can also pick up cases missed by the IMCI clinical algorithm, particularly in primary care settings, including small-capacity hospitals. In the absence of an oxygen system, introduction of routine pulse oximetry in primary care settings (no oxygen availability and pulse oximetry at levels 2, 1b, and 1a, or no oxygen availability and pulse oximetry at levels 2, 1b, 1a, and 0) had a comparable effect to the full scale-up of oxygen systems without pulse oximetry (high oxygen availability and no pulse oximetry), both resulting in almost 1000 deaths averted in 1 year. Moreover, when considering the costs, the INHBs of pulse oximetry only strategies are double that of the full oxygen scale-up only strategy.

We found that efficient oxygen systems are driven by the use of pulse oximetry. Access to oxygen therapy for children with ALRI and hypoxaemia doubles when

	Costs		Health workers' IMCI performance		Health system conditions		Scale-up constraints	Epidemiology		
	ALRI oxygen consumption of 50%*	Cost of outpatient/ inpatient ×2	Perfect 100%	Imperfect 50%	Referral rate 60%	All perfect†	Planned PSAs system: 70% availability	Reduce baseline incidence by half‡	Reduce baseline odds of death by half	Reduce effect of oxygen§
No oxygen availability and no pulse oximetry	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
No oxygen availability and pulse oximetry at level 2	3600 (2700 to 4600)¶	1600 (681 to 2544)	−1300 (−1700 to −900)	11 000 (9800 to 12 400)	3600 (2700 to 4600)	−1200 (−1677 to −731)	3600 (2700 to 4600)¶	1200 (464 to 1924)	2600 (1900 to 3400)	5500 (4600 to 6500)
No oxygen availability and pulse oximetry at levels 2 and 1b	13 400 (11 600 to 15 100)¶	8400 (6600 to 10 200)	−1300 (−2400 to −200)	29 100 (26 900 to 31 200)	13 400 (11 600 to 15 100)	−1500 (−2552 to −460)	13 400 (11 600 to 15 100)¶	6400 (5100 to 7900)	7800 (6600 to 9000)	18 700 (16 900 to 20 500)
No oxygen availability and pulse oximetry at levels 2, 1b, and 1a	14 000 (11 400 to 16 400)¶	4000 (1400 to 6400)	−10 100 (−11 700 to −8300)	38 300 (35 300 to 41 000)	14 800 (12 300 to 17 100)	−12 100 (−13 700 to −10 500)	14 000 (11 400 to 16 400)¶	5100 (3100 to 7000)	8700 (7000 to 10 300)	23 300 (20 900 to 25 600)
No oxygen availability and pulse oximetry at levels 2, 1b, 1a, and 0	13 500 (10 800 to 15 900)¶	2800 (48 to 5112)	−11 300 (−13 000 to −9500)	38 600 (35 500 to 41 200)	14 200 (11 600 to 16 600)	−13 900 (−15 700 to −12 200)	13 500 (10 800 to 15 900)¶	4500 (2400 to 6400)	8800 (7000 to 10 400)	23 300 (20 900 to 25 800)
Low oxygen availability and no pulse oximetry	−6100 (−7200 to −5000)	3300 (2200 to 4400)	7300 (6000 to 8500)	−1400 (−2300 to −500)	2400 (1400 to 3500)	8700 (7400 to 10 100)	3100 (2000 to 4200)¶	−1100 (−2000 to −212)	1800 (967·0 to 2580·0)	−2800 (−3500 to −1900)
Low oxygen availability and pulse oximetry at level 2	−554 (−2000 to 880)	6900 (5400 to 8300)	6400 (5000 to 7800)	13 400 (11 900 to 15 100)	8000 (6600 to 9400)	7800 (6500 to 9300)	8700 (7200 to 10 200)¶	1700 (458 to 2878)	5400 (4300 to 6500)	3600 (2300 to 4900)
Low oxygen availability and pulse oximetry at levels 2 and 1b	11 500 (9500 to 13 600)	16 100 (14 000 to 18 200)	7600 (5900 to 9300)	34 400 (32 000 to 36 800)	20 000 (17 900 to 22 100)	8800 (7300 to 10 600)	20 700 (18 700 to 22 800)¶	8600 (7000 to 10 300)	11 500 (10 000 to 12 900)	17 900 (15 900 to 19 900)
