CHARITY ENTREPRENEURSHIP

IMPROVING OXYGEN ACCESS FOR CHILDHOOD PNEUMONIA

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CONSIDERED

Research Report:
Large-Scale Global Health – Improving oxygen access for childhood pneumonia

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Executive Summary

There are few medical therapies more basic than oxygen. Unfortunately, despite being critical for numerous medical treatments, medical oxygen remains inaccessible to many. For example, medical oxygen is a crucial treatment for severe pneumonia, which is now the biggest infectious killer of children, claiming over 700,000 young lives every year. In addition, medical oxygen is also a key treatment for over 20 health conditions, including COPD, neonatal asphyxia, malaria, sepsis and meningitis, and now for Covid-19. Data suggest that this cumulative need is massive and largely underserved. Considering cases of hypoxaemic pneumonia alone; an estimated 7 million children who need medical oxygen therapy are admitted to LMIC hospitals each year, yet in many contexts only one in five actually receive it (Kitutu et al., 2022). Broad estimates suggest at least half of the world's population does not have access to medical oxygen. In the few places where in-depth studies have been carried out, availability is critically low. For instance, in the Congo, only 2% of healthcare facilities have oxygen; in Tanzania it's 8%, and in Bangladesh 7%, according to limited surveys for USAID.

Unfortunately, the COVID pandemic has only exacerbated the oxygen supply gap. Whilst more funding and resources have been diverted to address this gap, the room to operate remains large.

There is strong evidence that improving oxygen systems would save lives, though the effect sizes for all the above diseases remain quite uncertain. Although the empirical evidence is low (as RCTs withholding oxygen would be unethical), the theoretical evidence, limited empirical evidence, historical track record, and expert consensus are strong evidence for it having *some* effect. Our best understanding comes from childhood pneumonia mortality. Improved oxygen delivery systems could reduce childhood pneumonia-related mortality by 48 percent in high-burden, low-resource settings (Lam et al. 2021).

There are good case studies of countries improving their access to oxygen, and charities and social enterprises that facilitate this work.

Based on childhood pneumonia-related mortality, improving oxygen access can **be highly cost-effective**. Our cost-effectiveness analysis yielded an estimated cost (in USD) per DALY equivalent of:

- $38 for distributing and maintaining oxygen concentrators and pulse oximeters without additional electricity support
- $79 for the above and additionally distributing solar power and electricity storage

If the charity focuses just on maintenance of oxygen concentrators, without distributing new ones, the cost-effectiveness is modeled to rise to **$17 per DALY**, but this would be at a significantly limited scale.

However, there are still some important concerns. Distributing oxygen equipment and supporting a large team of biotechnicians is much more complex than distributing bed nets or deworming pills. Beyond concentrators themselves, there are different patient interfaces which need to be considered, depending on the patient condition, such as nasal cannulas, simple face masks, non-rebreather masks, and non-invasive and invasive ventilation. Oxygen delivery also needs to be adjusted to patient conditions via flow rates, and carefully observed to prevent adverse side effects of over oxygenation- such as retinopathy in neonates. If simply considering the distribution of equipment, it may not seem so complicated, but the downstream steps of patient care and management add additional complexity.

The overall effects on other health conditions are highly uncertain, and if oxygen concentrators are used for other health conditions, it may lower the overall cost-effectiveness. There is very little systematic data analyzing the level of oxygen access across all the countries, and little data on the reliability of electricity in these countries.

Overall, we currently lean against recommending a new charity to improve oxygen access, but we may revisit this idea in future research cycles.

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Introduction

This report has been produced by Charity Entrepreneurship (CE). CE's mission is to cause more effective charities to exist in the world by connecting talented individuals with high-impact intervention opportunities. We achieve this goal through an extensive research process and our Incubation Program. In 2022, our research process focused on the top highly scalable global health interventions.

Improving oxygen access was chosen by CE research staff as a potentially promising intervention within this category. This decision was part of a five-month process designed to identify interventions that were most likely to be high-impact avenues for future charity entrepreneurs. This process began by listing nearly 300 ideas and gradually narrowing them down, examining them in more and more depth.

In order to assess how promising interventions would be for future charity entrepreneurs, we use a variety of different decision tools such as group consensus decision-making, weighted factor models, cost-effectiveness analyses, quality of evidence assessments, case study analyses, and expert interviews.

This process was exploratory and rigorous, but not comprehensive – we did not research all 300 ideas in depth. As such, our decision not to take forward a charity idea to the point of writing a full report should not be seen as a view that the idea is not good.

Background

Oxygen is a vital medicine that has been used to treat a wide range of medical conditions since the 1800s. According to the Institute for Health Metrics and Evaluation (IHME), there are at least 20 conditions where oxygen treatment would be appropriate, including lower respiratory infections such as COVID-19, pneumonia, and influenza, as well as chronic obstructive pulmonary disease (COPD) (Vos, 2022). It is important to note that oxygen therapy is used to treat hypoxemia, which is a condition characterized by a low level of oxygen in the blood. Hypoxemia is a symptom and not the cause of these conditions; however, if left untreated, it can lead to serious complications. When the body is not getting enough oxygen, the cells and organs cannot function properly and this can lead to damage of the brain, heart, and other vital organs, and ultimately result in death.

