

DIGITAL PULMONARY REHABILITATION

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SDG+ – Digital Pulmonary Rehabilitation

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Note to readers: Our research is primarily aimed at AIM decision-makers and participants in our programs and is geared toward finding the best ideas for incubation. Reports on ideas that have not been recommended for incubation can often be less polished, given our commitment to focus on recommended ideas.

We are also grateful to the experts who took the time to offer their thoughts on this research. We also thank the team members at AIM, especially Samantha and Ben, who helped with the report.

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Executive Summary

Chronic Obstructive Pulmonary Disease (COPD) is a serious global health problem.

According to the global burden of diseases (GBD), it was the third most common cause of death worldwide in 2019, with about 212 million prevalent cases, leading to 3.3 million deaths and 74.4 million disability-adjusted life years (DALYs) lost.

In addition to the lives it claims, COPD also affects the quality of life of patients. The main symptoms of COPD are chronic cough, shortness of breath, frequent respiratory infections, and chest tightness. Together, these symptoms cause patients to have reduced exercise capacity, quality of life, and increased social isolation. If left untreated, the symptoms can become gradually more severe and lead to death during acute exacerbations.

It is estimated that over 90% of COPD deaths occur in low and middle-income countries (LMICs). Poor awareness and insufficient resources in terms of infrastructure for diagnosis, availability of essential drugs, skilled health professionals, and overall healthcare priorities exacerbate this issue.

While public health efforts have been largely focused on preventive measures such as smoking cessation, there is an opportunity and need to expand treatment options. This is critical because 50% of the global COPD burden is due to risk factors not related to smoking, such as air pollution, which affects LMICs disproportionately. While prevention efforts should continue, there is an additional need to serve the many patients who have already developed COPD.

Pulmonary rehabilitation (PR) is a low-cost and well-evidenced program that improves the health outcomes of patients with COPD. It encompasses exercise programs, chest physiotherapy, education on the disease, support for self-management, and lifestyle changes. PR is effective at reducing symptom severity, improving patients' quality of life, lowering hospital admissions and acute exacerbations, and decreasing mortality rates.

Despite its effectiveness, PR services are often underutilized or unavailable in LMICs and rural areas. In 2015, PR was available to only 2.7% of people with chronic lung diseases globally. Common barriers include long travel distances, lack of knowledge of benefits, lack of trained healthcare capacity, and cost of treatment.

Experts agree that COPD and PR are highly neglected in LMICs.

This report investigates how promising it is for a new charity to work towards increasing access to PR through digital PR (PR delivered through mobile applications), especially for severe COPD patients who have recently been

hospitalized. We previously refrained from recommending a charity to work on increasing access to in-person PR because we were concerned about the limited healthcare capacity in LMICs. Digital PR has the potential to overcome this main barrier to PR uptake.

There is strong evidence that in-person PR improves the quality of life in COPD patients and reduces the mortality of severe COPD patients post-hospitalization.

There is also moderate evidence that digital PR is equally effective as in-person PR in head-to-head comparisons. This is supported by weak to moderate evidence that digital PR improves exercise capacity and quality of life in COPD patients relative to no rehabilitation.

One of the leading digital PR apps, myCOPD, which is approved by the UK NHS, has expressed interest in partnering with charities to expand its service to LMICs. This highly scalable app is designed to provide remote and unsupervised digital PR to anyone with a smartphone and internet connection.

Any hospital outpatient department would be a good touchpoint for reaching recently hospitalized COPD patients. Patients are more likely to adopt new behavior changes after a life-threatening exacerbation. Severe COPD patients with a larger health burden also benefit more from PR. However, all COPD patients could benefit from the intervention, and public outreach could also be considered for broad user acquisition.

Our geographic assessment suggests that the charity would likely work in lower-middle-income countries. The higher smoking rates and higher air pollution in LMICs lead to a larger burden. Given this, India, Nepal, China, and Indonesia are the most promising countries. At this point, rolling out in English-speaking countries seems more straightforward, as the charity wouldn't have to translate the content from myCOPD to other languages. However, we expect achieving regulatory approval to be the main barrier and would be country-dependent.

Our cost-effectiveness analysis suggests that the intervention would be highly cost-effective. We modeled for the charity to partner with myCOPD to provide digital PR to recently hospitalized COPD patients in Nepal and India. Based on the prevented deaths and improved quality of life, the intervention is estimated to cost \$9-\$84 per DALY averted; this is equivalent to 11-108 DALYs averted per \$1000 spent.

Tractability is a moderate concern with this intervention. In the suggested theory of change, multiple causal chains require behavior changes, including for doctors to increase referrals to digital PR and for patients to take it up and complete the program.

The evidence base for interventions that increase PR referral and uptake is weak.

There are only several randomized trials of various interventions. The one with the largest effect size is an education program for outpatient health workers. Others include patient manuals to increase their awareness. Nonetheless, we do not think these recruitment challenges are insurmountable.

We have several remaining uncertainties regarding this intervention. A significant amount of the evidence base comes from high-income countries. Though we have discounted the external validity of the effects, we are uncertain how much this adjustment should be. It is plausible that PR is more effective in LMICs because of the lack of access to other treatments, such as pharmacological inhalers.

We expect regulatory barriers to be another challenge to overcome. Although we have some indication that LMIC governments recognize the importance of PR, we are still uncertain about the extent of their cooperation.

There are positive externalities expected with this intervention. Many studies have noted that reduced hospital readmission rates from PR are cost-saving for patients and hospitals. Patients are expected to have increased productivity based on increased health and mobility. Some studies have also documented the increase in mental health from PR.