Low oxygen availability and pulse oximetry at levels 2, 1b, and 1a	17 500 (15 000 to 20 100)	17 200 (14 700 to 19 900)	3100 (1100 to 5200)	50 300 (47 300 to 53 300)	26 000 (23 500 to 28 600)	3700 (1700 to 5700)	26 700 (24 200 to 29 400)¶	10 900 (8900 to 13 000)	15 300 (13 500 to 17 100)	26 300 (23 800 to 28 800)
Low oxygen availability and pulse oximetry at levels 2, 1b, 1a, and 0	17 500 (14 900 to 20 200)	16 600 (13 900 to 19 300)	2300 (200 to 4500)	51 300 (48 300 to 54 400)	26 000 (23 400 to 28 700)	2800 (730 to 4905)	26 800 (24 100 to 29 400)¶	10 600 (8600 to 12 700)	15 700 (13 800 to 17 500)	26 700 (24 100 to 29 200)
High oxygen availability and no pulse oximetry	−11 100 (−12 700 to −9400)	7100 (5500 to 8700)	14 800 (13 100 to 16 700)	−1900 (−3100 to −600)	5200 (3600 to 6700)	17 100 (15 400 to 18 800)	3600 (2200 to 5200)	−1700 (−2932 to −356)	4400 (3200 to 5600)	−4100 (−5300 to −2900)
High oxygen availability and pulse oximetry at level 2	−4400 (−6200 to −2500)	11 800 (10 000 to 13 800)	14 200 (12 400 to 16 100)	15 100 (13 300 to 17 200)	11 900 (10 100 to 13 700)	16 600 (14 800 to 18 500)	10 000 (8300 to 11 900)	1800 (339 to 3385)	8800 (7300 to 10 100)	2800 (1200 to 4300)
High oxygen availability and pulse oximetry at levels 2 and 1b	9900 (7500 to 12 500)	23 400 (20 900 to 25 900)	16 700 (14 600 to 18 700)||	39 700 (37 000 to 42 400)	26 200 (23 800 to 28 700)	19 200 (17 200 to 21 200)||	23 400 (21 000 to 25 800)	10 500. (8600 to 12 500)	16 200 (14 500 to 18 000)	17 900 (15 800 to 20 200)
High oxygen availability and pulse oximetry at levels 2, 1b, and 1a	21 500 (18 700 to 24 400)	30 200 (27 400 to 33 200)	16 500 (14 200 to 18 600)	62 600 (59 400 to 65 900)	36 800 (33 900 to 39 600)	19 000 (16 800 to 21 300)	33 600. (30 800 to 36 500)	16 400 (14 100 to 18 600)	23 100 (21 200 to 25 200)	30 300 (27 500 to 33 000)
High oxygen availability and pulse oximetry at levels 2, 1b, 1a, and 0	22 400 (19 600 to 25 300)||	30 500 (27 600 to 33 400)||	16 300 (14 000 to 18 600)	64 600 (61 300 to 67 900)||	37 600 (34 600 to 40 400)||	18 800 (16 600 to 21 200)	34 300 (31 400 to 37 200)||	16 800 (14 400 to 19 100)||	23 800 (21 700 to 25 900)||	31 200 (28 500 to 34 100)||

Full outputs of scenarios under sensitivity analyses (mortality, DALYs, costs breakdown, and ICERs) are detailed in the appendix (pp 118–163). Sensitivity analyses to pulse oximetry costs (doubled) are in the appendix (pp 158–160). ALRI=acute lower respiratory infection. DALY=disability-adjusted life-year. ICER=incremental cost-effectiveness ratio. IMCI=Integrated Management of Childhood Illness. NA=not applicable. OR=odds ratio. *Default ALRI consumption is 25·9% of total oxygen demand. †All perfect—100% health workers' IMCI performance, 100% referral rate of severe cases diagnosed, 100% pulse oximetry usage rate. ‡ALRI Incidence of 7·5 per 100 child-years makes up 13·2% of the national oxygen demand; thus, 13·2% of the total system cost. §OR of treatment failure without oxygen is 1·43. ¶Remains unchanged from the main analysis results. ||The cost-effective strategy.