Despite the importance of oxygen, there is a lack of understanding about the total hypoxemia burden, which is the burden of death and disability that would have been avoided if medical oxygen had been available in the correct settings. This lack of understanding makes it challenging to assess the global demand and supply of oxygen.

Pneumonia has probably been the dominant angle from which organizations have arrived at oxygen access as a focus. Pneumonia is the leading infectious cause of mortality among children under five in low-and middle-income countries (LMICs), with an estimated 700,000 deaths each year (IHME, 2019). The COVID-19 pandemic has further exacerbated the shortage of oxygen in many parts of the world.

The standard care for pneumonia is a course of antibiotics. And there is also a pneumococcal vaccine that is effective for preventing a significant number of pneumonia infections (JustActions, 2021).

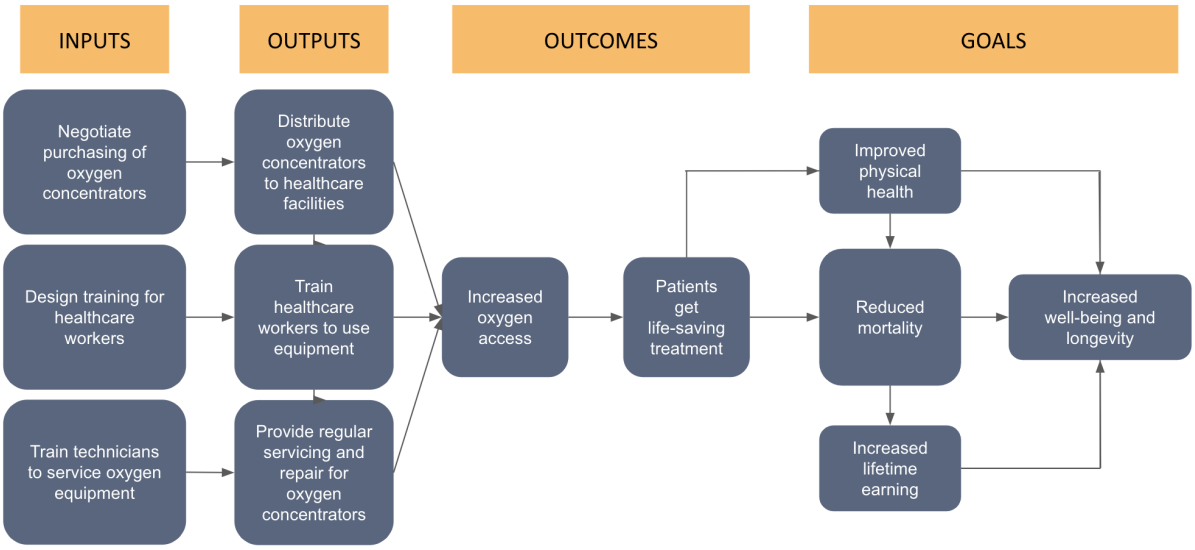
Our best understanding of the effects of improving oxygen access comes from studies on childhood pneumonia. A meta-analysis of four studies found that improving oxygen access was estimated to counterfactually reduce childhood pneumonia mortality by 48%. Based on this, the cost-effectiveness of improving oxygen access was estimated to be $62 per disability-adjusted life-year (DALY) (Lam et al. 2021).

Theories of Change

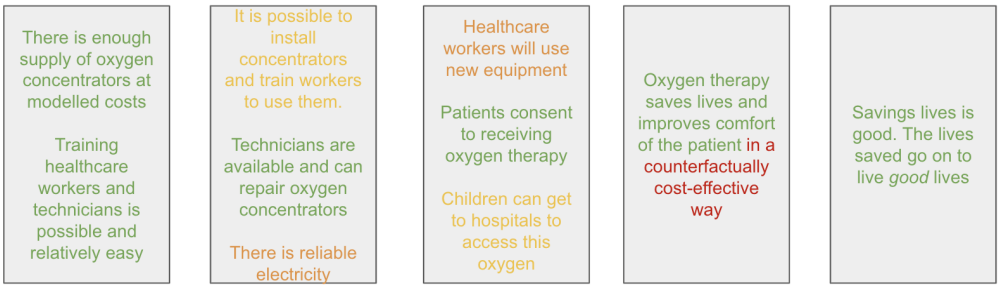
A new charity working to improve oxygen access will deliver a package of interventions, including:

- Going to hospitals to perform needs assessments: checking if there is equipment (oximetry and concentrators and canisters), well-trained staff to use the equipment, staff trained to maintain, and energy to use it
- Provision of equipment: pulse oximetry and O2 concentrators, potentially energy solutions (e.g., solar power) as well
- Provision of training
- Support to fix broken O2 equipment

The theory of change for this intervention is as follows:



These are the key uncertainties and assumptions regarding each stage of the theory of change:



Scale: key uncertainty, high uncertainty, some uncertainty, low uncertainty, unconcerning

Geographic Assessment

The geographic assessment is done in two stages. First, we look at where existing organizations are working and what they are doing. This information will later be used as an input in the formal geographic assessment as a measure of neglectedness (the greater the number of organizations already working in a country, the less neglected the problem is in that country, and therefore the less promising it is to start a new organization in). Second, we conduct the formal geographic assessment with the aim of finding the top priority countries for starting a new nonprofit.