Overall, we think this idea is worth recommending to Charity Entrepreneurship Incubation Program founders because we believe PR is effective, neglected, and needed in LMICs. Partnerships with organizations, such as the myCOPD app, simplify the implementation considerably. Because the incremental costs of additional patients are so low, once regulatory barriers are overcome, the upside of the charity is incredibly high, with the cost-effectiveness increasing per user acquired. With the rising burden of COPD and the increasing penetration of smartphone and digital health technologies, we think this charity idea is very promising.

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Glossary

Acronym	Stands for
AIM	Ambitious Impact
CEA	Cost-effectiveness analysis
CEO	Chief Executive Officer
COPD	Chronic Obstructive Pulmonary Disease
CRD	Chronic Respiratory disease
CRQ	Chronic Respiratory Questionnaire
DALY	Disability-adjusted life year
GBD	Global Burden of Disease
GDP	Gross Domestic Product
HIC	High-income country
LMIC	Low-middle income country
MD	Mean Difference
MID	Minimal important difference
NCD	Non-communicable disease
OR	Odds ratio
PR	Pulmonary Rehabilitation
RCT	Randomised controlled trials
SD	Standard Deviation
SGRQ	St. George's Respiratory Questionnaire
тос	Theory of Change
WHO	World Health Organization

1 Introduction

This report evaluates the idea of digital pulmonary rehabilitation for COPD patients in LMICs and its promise for the Charity Entrepreneurship Incubation Program.

This report has been produced by Ambitious Impact (AIM). AIM's mission is to create more effective charities by connecting talented individuals with high-impact intervention opportunities. We achieve this goal through an extensive research process and our Charity Entrepreneurship Incubation Program.

This process began by sourcing hundreds of ideas for potential new charities from the members of our wider network, then gradually narrowing them down and examining them in increasing depth. To assess how promising interventions would be for future charity entrepreneurs, we use various 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 is exploratory and rigorous but not comprehensive—we did not research all ideas in depth. As such, our decision not to pursue a charity idea to the point of writing a full report does not reflect a view that the concept is not good.

2 Background

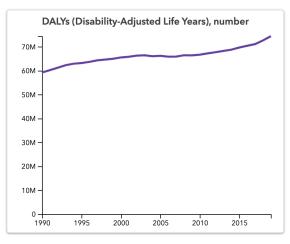
Chronic Obstructive Pulmonary Disease

The global health landscape is undergoing a significant transformation, characterized by an aging population and a rise in non-communicable diseases (NCDs). These shifts are leading to an increased prevalence of disabilities and functional declines, especially in LMICs. LMICs face a 'double burden' as they continue to combat infectious diseases while also experiencing a surge in NCDs, including chronic respiratory diseases (CRDs).

COPD is a major public health concern. CRDs encompass a range of lung and airway conditions, including asthma, COPD, cystic fibrosis, lung cancer, and sleep apnea. COPD, in particular, stands out as a leading global health issue. According to the global burden of diseases (GBD), it was the third most common cause of death worldwide in 2019, with about 212 million prevalent cases, leading to 3.3 million deaths and 74.4 million disability-adjusted life years (DALYs) lost (Safiri et al., 2022). The global economic cost of COPD is estimated to be \$2.1 trillion (Salvi, 2015).

The majority of COPD deaths occur in LMICs. It is estimated that over 90% of COPD deaths occur in LMICs, highlighting the disproportionate impact of COPD in these regions. Poor awareness and insufficient resources in terms of infrastructure for diagnosis, availability of essential drugs, skilled health professionals, and overall healthcare priorities limit adequate care.

There are several key risk factors for COPD. Key contributors to COPD-related DALYs include smoking (46.0%), air pollution (20.7%), and occupational exposures (15.6%)(Safiri et al., 2022; Yang et al., 2022). Low-income countries (LICs) generally have a higher percentage of COPD cases linked to non-tobacco-related risk factors compared to high-income countries (HICs) (Yang et al., 2022). While the DALY rate for COPD is on the decline, mainly due to decreasing smoking rates, the total number of COPD cases continues to increase because of the growing population. (Figure 2).



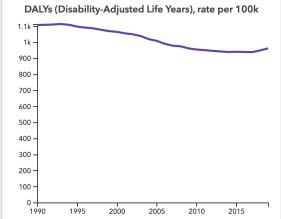


Figure 2: Global total and rate of DALYs lost per year due to COPD (source: Global Burden of Disease)

Two main conditions contribute to COPD: emphysema and chronic bronchitis.

Emphysema is a condition in which the air sacs of the lungs (alveoli) are damaged and enlarged, affecting gaseous exchange. Bronchitis is the inflammation of the lining of the bronchial tubes, which carry air to and from the air sacs. These two conditions usually occur together and vary in severity. Once developed, COPD cannot be cured, but the symptoms can be managed, and prognosis can be improved.

COPD patients suffer from many symptoms, and if not managed appropriately, the condition deteriorates over time. These symptoms include but are not limited to, a persistent cough, shortness of breath, frequent respiratory infections, wheezing, chest tightness, fatigue, weight loss, and frequent clearing of the throat (Table 1 indicates the categorization of disease progression). These symptoms can worsen over time and lead to reduced exercise capacity, diminished quality of life, social isolation, and psychological issues exacerbated by socioeconomic and geographical factors.