Table 3: **Sensitivity analysis results: incremental net health benefits (net DALYs averted) for each intervention strategy versus the null scenario under different conditions**

routine pulse oximetry is implemented at all levels of the health system compared with none (18% to 37% in the low oxygen system, and 35% to 72% in high oxygen system; table 2). Identifying oxygen need with routine pulse oximetry brings effective use of oxygen closer to the maximum availability.

If investments towards effective operation of the existing oxygen system achieved an oxygen service availability of 40%, the introduction of routine oximetry at all facility levels (low oxygen availability and pulse oximetry at levels 2, 1b, 1a, and 0) yields greater INHB (26 800 [95% CI 24 100–29 400]) net DALYs averted) than investing in additional planned PSA plants without concurrent implementation of pulse oximetry further into primary care hospitals (high oxygen availability and pulse oximetry at level 2; 13 400 [11 600–15 300] net DALYs averted; table 2). Thus, investing in additional oxygen capacity without implementing routine pulse oximetry means it will not fulfill its potential impact.

Indeed, in scenarios with oxygen availability, mortality further reduces by 15–20% (increasing percentage with increasing oxygen availability) when pulse oximetry implementation at outpatient settings covers all facility levels compared to none (table 2). In terms of population-level health gains, full implementation of pulse oximetry can nearly triple the net health benefit of oxygen implementation scenarios (low or high oxygen availability and pulse oximetry at levels 2, 1b, 1a, and 0 compared with low or high oxygen and pulse oximetry at level 2; table 2).

Sensitivity analyses (table 3) of cost changes consistently indicate that the strategy leading to the greatest incremental net health benefit is the full-scale implementation of both oxygen and pulse oximetry across all levels of the health system (high oxygen and pulse oximetry at four levels). Even if childhood ALRI were to consume 50% of the oxygen system's capacity, equivalent to near doubled oxygen costs, the full-scale implementation remains the cost-effective strategy.

Similarly, full-scale implementation consistently emerged as the cost-effective strategy across the epidemiological variations tested in sensitivity analyses, including a 50% reduction in ALRI incidence, halved baseline mortality odds, and diminished oxygen therapeutic effect.

In terms of health system constraints, sensitivity analyses of reduced quality of care and ineffective referral pathways confirm that full-scale implementation remains the strategy yielding the greatest net DALYs averted. In parallel, we ran simulations under improved quality care and within a theoretical optimal health system; both showed that scaling up oxygen systems is impactful in perfect conditions, while implementation of pulse oximetry can be limited to hospitals. This finding supports the importance of adhering to IMCI guidelines and maintaining an effective health system to optimise efficiency of oxygen systems, while also highlighting how routine pulse oximetry can help address and mitigate underlying system inefficiencies. Additionally, even a reduction in the oxygen service availability achieved with +planned PSA system reached the same conclusion on the cost-effective strategy.

Discussion

Scaling up oxygen to meet 80% of the national demand and pulse oximetry to all levels of the health system in Malawi is cost-effective. At $35 per DALY averted (with sensitivity analyses results ranges between $27–52), it represents outstanding value for money, even in comparison to competing essential interventions in Malawi's current health benefits package.[18] The incremental net health benefit of 40 200 DALYs averted is as good as a hypothetical intervention that eliminated, at zero cost, all DALYs due to African trypanosomiasis, schistosomiasis, onchocerciases, and lymphatic filariasis combined.[21] There is also strong complementarity of pulse oximetry and oxygen: the model shows that access to pulse oximetry drives the efficiency of oxygen systems.