4.1 Where existing organizations work

We identified many relevant organizations working to increase oxygen access (2022 LSGH - 123 - Oxygen access Stage 5 Catalogue). Among these, there were two large coalitions to note: Every Breath Counts Coalition (EBC) and Oxygen Alliance.

The EBC, as a coalition, is the largest actor in the space addressing pneumonia. However, because its main focus is on pneumonia, oxygen access is only part of its focus. The rest of their efforts are divided into PCV vaccine and antibiotic access. Its 40 members include UNICEF, PATH, Bill and Melinda Gates Foundation, and Clinton Health Access Initiative.

On the other hand, Oxygen Alliance is mainly focused on oxygen concentrators. Most of their partners work on access to Oxygen concentrators, mainly through maintenance of broken ones, and some through distribution of new ones. Their partners include, but are not limited to, HealthPort, Open O2, Glomed Technologies, and Sanrai International.

There are several large funding bodies that fund work in this space, namely WHO, USAID, Unitaid, Bill & Melinda Gates Foundation, and the Global Fund. Several of these organizations have only recently paid more attention to oxygen access, since the start of the COVID-19 pandemic. Additionally, there are smaller funders that invest in early-stage ventures, including D-Prize, Brink (through Oxygen Colab) and Skoll foundation (through Oxygen Hub).

Of note, there's also a recently announced Lancet Global Health Commission for medical oxygen, which aims to produce a report by 2024 to (1) address major gaps in oxygen research, (2) mobilize a broad coalition to promote best practices in addressing the gaps in medical oxygen delivery systems, facilitating and conducting the relevant research to inform implementation, and (3) accelerate impact towards strong oxygen systems and reduced mortality and morbidity globally (Kitutu et al., 2022). As part of this effort, the IHME is seeking $1.4 million in funding for a proposal to formally capture and map the hypoxemia burden, similarly to the Global Burden of Disease project.

4.2 Geographic Assessment

To assess which countries could be promising for a new organization to work in, we completed a formal geographic assessment, taking into account each country's DALY burden from pneumonia and COVID, the historic trends, and ease of operation.

It is important to note that there are several uncertainties that make it difficult to conduct a completely comprehensive geographic assessment. These include the limited data available on current oxygen access in many countries, and the reliability of electricity supply.

Based on this assessment, the five most promising countries for a new organization to work on improving oxygen access are Burkina Faso, Niger, Nigeria, Sierra Leone, and Somalia.

Quality of evidence

Evidence that improved oxygen access reduces mortality rates

The question of whether improving oxygen access would reduce mortality rates is complex. On the one hand, oxygen therapy is a well-established treatment in modern medicine and has been used since the 19th century. However, due to its early and enthusiastic uptake, there is very little empirical evidence for its benefit. There are very few randomized controlled trials (RCTs) on the effects of oxygen therapy, because any fully randomized controlled trial to establish the efficacy of oxygen therapy would require the withholding of oxygen from a control group, but once the theoretical basis for oxygen is understood, withholding oxygen in this way immediately becomes unethical.

Furthermore, because there are so many conditions that require oxygen treatment, it is also very difficult to estimate the overall effects on mortality. Our best understanding of the effects on mortality comes from studies on childhood pneumonia. A meta-analysis of four studies found that improving oxygen access was estimated to reduce childhood pneumonia mortality by 48% (Lam et al. 2021). Based on this, the cost-effectiveness of this intervention is estimated to be $62 per disability-adjusted life-year (DALY). A study of expert opinions also concluded that most experts were highly optimistic that improving oxygen therapy would decrease childhood pneumonia mortality, at an estimated 20% (Catto et al., 2011).

Animal studies also suggest that improving oxygen access may reduce mortality rates. For example, in pigs infected by streptococci, mortality reduced by 48% when treated with oxygen (Catto et al., 2011).

The second line of evidence comes from studies on COVID-19. One study found that in 26 countries, conservative oxygen strategies lead to higher mortality rates in COVID patients. Conservative oxygen strategies mean delaying oxygen therapy until blood oxygen saturation levels reach <92% and targeting levels of 88-92%, rather than liberal strategies of 94-98% (Mansab et al., 2021). A retrospective analysis published in March 2020 investigated the optimal oxygen saturations (SpO2) for patients admitted to Intensive Care Units (ICU). The investigators analyzed over 35,000 patients, and concluded that the optimum oxygen range for patients in ICUs was 94–98%. Patients who spent only 40% in the optimal range had a 50% increased mortality than those who spent 80% in the optimal range of SpO2 94–98% (Goyal et al, 2021). The investigators corrected for a number of

confounders, including disease severity. This RCT found that liberal oxygen provision vs. conservative oxygen provision reduced deaths by 32%. The RCT was cut short due to excessive deaths in the conservative group.

The remaining hypoxemia burden from conditions such as COPD and malaria were beyond the scope of this investigation. However, based on our understanding of the biological mechanism behind oxygen and hypoxemia, it seems there is a strong case that increasing oxygen access is indeed very effective at reducing mortality.

Evidence that a charity can make change in this space

Increasing oxygen access is a complex task that is more challenging than distributing bed nets or deworming medicine, especially in low-resource settings. This is because increasing oxygen access requires multiple pieces of equipment, such as a pulse oximeter, oxygen concentrator, and a reliable electricity supply, and often requires working with national programs. Additionally, oxygen concentrators are not originally designed for use in low-resource settings, and often face challenges such as high dust and lower electricity reliability. These factors can cause damage to the equipment, and make it difficult to maintain and operate them in these settings.