Table 1: Categorization of COPD (<u>GBD 2015 Chronic Respiratory Disease</u> <u>Collaborators</u>, 2017)

COPD Category	Description	Disability weight (95% UI)
Mild	Has cough and shortness of breath after heavy physical activity but can walk long distances and climb stairs.	0.019 (0.011–0.033)
Moderate	Has cough, wheezing, and shortness of breath, even after light physical activity. The person feels tired and can walk short distances or climb only a few stairs.	0.225 (0.153-0.31)

Severe	Has cough, wheezing, and shortness of breath all the time. The person has great difficulty walking even short distances or climbing any stairs, feels tired when at rest, and is anxious	0.408 (0.273-0.556)
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COPD is commonly associated with one or more medical comorbidities. These include cardiovascular disease (hypertension, coronary artery disease, systolic and/or diastolic congestive heart failure, arrhythmias), metabolic disturbances (hyperlipidemia, diabetes mellitus, osteoporosis, and osteoarthritis), skeletal muscle dysfunction, anemia, infections, obstructive sleep apnea, renal insufficiency, swallowing dysfunction, gastroesophageal reflux, and lung cancer.

Acute exacerbations can occur in severe cases of COPD, leading to hospitalization and death. Acute exacerbations are the most common reason for hospital admissions and death among patients with COPD. Post-hospitalization discharged patients have a ~35% chance of mortality and ~60% chance of rehospitalization in the following year (Puhan et al., 2016). On average, COPD patients from HICs experience about one exacerbation per year, and 1 in 5 exacerbations are severe enough that they require hospitalization (Sadatsafavi et al., 2016).

COPD's impact extends beyond physical symptoms, significantly affecting mental health. A meta-analysis by Coventry (2009) revealed high prevalence rates of depression (40%) and anxiety (36%) in older adults with COPD, highlighting the need for holistic treatment approaches. One reason is patients become locked in a spiral of decreasing mobility due to shortness of breath, thus reducing social activities and exercise, leading to poor mental health and further reduced mobility.

COPD is diagnosed by lung function tests, mainly spirometry, as well as questionnaires. Spirometry measures how much air you breathe out and how fast you can blow air out.¹ There are two main questionnaires: the Chronic Respiratory Questionnaire (CRQ) and the St. George's Respiratory Questionnaire (SGRQ).²

There are many different ways to manage COPD. In rough order of importance and cost-effectiveness, these are smoking cessation, vaccination against pneumonia, PR, pharmacotherapy, high-flow oxygenation, and extracorporeal carbon dioxide removal for treating exacerbations (See Expert Section). We focus on PR in this report.

¹ COPD is diagnosed when the FEV1/FVC ratio is below 0.7 after bronchodilator. The FEV1/FVC ratio is the ratio of the forced expiratory volume in the first one second to the forced vital capacity of the lungs ² Both the CRQ and the SGRQ are standardized questionnaires designed to measure impaired health and quality of life in airway diseases. They both have a symptoms component.

Pulmonary Rehabilitation: An Effective Strategy for COPD Management

PR is a multidisciplinary, cost-effective intervention that has shown great promise in reversing disabilities associated with CRDs. It encompasses exercise programs, chest physiotherapy, education on the disease, support for self-management, and lifestyle changes. The program usually consists of 2 or 3 weekly sessions lasting several weeks or months.

The exercises are simple, including breathing and physical exercises targeted at improving breathing. There are specific techniques, such as pursed-lip breathing and yoga breathing, to increase breathing control and avoid breathlessness. Techniques are also taught to clear mucus from the lungs. Physical exercise training aims to strengthen the back, arms, legs, and muscles for breathing. Training can also help you build stamina and flexibility, making everyday tasks and activities easier.

Despite its established effectiveness and recommendation in WHO guidelines, PR services are often unavailable, particularly in LMICs and rural areas (Habib et al., 2020). Globally, in 2015, PR was available to only 2.7% of people with CRD (including asthma, cystic fibrosis, and pulmonary fibrosis) (Lahham & Holland, 2021). The WHO's Rehabilitation 2030 initiative calls attention to the significant unmet need for accessible and affordable rehabilitation in LMICs, where the gap between demand and capacity is vast.

While this report focuses on COPD, the principles of PR can benefit other diseases like asthma and tuberculosis. More broadly, enhancing rehabilitation capacity within health systems could address a wider range of conditions. According to the WHO Rehabilitation Need Estimator, one-third of the global population, which has risen from 1.48 billion in 1990 to 2.41 billion in 2021, could benefit from rehabilitation services. Due to its severity COPD, representing only 5% of these cases, contributes disproportionately to the DALY burden (WHO, 2021).

However, a major concern for implementation is the lack of trained physiotherapists who could provide PR in LMICs. Despite the idea being strong in many other respects, we previously decided against the recommendation of a charity providing free in-person PR in LMICs because of this barrier. Digital PR³ is promising because it does not (neccessarily) require local physiotherapists.

³ Interchangeably refered to as "digital PR", "e-health PR".

Digital PR

Traditionally, PR is delivered in person in an outpatient or community setting. One of the reasons why in-person PR has such low uptakes, even in the developed world, is the inconvenience of patients' having to access clinics while they are struggling with physical activity due to breathlessness. Patients living in rural areas and LMICs may also have limited access due to a lack of services and trained professionals.

Digital PR is emerging as a cheaper and more cost-effective way to deliver the program and is often preferred by patients because of the convenience of not needing to travel to a clinic. By providing healthcare at a distance through the use of telecommunications or virtual technology, digital PR can provide greater healthcare access and service delivery options for individuals who are geographically or socially isolated, for patients in full-time work or study, or for individuals who find travel difficult due to their disease severity or comorbidities.

Notably, some of the apps that have been developed can deliver digital PR without the need for physiotherapist supervision. This circumvents the major barrier of the lack of trained physiotherapist capacity, allowing for high scalability.

The shift to telehealth in COVID and the increasing uptake of smartphones and internet access provide a unique opportunity for digital PR. COVID has accelerated the digitization of healthcare, and both patients and healthcare systems are now more open to telehealth. Smartphone and mobile internet connection adoption is increasing at 1.7%-2.3% per year. And there are now 5.6 billion people (69% of the global population) with mobile service (GSMA, 2024).