When quality of IMCI implementation (and therefore diagnosis of severe pneumonia requiring inpatient management) is low, the incremental net health benefits of scaling up pulse oximetry alone or in combination with oxygen are even greater. This finding is particularly relevant to settings where implementation of IMCI for pneumonia diagnosis is generally poor (eg, Malawi), with respiratory assessments such as respiratory rates often not being performed.[22–24] The main signs used to classify severity in IMCI are also subjective, further affecting misdiagnosis. Pulse oximetry detects hypoxaemia in cases that would be missed because they do not have clinical signs that could be detected with the current IMCI algorithm,[25] including fatal hypoxaemic cases.[26] Therefore, a focus on quality pulse oximetry adoption provides a clear opportunity for a more objective measure of disease severity, but only if health-care workers are motivated and equipped to conduct these measurements.[27]

Additionally, there is potential for further effect from routine pulse oximetry use and oxygen treatment not covered in this economic evaluation. Such potential impact includes the effect of providing oxygen therapy to children with moderate levels of hypoxaemia (SpO_2 measurements between 90% and 92%),[28] and the potential effects of pulse oximetry in correctly prescribing antibiotic therapy for non-hypoxaemic cases presenting with an abnormal SpO_2 (below 95%).[29] Therefore, the impact and cost-effectiveness of both interventions could potentially be greater than presented in this analysis, depending on the other implementation considerations.

Implementation of routine pulse oximetry across the health system should be a priority in any oxygen system expansion. Currently, there is an unrealised opportunity to maximise the efficient use of existing oxygen systems. Our findings feed into wider calls to expand access to oxygen as an essential medicine globally, which have gained momentum since the COVID-19 pandemic. Efforts by *The Lancet Global Health* Commission on Medical Oxygen Security[5] and the Global Oxygen Alliance, which aims to raise $4 billion in oxygen investments from 2024–30,[30] should lead to scale-up of both routine pulse oximetry and oxygen concurrently, especially in the highest burden countries.

This modelling study provides a comprehensive analysis of the potential benefits of oxygen and pulse oximetry implementation in the Malawi health system context. However, the successful implementation of these interventions is hindered by a multitude of crucial factors[14] including subpar quality of care and referral systems as analysed and surging demand for health services resulting from the expansion of interventions. This expansion requires a well equipped health workforce, which poses a substantial challenge in Malawi.[31] Although the cost of increased demand for care services is included in outpatient and inpatient costs, translating these projections into the reality of increasing staff numbers poses another bottleneck in improving oxygen accessibility and quality of care.

It is possible that we overestimated or underestimated the effect of pulse oximetry, as we had to assume 100% sensitivity and specificity in measuring SpO_2. This assumption is because the modelling of hypoxaemia and SpO_2 levels is informed by published studies that use pulse oximeter devices with the same level of accuracy (+/–2%).[12] Thus, non-detected or overdiagnosed cases are reflected in the mortality rates. For the model to truly handle accuracy we would need arterial blood gas measurement data from children in LMICs, which are not currently available. We also acknowledge the concerns regarding potential lower accuracy in individuals with darker skin tones.[32] However, the magnitude of these issues and their actual effect on the identification of true hypoxaemia cases is unclear, given that SpO_2 measurement accuracy is multifactorial. We did not model oxygen overuse, as pulse oximetry for monitoring oxygen use is a key component included in the oxygen system to guide oxygen therapy.

Further limitations of the model are that it assumes complete availability of antibiotics as the base intervention for pulse oximetry and oxygen to be effective. The model also assumes a uniform distribution of oxygen supply across the country and does not include transportation costs associated with referrals (appendix pp 101–103). As with all modelling exercises, we relied on data from many published studies to inform our model parameters. It is not always clear from these studies how they addressed issues such as missing data, which could potentially introduce bias in our parameter estimates. Stochastic uncertainty arising in the model due to random variability was quantified through bootstrap iteration, and parameter sensitivity was examined through one-way sensitivity analyses across plausible and extreme parameter ranges. Both approaches confirm the robustness of the findings on the cost-effectiveness of pulse oximetry and oxygen. Nevertheless, structural uncertainty related to conceptual modelling assumptions could not be fully assessed, and implementation challenges or unexpected clinical usage patterns could potentially influence the cost and effect of oxygen beyond our considered ranges.