Despite these challenges, there is evidence that efforts to increase oxygen access have been successful in improving access to oxygen. For example, studies have shown that programs to increase oxygen access in Papua New Guinea, Nigeria, and Laos have been cost-effective (Lam et al. 2021). Additionally, there have been successful national programs in Ethiopia to increase oxygen access.

Charities/social enterprises have also been successful in increasing oxygen access in low-resource settings. For example, OpenO2 in Malawi, HealthPort in Nigeria, and FreO2 in Tanzania have all implemented programs to increase access to oxygen in their respective countries. However, due to how young these ventures are, there is very little robust measurement and evaluation to assess their cost-effectiveness.

Expert views

This section summarizes conversations with experts working to increase oxygen access, including funders, direct actors, and leaders of think-tanks. In general, experts consider this to be a highly cost-effective intervention that is very neglected. Lack of maintenance culture is cited as a key reason why the problem is so large.

Will Snider, D-Prize

Profile: D-Prize gives out small grants to new ventures that distribute proven poverty interventions. Oxygen access is one of their challenges, and other examples include the distribution of water filters or self-injectable contraception. Will Snider leads the operations for D-Prize and is a founding judge on the team. He directly works with some of the winning teams of the prize, so he has a broad understanding of the challenges in the space.

Summary: Will was very excited to hear that CE was considering improving oxygen access as a charity idea, and thinks the problem is very large and neglected. D-Prize has seeded five social enterprises so far, addressing oxygen concentrator maintenance across Nigeria, India, Ghana, Gambia, and Uganda. Interestingly, all of the social enterprises have reported needing to offer repairs for free at the beginning, because hospitals are unable to afford- or unconvinced of the need for- the repairs. Will is also not very concerned about finding technicians, as there doesn't seem to be a shortage, and some of these repairs need not be done by established biomedical technicians. For example, Oxicare was able to retrain jobless TV repairmen to perform the maintenance. When asked whether the five social enterprises may fill the needs sufficiently, Will was not worried and said that not all of them intend to scale massively. He certainly thinks there could be room for more organizations to work on this problem.

Aishat Adeniji, HealthPort

Profile: Aishat was born and raised in Nigeria. She is a medical doctor and has practiced medicine in the USA and Nigeria. Having experienced the lack of access to proven medical treatments and equipment, she founded HealthPort, which received a seed grant from D-Prize in 2021. As a young start-up, HealthPort operates in Nigeria, with ambitions to scale across Sub-Saharan Africa and more.

Summary: HealthPort initially focused on maintaining oxygen concentrators through training and hiring technicians. However, they have found that, specifically in Nigeria, there is also a lack of circulating oxygen concentrators. They have since partnered with O2 Cube, a company that manufactures solar-powered oxygen concentrators, and are selling them to hospitals alongside their traditional maintenance service contracts. This is spurred by the fact that the electric grid in many parts of Nigeria is too unreliable. Aishat thinks that even though WHO has focused more on oxygen access since COVID, the landscape is still very neglected and needs far more attention. In the future, HealthPort will complete the evaluation of their pilot, which they would be happy to share.

As a side note, Aishat and Will may share very similar views because they work and share information. Both Aishat and Will think there might be some inertia with health workers being accustomed to practices that do not rely on oxygen access, because they have historically not afforded it. When asked whether hospitals reject their business, Aishat said it often happens because of this inertia and affordability. Another important takeaway is that operations in the urban areas often end up subsidizing operations in the rural areas.

Leith Greenslade, coordinator of Every Breath Counts Coalition

Profile: Leith is the founder of JustActions, and manages the Every Breath Counts Coalition, the largest coalition of stakeholders fighting pneumonia. As such, oxygen access is one of their major points of focus. Members include PATH, UNICEF, Bill & Melinda Gates Foundation, and more.

Summary: Leith is very positive about seeing a new CE charity working on oxygen access. She thinks the problem is hugely neglected because the Global Health Community has primarily focused on single diseases such as TB, HIV, and Malaria, or single solutions, such as vaccines. Oxygen access is an issue that affects many diseases, so it gets left behind. Another reason is because we have large knowledge gaps in the current status of oxygen access, as well as the hypoxemia burden. She thinks Childhood Pneumonia wouldn't even account for 10% of the entire hypoxemic burden that Oxygen access improvements could address. A preliminary list from IHME has identified at least 20 diseases that can require oxygen treatment, and they are seeking 1.4 million in funding to quantify the hypoxemia burden. While EBC is one of the organizations working on the problem, and is very cost-effectiveness minded, she doesn't think all the members of EBC explicitly prioritize cost-effectiveness, and as a result, work in countries with less need. She thinks a charity working with boots on the ground, distributing or maintaining equipment, is much more needed than a policy/advocacy charity, but she has stressed the importance of financial sustainability and would be more excited by social enterprises doing this work. Location-wise, she thinks it would be most promising to work in West Africa, probably starting in Nigeria as a base. Leith think that it will be important for the charity to be flexible and not tunnel vision on a specific kind of oxygen support, for example, but be able to provide or source liquid oxygen, PSA plant-generated oxygen, or mobile concentrator oxygen, depending on the health system's specific needs and local cost-effectiveness analysis.