Another benefit of digital PR is that digitization lends itself to easier measurement and evaluation, as well as faster feedback loops. Implementers can easily track the progress of individuals and cohorts via symptom questionnaires and live feedback from the patients themselves. It also enables the monitoring of quality standards and audits.

3 Theories of change

We think delivering a well-designed digital PR program would be highly promising in LMICs. As described in the expert interview section, we have had initial discussions with *my mhealth*, the company that developed the NHS-approved digital PR app called myCOPD. They are excited to partner with charities to expand into LMICs. We think this partnership model is especially promising, as demonstrated by the cost-effectiveness analysis we conducted.⁴

The myCOPD app⁵ is a well-evidenced web-based app uniquely designed to not require physicians to supervise the exercises. This makes it incredibly scalable, and it is the only COPD app approved for national use in the UK (see evidence section).

We think it is most promising to target patients who have just had hospitalization events. Pulmonary rehabilitation is beneficial for all COPD patients of different severities. However, we speculate that targeting severe COPD patients who have just had exacerbations could be most cost-effective. This is because of three reasons: 1) the effect size would be greater on both qualities of life and mortality; 2) the hospital would be a convenient touchpoint to refer the patient to digital PR; and 3) We speculate that uptake and adherence to the PR program would be greater immediately post-exacerbation because patients are more likely to adopt new lifestyle behaviors after a negative health event.

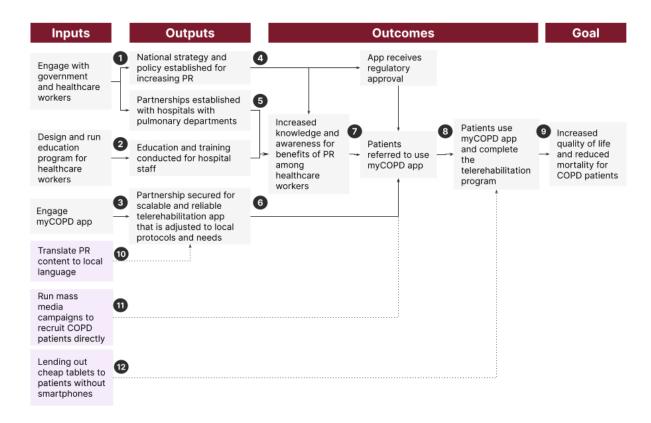
The charity would likely have to engage the local health system to ensure that hospitalized patients get referred to download the app and access the service. This could be done at the policy level, through health ministers, or at the hospital level.

We expect the main barrier to be achieving local regulatory approval for the app. Work is needed to ensure that the myCOPD app is adapted to local PR protocols and languages.

The following is the detailed theory of change we imagined for the intervention.

⁴ In case the partnership does not work out, we also modeled separately for the charity to develop its own digital PR platform that utilises group-based video supervised digital PR. This was less cost-effective but still above our bar for cost-effectiveness (see CEA section).

⁵ myCOPD app is the flagship product of <u>my mhealth</u>, which is a for-profit social enterprise dedicated to providing digital solutions to managing long term health conditions.



The following assumptions relate to each step within the ToC, color-coded by our uncertainty. The numbers correspond to the steps in the ToC.

- 1. Governments and health systems are supportive of efforts to increase PR.
- 2. There is enough information about PR to design education programs and the hospital agrees to allow us to provide the training to staff.
- 3. MyCOPD is willing to partner with us. There is enough information to adjust the protocols to local needs.
- 4. Healthcare workers pay attention to national policies, and the government approves the app from a regulatory perspective.
- 5. Educational materials succeed in increasing knowledge and awareness around PR for healthcare workers.
- 6. Patients have smartphones and internet access⁶. There is physical infrastructure enabling the app to operate in LMICs. The app is adaptable to LMIC needs.
- 7. Increased knowledge from health workers increases referral of patients to PR.
- 8. Increasing referral and uptake leads to the completion of PR. Older patients can navigate the myCOPD app technologically.
- 9. PR is effective at increasing quality of life and reducing mortality for severe COPD patients. Digital PR is equally effective.
- 10. Content can be translated.

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⁶ We have evidence that suggest access to smartphones amongst older populations in LMICs are low, but we have also discounted for this in our CEA.

- 11. COPD patients will respond to campaigns and sign up for the app.
- 12. Patients will give the tablets back, and they are able to use them correctly.

Adaptation of myCOPD app to local contexts

The pulmonary rehabilitation program and the actual exercises will be largely the same across the world in any context. As myCOPD is a web app, even older and slower phones should be able to use the service as long as there is an internet connection. The myCOPD app has expressed willingness to work with the charity to adapt the app to LMIC needs.

Some potential adaptations to the app that we think are possible:

- Translation to local languages.
- Adding warnings about going outside when the air pollution is heightened.
- Allowing content to be downloaded to circumvent intermittent internet connectivity.

Although we have accounted for limited access to smartphones amongst the elderly population in LMICs, there are optional activities that the charity could undertake in order to increase reach to these populations.

Loaning cheap tablets to patients who do not have smartphones. We have
previously investigated the costs of these tablets for <u>digital personalized</u>
<u>learning</u> and family planning decision apps (analysis available upon request),
and we think it would be cheap and cost-effective to provide them to COPD
patients as well. However, this would add an extra step of complexity to the
Theory of Change, and we have not modeled this in the CEA.

Scaling potential

Once established, the digital PR program can be scaled to patients with moderate or mild COPD. We think that focusing just on severe COPD patients would already generate an impact at a large enough scale. However, under the myCOPD app partnership model, the incremental costs of extra users would be close to zero, which makes it potentially promising to scale the program to moderate or mild COPD patients. We suspect the uptake would be lower due to a lower perceived need for rehabilitation.