In the scale-up of pulse oximetry and oxygen, especially in primary care, implementation needs to be carefully considered beyond the costs and logistics. Supply-side barriers relating to health-worker competency need to be addressed (including delivering training, mentoring, and creating the right conditions for staff motivation) for sustained high-coverage use of pulse oximetry and oxygen by all cadres of staff tasked with implementing them at each level of care.[27] Demand-side barriers also require attention, as oxygen therapy can be unacceptable to caregivers or patients in contexts where knowledge of oxygen therapy is low[33,34] or unaffordable[35] (eg, in health systems where care is funded directly via out-of-pocket payments by patients).

In conclusion, our modelling results indicate that pulse oximetry and oxygen are complementary cost-effective interventions in Malawi and should be scaled up in parallel. However, the way in which scale-up is done should depend on government priorities and feasibility, and a phased approach might be sensible.[36] Given the key message that routine pulse oximetry is crucial to realising the benefits of oxygen investments, there needs to be a focus on quality pulse oximetry implementation across the health-care system. Previous work has shown that pulse oximetry uptake among health-care workers in routine care settings can be achieved.[37] Additional modelling should be done in high-burden countries that face different health system constraints. However, given our findings of low cost per DALY averted across a range of sensitivity analyses, and in comparison to other essential health interventions, it seems likely that pulse oximetry and oxygen will be cost-effective in these countries too.

Contributors

ILL, EDM, VC, PR, ANP, TC, and TBH contributed to conceptualisation of the study. ILL, EDM, EB, JHC, MMG, EJ, TDM, JM-B, EM, SM, MM, DN, AR, BS, LS, AUT, PR, VC, ANP, TC, and TBH contributed to the methodology. ILL contributed to data curation, formal analysis, and visualisation. ILL and TC wrote the original draft. ILL, EDM, EB, JHC, EJ, CK, NL, TDM, JM-B, EM, SM, MM, DN, HN, AR, BS, LS, AUT, PR, VC, ANP, TC, and TBH contributed to reviewing and editing. ILL, PR, ANP, TC, and TBH contributed to funding acquisition. ILL, TC, and TBH accessed and verified the data and are responsible for the decision to submit the manuscript. All the authors had access to the data in the study and accept responsibility for the decision to submit for publication.

Declaration of interests

Besides funding from the Wellcome Trust and UK Research and Innovation going towards authors' institutions, some authors took on private projects, outside the submitted work. ILL declares receiving consulting fees from ICDDR-B for her work for The *Lancet* Commission on Medical Oxygen Security related to this study. TC declares consulting fees donated to his institution from the Global Fund for related work, personal consulting fees from the UN Economic Commission for Africa, and non-paid work chairing a Trial Steering Committee for a trial of adolescent mental health interventions in Nepal. ANP declares receiving consulting fees from the Bill & Melinda Gates Foundation. All other authors declare no competing interests.

Data sharing

All data used in this study are available in our supplementary material and via our GitHub repository: https://github.com/UCL/TLOmodel/releases/tag/Li_Lin_et_al_ALRI_CEA_Ox_PO.

Acknowledgments

The first phase of this study was funded by UK Research and Innovation as part of the Global Challenges Research Fund (*Thanzi La Onse*; reference MR/P028004/1) and the second phase was funded by The Wellcome Trust (*Thanzi La Mawa*; reference 223120/Z/21/Z). BS, TDM, MM and TBH are jointly funded by the UK Medical Research Council and the UK Department for International Development under the Medical Research Council and Department for International Development Concordat agreement and are also part of the EDCTP2 programme supported by the EU (reference MR/R015600/1). This project was also made possible thanks to funding and support from the Clinton Health Access Initiative and Unitaid.

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