Lynne Ruddick, Innovation Lead at Brink, Lead for the Oxygen Colab

Profile: Lynne is a nurse by background, and has worked in the NHS for over 20 years. She works as an Innovation Lead for Brink, Behavioural Innovation Consultancy and Leads the Oxygen CoLab (a partnership between Brink, UNICEF and DT Global) funded by the FCDO. The Oxygen CoLab was an initial response to the lack of access to oxygen during COVID; it was created as a part of the UK Government's COVID action plan. The Oxygen CoLab brings together innovators, experts in oxygen systems, and other stakeholders to understand the reasons for the barriers to oxygen access in low-income countries and develop solutions. This deeper understanding has meant they have provided targeted funding to accelerate product development and test innovative business models which provide wrap-around service models which includes training, maintenance and the provision and implementation of diagnostic and delivery equipment.

Summary: Oxygen concentrators were initially designed for domestic use in the Global North. Innovators and manufacturers are increasingly seeing their value in low-resource settings and are working on developing new models that are more resilient to dust, humidity and poor power conditions and which require less maintenance. There is growing evidence that these changes can be made without significantly increasing their current market price. Oxygen concentrators are donated or procured with little or no consideration of the maintenance and training costs. There is an opportunity for entrepreneurs and social enterprises to provide the wrap-around service that ensures the sustainability and cost-effective distribution and delivery of medical-grade oxygen for a subscription fee. There is also an opportunity for them to reduce the cost of peripherals through bulk purchase and then distribute locally to smaller, more remote health centres.This allows health care professionals to focus on the delivery of the care, and not the operational elements. The Oxygen CoLab is in the early stages of testing a number of different business models (Oxygen as a Service or O2aaS) to fully understand their ability to break even given the high initial capital expenditure. This is currently supported through donor funding, and we are investigating the value of financial mechanisms to encourage the development of these businesses in the longer term. Our six O2aaS programs are in Kenya, Uganda, India, Tanzania, DRC and Philippines. The pilots serve a number of different patient groups, including children and adults. In some cases the oxygen is being re-compressed into an oxygen cylinder, and so can be used at all the required flow rates. The oxygen concentrator should be considered a vital part of the oxygen ecosystem, alongside the PSA plant and liquid oxygen. We believe the ideal use case is in remote and rural settings.

Felix Lam, Clinton Health Access Initiative

Profile: Felix is an Associate Director at the Clinton Health Access Initiative (CHAI), and leads a team that focuses on child health, including pneumonia. He has been working on oxygen through a child pneumonia lens since 2015, and the pandemic has expanded his work to include other areas beyond child pneumonia. His role includes program implementation and researching evaluation. As part of this work, he was the lead author in the meta-analysis analyzing the cost-effectiveness and efficacy of improving oxygen access and child pneumonia mortality.

Summary: There is not a one size fits all solution for oxygen access across all countries. It will take a lot of research and thinking about each country's context to figure out the most effective solution for increasing oxygen access. The solutions may vary, depending on the country, such as using concentrators, PSAs, or liquid oxygen, and whether electricity support is needed. Importantly, oxygen concentrators were most useful for pediatric and neonatal patients, because adults tend to require higher flow rates of oxygen that concentrators cannot provide. For this reason, the charity should not dismiss increasing access to large-scale PSA plants, and liquid oxygen production as potential cost-effective solutions. Another important takeaway is that studies on cost-effectiveness of improving oxygen systems' solar components do not take into account the reduced running costs from not needing to pay for grid electricity. Therefore, the cost-effectiveness of including solar components may be underestimated. CHAI will be doing more research to understand the additional benefits of expanding oxygen access, beyond childhood pneumonia. In terms of country selection, Felix is most excited by countries that already have high pneumococcal vaccine coverage and need higher oxygen access, like Bangladesh; however, other places like Chad could really use help with both vaccination and oxygen access.

Expert takeaways

All experts were very positive about the idea of a new charity addressing oxygen access, as they believed that there is still a lot of room for improvement and the problem is still neglected. However, they also stressed the importance of taking into account the local contexts and deciding on the best approach to improve oxygen access. They noted that oxygen concentrators may be most suitable for neonatal and pediatric patients, because of their lower flow rates. However, they are not currently optimally designed for use in low-resource settings, and it is possible to lower costs and make them more durable for such contexts. The published cost-effectiveness analyses (CEAs) don't account for electricity costs, which could underestimate the cost-effectiveness of including solar power assistance. All experts also stressed the importance of financial sustainability, and preferred a social enterprise scaling

model. Some experts remarked that most social enterprises doing this work needed to start as non-profits before they have proven value to clients.

Cost-effectiveness analysis

We conducted a cost-effectiveness analysis on distributing and maintaining oxygen concentrators and pulse oximeters, with and without solar energy components in Nigeria, modeling the effects solely on the reduction in childhood pneumonia mortality. We focused on Nigeria because it was one of the top countries identified from our geographic assessment, and because Leith Greenslade from EBC had strongly advised that it should be a priority country.