Once the program is established and the benefits are proven, the government could internalize the costs. In a similar way to the NHS contracting *my mhealth* for the myCOPD app, once LMIC governments understand the value and impact of the app, they can also take over the funding to *my mhealth* for the service they provide.

After establishing regulatory approval for COPD, the charity can expand to other diseases, such as asthma and tuberculosis. There is also long-term potential for implementing chronic disease management programs like cardiac rehabilitation, diabetes management, etc., which my mhealth has already developed.

4 Quality of evidence

4.1 Evidence that a charity can make a change in this space

Governmental support

There is weak evidence that governments would support favorable policies to increase PR access and uptake.

We found a situation assessment by the Ministry of Health in Nepal, one of the
top target countries, acknowledging the significant unmet need for
rehabilitation and the need for the government to strengthen leadership and
increase investments in rehabilitation capacity (Government of Nepal 2022).

Increasing referrals and uptake

We feel most uncertain about this part of the ToC – the ability of the charity to increase referrals and acquire users for the app. From what we found, baseline referral rates are low across the world, but there are interventions that can increase the referral rates. Additionally, the charity could benefit from directly acquiring users through public campaigns, similar to the approach by Kaya Guides. Therefore, we do not feel these challenges are insurmountable.

The baseline referral rates at hospitals are low. This presents a challenge for the charity to reach potential app users. However, it also represents an opportunity to reach users that wouldn't otherwise be reached.

- A study in the UK found that only 9.3% of eligible patients were referred to PR (Moore et al., 2017).
- Data from the US suggests 19% of patients with idiopathic pulmonary fibrosis were referred to PR (de Andrade et al., 2021).
- Referral rates at specialist clinics in Melbourne are higher, with 40% of patients with Interstitial lung disease having been referred (Hoffman et al., 2021).

⁷ Kaya guides provides guided and unguided self-help programs through a whatsapp chatbot in India.

We assume the referral rates will be similarly low in LMICs.

Once referred, uptake of in-person PR is generally moderate. As discussed in the background section, the main barriers to uptake are patients struggling with the physical exertion of traveling to physiotherapy clinics and the lack of capacity, especially in rural areas.

- An audit in England and Wales found that 69% (47,020) of the 68,000 COPD patients referred attended pre-assessment, with 85.2% to 90% enrolling in PR afterward. Suggesting that uptake is 58.9% to 62.2% (Watson et al., 2023).
- During a webinar, Henrik Hansen, the co-author of the Cochrane review on digital PR (2021), noted that among patients who didn't take up in-person PR, 50% took up digital PR (Europe Region World Physiotherapy 2021).

There has been an acceleration of digital tools in LMIC healthcare systems, especially since COVID. This is highlighted by this infographic by McKinsey (2021)

Digital tools have helped lower- and middle-income countries address major healthcare system challenges.

Primary healthcare use cases in eight lower- and middle-income countries

1 Burkina Faso: Rapidly and widely deployed COVID-19 modules enabled by digitalhealthcare tools and scaled over a decade (Company: CommCare)

2 Nigeria:

- •Quickly scaled existing disease-surveillance platform (Company: SORMAS)
 •Implemented data system to manage public-health-goods supply chain (Company: LMIS)
 •Provides self-managed care platform for users with chronic health issues (Company: mDoc)
- 3 South Africa: Chatbot app enabled around 11 million symptom checks across various industrial sectors during COVID-19 pandemic (Company: Turn.io)
- 4 Uganda: Mobile app supported healthcare workers in pandemic response and primary care (Company: SmartHealth)



5 Kenya:

- •Text messaging enables healthcare payments; connects patients, providers, and payers (Company: CarePay) •Telemonitoring model
- supports case-based learning on broad health topics (Company: Project ECHO)

6 Rwanda:

- •Wide uptake of telemedicine tool with users/providers (Company: Babyl) •Pemete monitoring via text
- •Remote monitoring via text messaging improves workflows and adherence (Company: WelTel)
- 7 Sri Lanka: Digital tool helped launch nationwide response to COVID-19 before first case was detected (Company: DHIS2)
- 8 Vietnam: Suite of digital tools tracks and traces COVID-19 (Companies: NCOVI, Bluezone, and others)

Note: The boundaries and names shown on this map do not imply official endorsement or acceptance by McKinsey & Company.

Source: McKinsey analysis based on 12 large-scale digital-tool implementations in 8 lower- and middle-income countries in Africa and Asia

There is weak evidence that interventions to increase PR referrals are effective. A systematic review of interventions to increase referral and uptake of PR in people with

COPD found several interventions to work (<u>Early et al., 2018</u>). However, the results are fairly mixed, and the quality of the evidence is generally poor.

- Fourteen papers were identified: Ten assessed referrals and five assessed uptake (46,146 patients, 409 clinicians, 82 hospital departments, 122 general practices).
- Four studies reported statistically significant improvements in referral (range 3.5%-36%). Two studies reported statistically significant increases in uptake (range 18%-21.5%). The largest effect sizes came from the following interventions:
 - By introducing mandatory monitoring of quality indicators, the outpatient department in Denmark increased PR referrals by 65%, from a baseline referral rate of 55% to 91%.
 - A patient manual summarizing the evidence for COPD treatments (a non-randomized controlled before and after trial, 18% increase in uptake rates; <u>Harris et al., 2009</u>).
- It is uncertain whether the charity will be able to persuade hospitals and healthcare workers to refer patients to the digital PR app, but we do not think it's impossible.

Since the incremental costs of additional users of the digital PR app are almost zero, the charity does not need to worry about targeting. Each additional COPD patient, no matter the severity, would benefit from using the app and increase the cost-effectiveness. This may improve the ease of recruitment, as the strategy is simpler. This may be done through mass media campaigns, for example.

By analogy, <u>Kaya Guides</u> (a previously CE-incubated charity) has recruited patients through these targeted campaigns (on Facebook and Instagram).

Smartphone penetration among LMICs and older populations

Smartphone penetration is lower in LMICs and especially in older populations.

For India:

- A paper published in 2015 found that smartphone usage among Indian elders aged 55 years old and above is at 5% (Sujata et al., 2015).
- More recent data from 2019 found that 10% of 45-year-olds and above use smartphones in India (Statista, 2022).

 A study with 42 participants found that training elderly people in India to use smartphone technologies is highly feasible (Das and Sethi 2020).

For Nepal:

- Smartphone penetration is about 49.6% of the total population in 2024 (<u>Kemp. 2024</u>). Another report of the 2022 national census suggests the number is 73% (<u>Republica, 2023</u>).
- This source suggests that only 2.6% of the elderly population (aged 55 and above) have smartphones (<u>Smartphone Users in Nepal 2023</u>). However, we have some doubts about the validity of this data, as other data sources for countries like Denmark seem potentially inaccurate (<u>Smartphone Users in Denmark 2023</u>).

Thailand

 84.3% of elderly Thai seniors (aged 60 or above) have smartphones in 2024 (<u>Krisanaraj, 2024</u>).

Regardless, smartphone penetration trends toward increased adoption. As current generations age, more elderly people will have access to the technology. Smartphone and mobile internet connection adoption is increasing at 1.7%-2.3% globally (<u>GSMA</u>, 2024).

4.2 Evidence that the change has the expected health effects

Most of the evidence for PR is generated from studies of in-person PR, and most of the evidence for digital PR is in the context of its comparison to in-person PR. Thus, in this section, we first summarize the evidence for in-person PR and then digital PR⁸.

In-person PR.

There is strong evidence that in-person PR improves patients' quality of life and moderate evidence that it is effective at reducing mortality if initiated immediately post-exacerbation.

⁸ A third option is Home-based PR, which allows the patient to stay at home, attended by physiotherapist who travel to the patients. We do not consider this ToC because it faces the same concerns we had for traditional in-person PR - the lack of qualified physiotherapist capacity in LMICs. Some of the evidence for home-based PR is summarised in the Annex.

- A Cochrane review of 65 RCTs of 3822 participants found that PR significantly improved all outcomes relating to quality of life, including dyspnoea (a sensation of running out of air and of not being able to breathe), fatigue, emotional function, and mastery (McCarthy et al., 2015). The effect sizes are measured by questionnaires.
- A Cochrane review analyzed 20 randomized controlled trials (RCTs) with 1,477 participants, revealing moderate-quality evidence that pulmonary rehabilitation following an exacerbation significantly reduces the likelihood of hospital readmissions by 56% within a year (95% confidence interval [CI]: 0.21 to 0.91), despite the results being heterogeneous (I² = 77%) (Puhan et al., 2016).
 - However, the evidence quality was deemed low regarding the impact of rehabilitation on mortality, showing no statistically significant effect (pooled odds ratio [OR] 0.68, 95% CI: 0.28 to 1.67), with noted heterogeneity in results (I² = 59%)⁹. Subgroup analysis highlighted significant differences in effects between trials with varying lengths of rehabilitation programs and trials differentiated by a low and high risk of bias, suggesting potential causes for the observed heterogeneity.
 - Further, high-quality evidence supports pulmonary rehabilitation's role in enhancing health-related quality of life post-exacerbation. Specifically, eight studies employing the SGRQ observed a significant improvement in SGRQ total scores, surpassing the minimal important difference (MID) by four points (mean difference [MD]: -7.80, 95% CI: -12.12 to -3.47; I² = 64%). This improvement was also significant and exceeded the MID in the impact and activities domains of the SGRQ.
 - \circ Regarding physical function, high-quality evidence indicates an average increase of 62 meters in the six-minute walk distance (6MWD) (95% CI: 38 to 86; I² = 87%).
 - Out of five studies that specifically monitored adverse events among 278 participants, four reported no adverse events during the rehabilitation programs, while one noted a single serious event.
- A more recent meta-analysis looking at early initiation of PR post-exacerbation did find significant mortality benefits (<u>Ryrsø et al., 2018</u>).
 - Thirteen randomized trials were included (801 participants). There was a clinically relevant reduction in mortality after early PR (4 trials, 319 patients; RR = 0.58 (95% CI: [0.35 to 0.98])). The follow-up times were generally around six months to a year.
 - Early PR reduced number of days in hospital by 4.27 days (1 trial, 180 patients; 95% CI: [- 6.85 to 1.69]) and hospital readmissions (6 trials,

⁹ We believe the study is probably underpowered to detect mortality rates, and therefore we do not update much based on this evidence.

319 patients; RR = 0.47 (95% CI: [0.29 to 0.75])). Moreover, early PR improved HRQoL and walking distance and did not affect the drop-out rate.

- This is corroborated by observation studies that show that amongst ~190,000 hospitalized COPD patients in the US, initiation of PR within three months of discharge significantly reduces 1-year mortality by 37% (<u>Lindenauer et al.</u>, 2020).
- Other pre-post studies also show clinically significant improvements, such as reduced hospital days (<u>Katajisto & Laitinen, 2017</u>).
- However, most evidence is generated from HICs. In addition, PR services
 developed in HICs may not be deliverable in the same format as LMICs, with
 substantial differences in resources, awareness, culture, healthcare
 configuration, and disease profile, which may affect overall management
 strategy.
 - An expert also noted that since LMIC patients have lower access to other management strategies for COPD, such as inhalers and vaccines for pneumonia, the effect sizes of PR in such countries could be larger than in HICs.