We consider staff costs for biotechnicians, the cost of oxygen equipment (including pulse oximeter, oxygen concentrators, supporting equipment like nasal cannulae, tubings) and the cost of training health workers to use and maintain the equipment. Our endline metric is the total child deaths saved, converted into DALYs averted.

Here are the cost-effectiveness estimates for different intervention packages for this charity:

Intervention package (Nigeria)	$ per DALY
Maintenance only	**$17**
Maintenance + distribute solar only	**$64**
Distribute + maintenance of concentrators w/o solar	**$38**
Distribute + maintenance of concentrators and solar	**$79**

Although it would be much more cost-effective to only provide free maintenance work as a Charity, it would significantly limit the scale of the charity. The most guaranteed scenario with the least amount of uncertainty and large scale, has the lowest cost-effectiveness at $79 per DALY. However, this is still a highly cost-effective charity.

7.1 Effects

Deaths averted

The model only estimates the annual number of childhood pneumonia-related deaths averted by increasing access to oxygen therapy.

- Number of children beneficiaries: We estimated this to be 393,293. This is a function of multiplying the following:

    - The number of child pneumonia case incidence per year in Nigeria: 2,537,373
    - Our targeted % reach: 50%
    - The percentage of child pneumonia cases that need oxygen therapy: 31%. (Graham et al, 2022)
    - (Graham et al., 2022)
- The number of deaths averted: 15,533
    - The childhood pneumonia death rate in our region: 5.1%
    - The expected reduction in death rate from improving oxygen access: 48% (Lam et al., 2021)
    - A discount for lower expected effect sizes if oxygen concentrators are used for other diseases: 50%
    - The number of childhood pneumonia patients we serve:
        - The number of child pneumonia case incidence per year in Nigeria: 2,537,373
        - Our targeted % reach: 50%
- DALYs per child <5: 36.53 (GiveWell)

Then, to estimate the overall impact of the charity over its lifetime, we also used the following:

- Discount for historical trend in pneumonia death reduction in Nigeria
- Duration of setting up; one year including:
    - Half a year for advocating and designing strategy
    - Half a year to deploy plans
- Years to reach scale: four years
- Charity years operating: 50 years (As per historic Charity Entrepreneurship models, e.g., Road Traffic Safety)
- A discount rate of 4%, as we were evaluating impact in the future and we wanted to evaluate impact in present-value terms

7.2 Costs

The costs are based around the maintenance costs and purchasing associated with oxygen concentrators. This takes into account the following:

- Fixed charity costs during pilot: $125,000. This is our best guess, and is being held constant across all other cost-effectiveness analysis models created by CE in 2022.
- Fixed costs at scale: We assume that you need four additional staff members - which we have estimated costs $225,000. This estimate of $225,000 is our best guess and is being held constant across all other cost-effectiveness analysis models created by CE in 2022.

- The number of oxygen concentrators needed to treat this many children: 5,371. This is a product of the following:
    - Average number of hours of oxygen needed per child: 88
    - Number of children needing oxygen: 393,293
      Divided by:
    - Average number of hours concentrators are per year: 6456.5 (Usage rate of 73%)
- Cost of maintenance staff: $4,876,710
    - Number of biotechnicians and managers needed to maintain that many concentrators.
        - Assuming each biotechnician can maintain 12 concentrators: 448 biotechnicians
        - Assuming each manager can manage 10 biotechnicians: 45 full time managers
    - Median salaries
        - Biotechnician assumed to be paid median salary for governmental army jobs: 4,530,000 naira
        - Managers assumed to be paid median salary of an "electoral project coordinator": 4,870,000 naira
        - Converted to USD: 1 USD = 461 naira
- Cost of equipment per year per concentrator: $1,151.31
    - Average costs from two studies of total program costs per oxygen concentrator, broken down into equipment, installation and maintenance, training of health workers and solar power capacity
    - Expected years of use for the equipment: five years
- Costs of solar power components are adjusted by the % of electricity that is unreliable

Not modeled

For simplicity, the following factors are not modeled in the CEA:

- The cost of electricity to run the concentrators: this would overestimate the cost-effectiveness of distributing concentrators without solar power components and vice-versa, underestimate the cost-effectiveness of providing the solar support.
- Of note, it would also be possible to provide other reliable sources of electricity by non-solar means. The trade-offs with different electricity support is beyond the scope of the report.
- Non-death related DALYs lost due to lack of oxygen therapy for children with hypoxemia.
- Non-pneumonia and non-adult-related DALYs averted. With 73% usage rates, the concentrators should be near maxed out already.
- Income benefits to the surviving children and economy.
- Negative externalities of over-oxygenation if equipment used incorrectly

- Healthcare worker costs. We assume that the existing healthcare system can incorporate the equipment without additional staffing needs.

Implementation

8.1 Talent

Whilst some background in engineering and biomedical equipment maintenance could be helpful, it doesn't seem to be prohibitive. Experts have noted that there are a lot of trained technicians who are looking for work, so that shouldn't be a concern either.

8.2 Access

Information

There is lots of information available on oxygen concentrator maintenance. WHO has a free online course, alongside video demonstrations, for health workers and biotechnicians. Oxygen Alliance also has a website with the manuals of all types of concentrators and advice on how to maintain/repair them. The organizations and coalitions working in this space are extremely approachable and willing to help.