In addition, there is moderate evidence that PR is beneficial for improving mental health, particularly anxiety and depression among COPD patients (Coventry, 2009).

There is weak evidence that PR is cost-effective.

 An RCT in Brazil showed that PR only costs \$75 per patient and saved the health system substantial costs in terms of hospital admissions, which were averted whilst increasing clinical improvements based on walk activity.

Digital PR

Many recent studies have compared digital PR to in-person PR. It's important to note that digital PR protocols still have differences; some, for example, are based on digitally supervised group rehabilitation sessions, while others are based on unsupervised phone apps. Here, we consider both under the umbrella of Digital PR, as the literature usually does.

There is moderate evidence that digital PR is effective and comparable to facility-based PR.

 A Cochrane review of 15 studies looking at digital PR for chronic respiratory disease found that there is little to no difference in effect on exercise capacity and quality of life between in-person PR and digital PR. Participants were found to be more likely to complete a program of digital PR (93% completion rate) than in-person PR (70% completion rate). Compared to no rehabilitation, digital PR significantly improved exercise capacity. Evidence also showed that digital PR could improve exercise capacity when delivered as a maintenance program post-PR. The review also found no adverse effects of digital PR (Cox et al., 2021).

- A meta-analysis of 8 studies found that digital PR was effective at improving the quality of life for patients and was comparable to facility-based PR (<u>Ora et al.</u>, 2022)
- There is some weak evidence that digital PR can help maintain PR's benefits in the long term as a post-rehabilitation program (<u>Uche-Okoye et al., 2023</u>).
- Experts have suggested that in-person PR is more effective and preferable but agreed that digital PR is more cost-effective. A review of cost-effectiveness studies found that digital PR was more cost-effective than home-based PR, which was more cost-effective than usual care (Liu et al., 2021).
- These meta-analyses didn't look at mortality outcomes (they were too underpowered to detect); however, considering how similar the program and exercises are, we believe this evidence would translate to mortality outcomes as well.

There is also evidence specific to the myCOPD app that demonstrates its effectiveness. We find this evidence encouraging but weak due to the studies' small sample sizes:

- An RCT of 41 COPD patients recruited through recent acute exacerbations showed that the app improved the CAT score and patient inhaler technique.
 Exacerbations were less frequent in users, and hospital readmission risks were lower (North et al., 2020).
- An RCT of 60 mild-moderate COPD patients found that patients with increased app use were associated with greater CAT score improvement. The myCOPD group showed a greater mean improvement in CAT scores, but the result was not statistically significant. The study found non-significant improvements in inhaler use (Crooks et al., 2020).
- An RCT of 90 patients with dyspnoea of grade 2 or higher found that myCOPD was non-inferior to in-person PR in terms of effects on walk tests and symptom scores. The myCOPD group showed favorable results compared to the in-person group (Bourne et al., 2017).
- In an unpublished study by Stonehaven Medical Group, 23 real-world patients were evaluated at five months. The average improvement in CAT score was 2.1.

The inhaler technique was improved, and the need for inhaler use was reduced. Hospital admissions were reduced from 6 to 0, with 19% fewer unscheduled GP appointments. The proportion of patients describing their ability to manage exacerbations very well rose from 29% to 55%, and those who felt confident using an inhaler rose from 76% to 90% (McLaughlin & Skinner, 2020).

 Based on this evidence, the myCOPD app is the only app approved by NHS/NICE in the UK (NICE 2024).

Combining this evidence with the wider evidence on digital PR, we are moderately confident in the effectiveness of the myCOPD app. We think it is likely that the app would be effective even in LMIC settings, as the exercises are entirely doable from within a small home without specialized equipment. There is also sufficient evidence from LMICs demonstrating the effectiveness of PR, whether delivered in-person or digitally.

Adherence

Although the adherence rates should be reflected in the effectiveness of the PR programs, evidence suggests that once patients take them up, adherence to in-person PR programs is moderately high.

- In Cali, Colombia, a cross-sectional model with 150 patients diagnosed with COPD found a high PR adherence rate (57%) (Betancourt-Peña et al., 2023).
- Another cross-sectional study in the US with 455 patients found that 26% of patients had low adherence, 23% were moderately adherent, and 51% were highly adherent (<u>Oates et al., 2017</u>).
- Hayton et al. noted that 71% of patients attended at least 63% of the planned eight sessions (Hayton et al., 2013).
- In New Zealand, an audit showed that 46% to 75% of participants completed all 16 planned PR sessions (McNaughton et al., 2016)

Digital PR has higher acceptability and, therefore, take-up and adherence.

- As mentioned, the Cochrane meta-analysis found that participants were more likely to complete a digital PR program, with a 93% completion rate compared to a 70% completion rate for in-person PR (Cox et al., 2021).
- The expert from the myCOPD app we consulted also mentioned that their adherence is very high and more favorable compared to head-to-head comparisons of in-person PR, which is a large reason it was recommended by NHS/NICE (NICE 2024).

5 Expert views

<u>In earlier research</u>, we interviewed two experts on in-person PR. One of them is the chief scientific officer of a prominent COPD NGO in the US, and the other is the CEO of a global NGO focused on chronic respiratory diseases at the primary care level. This round, we interviewed one additional expert, the CSO of *my mhealth*.

CSO and CEO of two COPD NGOs

Both experts agree that COPD is extremely neglected. It affects disenfranchised populations more. There is very little awareness and prioritization, even in high-income countries.

COPD affects more people and has a higher DALY burden; however, one expert made the case for Asthma as well. People with Asthma are, on average, younger and live with the disability for longer. Asthma may also be more tractable – there is also one treatment for asthma: corticosteroids, which are very under-utilized. COPD, on the other hand, requires a package of interventions.