There are critical gaps in our knowledge about oxygen access at a country by country level, as well as hypoxemia burdens and the effect of improving oxygen systems on reducing overall mortality. Hopefully these gaps will be eased with the release of the Lancet Global Health Commission report on medical oxygen.

Government

Since the increased interest from the COVID-19 pandemic, many high-burden countries are drafting/ have drafted National Oxygen plans. As such, we expect governments to be quite cooperative.

Hospitals

It is important to note from the interview with HealthPort that a significant number of hospitals have rejected their service due to high costs. A CE charity could mitigate this by offering the service for free, or at a subsidized cost. It remains unclear how willing healthcare workers are to change their existing practices, since they are used to operating without oxygen, or there may be inertia with changing from using oxygen cylinders to oxygen concentrators. As case studies above suggest, it is certainly not an eliminating concern, but the charity should be sensitive and mitigate this risk.

8.3 Feedback loops

We are not too worried about the feedback loops in this intervention. Seems like a lot of the factors would be measurable: 1) whether hospitals and health ministers are on board, 2) how many oxygen concentrators we provided/ repaired, 3) mortality rates in the hospitals.

8.4 Funding

EA funding

As far as we are aware, oxygen access has largely not been in the radar of EA organizations. The closest thing we found was a forum post about COVID-19 charities in India (gotech, 2021). With the partnership of GiveWell and CHAI, which is a large player in the oxygen access space, one might expect more EA funding in the space to come.

Non-EA funding

There has been more funding for increasing oxygen access since the pandemic; however, it is yet to be seen whether this interest can be maintained as the world moves on. We expect the funding to decrease in the coming years, but for there to still be a substantial amount.

There are several large funding bodies that fund work in this space, namely WHO, USAID, Unitaid, Bill & Melinda Gates Foundation, and the Global Fund. Additionally, there are smaller funders that invest in early stage ventures including D-Prize, Brink (through Oxygen Colab) and Skoll Foundation (through Oxygen Hub).

8.5 Scale of the problem

The scale of the problem is really large. Oxygen therapy is a treatment for more than 20 different conditions. Pneumonia alone is the leading infectious cause of mortality among children under five in low-and middle-income countries (LMICs), with an estimated 700,000 deaths each year. Over half of the health facilities in LMICs don't have access to oxygen.
Without proper quantification of the hypoxemia burden, it is difficult to understand the full scale of the problem. However, it can hardly be understated. It should also be noted that the scale is only as big as the percentage of the population with access to the health facilities we serve. On this point, some experts have suggested that healthcare attendance rates will go up as a result of the increase in oxygen access, since in many places, parents assumed that this wasn't available.

From a nuanced perspective, experts have cautioned that scale-up should be context sensitive. In certain situations, PSA plants or liquid oxygen plants would be more cost-effective. Assuming concentrators are optimally cost-effective for the pediatric or neonatal unit, there is sufficient scale there alone.

8.6 Neglectedness

The question of whether this work is neglected is complex.

While COVID-19 has brought increased attention and funding to the issue of oxygen access, the increased demand for oxygen as a result of the pandemic may have overwhelmed any additional resources gained. Historically, pneumonia has been neglected in comparison to other global health priorities such as HIV/AIDS, TB, and vaccination efforts. Between 2000 and 2019, global pneumonia deaths fell by just 14%, while deaths from other infectious diseases, such as measles which fell by 86%, HIV/AIDS by 45%, diarrhea and malaria by 37%, and tuberculosis by 31%.

Oxygen therapy is used to treat multiple conditions, but is not the primary treatment for any one of them, which has led to its deprioritization. Additionally, a lack of strong empirical evidence for the impact of oxygen therapy on reducing overall mortality has also contributed to its neglectedness.

Within pneumonia, other interventions such as the PCV vaccine and antibiotic availability have been more focused, and experts have suggested that oxygen is more neglected.

There are many organizations working in the space, but these seem to be of two categories: 1) large multilateral organizations that work with governments, but not just focused on oxygen access, and 2) small social enterprises/ organizations that work directly to increase oxygen access via distribution or maintenance of oxygen concentrators. A lot of the smaller organizations don't have strong ambitions to scale massively at the international level, nor are they making decisions from a strictly cost-effectiveness perspective. Our sense is that there is definitely room for a new charity to work in the space, especially with such a large-scale problem.

8.7 Tractability (execution difficulty)

Tractability is probably the larger concern of this intervention. Distributing oxygen equipment and supporting a large team of biotechnicians is much more complex than distributing bed nets or deworming pills. Beyond concentrators themselves, there are different patient interfaces which need to be considered, depending on the patient condition, such as nasal cannulas, simple face masks, non-rebreather masks, and non-invasive and invasive ventilation. Oxygen delivery also needs to be adjusted to patient conditions via flow rates, and carefully observed to prevent

adverse side effects of over oxygenation, such as retinopathy in neonates. If simply considering the distribution of equipment, it may not seem so complicated, but the downstream steps of patient care and management add additional complexity.

There are additional considerations to keep in mind, namely 1) the willingness of the government and healthcare system to cooperate, and 2) understanding the local context enough to provide the correct oxygen access solution.

However, if we keep the focus narrow, on oxygen concentrators in pediatric and neonatal care settings, there are still case studies to suggest this is tractable.

8.8 Externalities

There is likely to be positive externalities associated with increasing oxygen access, most obviously on the hypoxemia burden not captured by childhood pneumonia that was modeled in the CEA. If a solar power component is included in the distribution of concentrators, there may also be further positive externalities associated with increased reliability in electricity. The CEA is currently only modeling DALY benefits from averting deaths; it is expected that oxygen therapy would alleviate additional DALYs from providing comfort to patients that wouldn't have died. Neither are the income benefits modeled.

There may be risks associated with improper use of oxygen therapy. It would be important to train healthcare workers to use the equipment properly, as over oxygenation has negative effects.

Several experts have also remarked on the importance for the intervention to be financially sustainable. Our interpretation is that if the intervention is perpetually delivered at no cost to hospitals, and relies exclusively on donations, there is a risk of Dutch disease, where local social enterprises that would otherwise provide this service become outcompeted.

8.7 Macro-level considerations

Why does the government not do this?

"Oxygen is often overlooked as a perfunctory treatment, useful but not glamorous, and widely assumed to be a commodity that is readily available." (PATH, 2019)

Until 2017, oxygen wasn't even on the World Health Organization's list of essential medicines. Some of the reasons are listed in the neglectedness section. The global health development community has focused more on single diseases and solutions such as HIV/AIDS, TB and vaccination.

On a relative basis, improving oxygen systems is more complex than just delivering bed nets and deworming pills. It is context-dependent and depends on factors such as electricity access, and access to primary treatments for underlying causes of conditions.

With the large initial capital expenditure to expand oxygen access, there is certainly a market failure that causes hospitals to source cheaper short-term options, such as the oxygen cylinder. The extra costs are usually borne by the patients who can rarely afford the treatment.

The counterfactual considerations of the Lancet Global Health Commission on medical oxygen

The recently announced Lancet Global Health Commission for medical oxygen, which aims to produce a report by 2024, is noteworthy because it should clear up a few big gaps in our uncertainty. Namely, what is the total hypoxemia burden in the world, and what is the state of oxygen access across LMICs. This could be seen as a benefit for any new charity entering the space in the next year or two, to gain access to such information.

However the commission also aims to mobilize a coalition of stakeholders to advance oxygen access. On the one hand, this may potentially speed up progress in the area, and lower the counterfactual impact of a charity. On the other hand, this could also make stakeholders more cooperative, and therefore the idea could be more tractable.

To us this seems difficult to update on, for or against.

Conclusion

After careful consideration, we have decided not to recommend a charity that works on oxygen access. While the idea met our cost-effectiveness bar, we ultimately felt that increasing oxygen access was a bit more complex for the implementation than we had initially anticipated. We also found it very encouraging to see the number of small enterprises entering this space, and felt that the solution may be more fitting for a social enterprise approach rather than a traditional nonprofit. We are excited by the Lancet Commission, which will hopefully shed more light on the hypoxemia burden, and we may revisit this idea when that data becomes available.

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Appendix 1 - what are the different types of oxygen therapy and respiratory aid?

According to this blog post: Oxygen therapy comes in a few forms: Low-flow Oxygen therapy, High-flow oxygen therapy and ventilator.

Ventilation – Ventilation is the activity of normal, spontaneous breathing, including the processes of inhalation and exhalation. If a patient is unable to do these processes on their own, they may be put on a ventilator, which does it for them.

Oxygenation – Ventilation is essential for the gas exchange process i.e., oxygen delivery to the lungs and carbon dioxide removal from the lungs. Oxygenation is only the first part of the gas exchange process i.e., delivery of oxygen to the tissues.

Difference between High-Flow Oxygen therapy and Ventilator, in essence, is the following: Oxygen therapy involves only giving you additional oxygen – your lung still does the activity of taking oxygen-rich air in and breathing carbon-dioxide-rich air out. A ventilator not only gives you additional oxygen, it also does the work of your lungs – breathing in and out.

Respiratory Failure could occur due to:

- an oxygenation issue resulting in low oxygen but normal – low levels of carbon dioxide. Also known as hypoxaemic respiratory failure – this occurs when the lungs are unable to absorb oxygen adequately, generally due to acute lung diseases that cause fluid or sputum to occupy the alveoli (smallest sac-like structures of the lung which exchange gasses). Carbon dioxide levels may be normal or low as the patient is able to breathe out properly. A patient with such a condition – hypoxaemia, is generally treated with oxygen therapy.
- a ventilation issue causing low oxygen, as well as high levels of carbon dioxide. Also known as hypercapnic respiratory failure – this condition is caused by a patient's inability to ventilate or breathe out, resulting in carbon-dioxide accumulation. CO_2 accumulation then

prevents them from breathing in adequate oxygen. This condition generally requires support of a ventilator to treat patients.

Low-flow systems have flow lower than inspiratory flow rate (normal inspiratory flow is between 20-30 liters/minute). Low-flow systems, such as oxygen concentrators, generate flow rates of 5-10 liters/m. Even though they offer oxygen concentration even up to 90%, since the patient needs to inhale room air to make up for the balance inspiratory flow requirement – the overall FiO2 may be better than 21% but still be inadequate. Additionally, at low oxygen flow rates (<5 l/min), significant rebreathing of stale exhaled air may occur because exhaled air is not adequately flushed from the face mask. This results in higher retention of carbon dioxide, and also reduces further intake of fresh air/oxygen.