Multiple interventions and treatments exist for COPD. These include 1. smoking cessation 2. vaccinations 3. respiratory rehabilitation 4. pharmacological interventions like bronchodilators and 5. oxygen therapy, which should only be used if the blood oxygen level is low.

On the COPD landscape, there are a few actors in the space, but none have been very effective at driving change. The WHO has only recently (3 years ago) added a medical respiratory office, and it has taken a lot of time for them to coordinate and organize the many actors in the space. The NCD alliance is a significant player, but its respiratory focus is weak. The other major players are the Global Allergy & Airways Patient Platform (GAAPP) and the Global Alliance against Chronic Respiratory Diseases (GARD). The pharma industry ends up being a major player because they have money to donate. Still, they tend to advocate for pharmaceutical interventions, which is not the most essential or cost-effective intervention for COPD.

Both experts also agree that focusing on smoking cessation may be more promising. If someone has COPD and they still smoke, the most effective action they can take is to quit smoking. Both experts think that smoking cessation is underutilized because there is still a pervasive narrative, even amongst doctors, that smoking is a lifestyle choice and should not be influenced by health professionals. However, one

expert noted that the success rates for cessation are low (~10%), and patients often relapse. Despite this, the experts still think it is promising and worthwhile.

Both experts agree that PR is effective but extremely under-utilized, especially in LMICs.

The hardest part of in-person PR is getting COPD patients to initiate it. It requires three levels of behavior change: 1. more referrals, 2. more uptake and completion, and 3. maintenance. This is also true for smoking cessation.

The capacity for in-person PR in LMICs is low. There are not enough physiotherapists, which makes digital PR promising. At a higher level, advocacy is needed for the government to establish policies to increase capacity.

Although the evidence for PR is highest in post-exacerbation scenarios, there are also reasons why the effect sizes would be lower in the real world. The thought of needing to do exercise at that point is anxiety-inducing because patients are afraid of being more breathless, even though PR helps them in the longer term. It would be easier for patients to initiate PR at less severe stages. However, patients with milder symptoms are harder to reach.

Hospitals are the best touchpoints to initiate PR post-exacerbation, but it is also most challenging when patients are still frail, breathless, and afraid to exercise. Patients who stay longer in the hospital have a higher chance of initiating because they are less frail by the time they are discharged.

Most COPD patients interact with primary care (80%). However, diagnosis and referral rates are low because doctors lack awareness. They do not tend to intervene when patients say they have a smoker's cough, especially because it is common for patients to go to the doctor for another medical issue and mention COPD symptoms as a side note.

It is difficult to interpret quality-of-life improvement measurements from studies because each patient is different.

Adherence rates of in-person PR are also a secondary concern and challenge. The best guess is that once initiated, adherence is about 50%.

Digital PR may greatly lower the cost and be suitable for LMIC contexts where patients can access the internet and smartphones. However, its effectiveness is less

proven, and adherence rates are usually lower. Nonetheless, with the cost savings, it would probably still be more cost-effective.

Experts are not too concerned about whether there is space for LMIC patients to perform exercises at home. They comment that the program is adaptable to a wide variety of contexts.

There is not one major provider for digital PR yet. Different countries are creating their own platforms, and some small start-ups are working on platforms, too. However, many of them still require testing and evidence generation.

One expert commented that perhaps radio campaigns could be promising.

Anecdotally, they have seen success with their organizations' social media campaigns.

There are some minor risks to consider. One expert mentioned that there might be a risk of allowing patients to feel like they can still smoke if PR is effective at improving their symptoms. However, they said that those patients would likely never quit anyway.

Tom Wilkinson, CSO of my mhealth (myCOPD)

My mhealth was first spun out from Southampton University. They have developed an app that serves patients with chronic diseases such as diabetes, COPD, asthma, and cardiac disease. Amongst them, the most developed and well-evidenced in COPD.

The company has been thinking about how to scale to LMICs and would be excited to partner with a charity. However, they currently have no plans to scale to LMICs and have only done a small pilot with some private clinics in India (for cardiac rehabilitation), Ethiopia, and Bangladesh. Most organizations in the space operate in the US, with very few focused on LMICs.

The main barriers to scale are regulation and capacity. The team is busy expanding in the UK and US and can't support LMICs. A charity could potentially solve many of these constraints.

The app has been proven in RCTs and compared head-to-head with in-person PR, which led to its approval by NICE and NHS.

Digital PR does not require video-supervised sessions, making it much cheaper and more scalable. Over the years, the program has been carefully designed to be highly

personalized, with video instructions and adjustments to the exercises according to the patient's needs and progress. Head-to-head comparisons have also shown that this app is better than video-supervised PR.

The app also allows for consistent monitoring and evaluation. It continuously receives patient feedback, and progress can be monitored at a population level on a dashboard.

Because the program doesn't require video supervision from staff, the incremental costs per patient are almost nothing. It costs almost the same to deliver it to 10,000 people as to a million people. The main costs are dealing with the regulatory side, training hospital staff, and adjusting the PR to local medical protocols. He estimates that serving 100,000 people would cost around 100,000-300,000 pounds (~2 pounds per patient), but to scale this to millions of people in the same regulatory jurisdiction would not increase much in costs. Therefore, the scaling costs should be thought of more as a cost per region or jurisdiction, not cost per patient.

Adherence and activation are very high. Exacerbations cause patients to reflect on their behaviors and motivate them to adopt new behaviors. Even older populations use the app more frequently. On average, in the UK, 74% of patients complete the program. Because COPD patients have symptoms almost every day, they are motivated to do the exercises. This is in contrast to in-person PR, where even in the UK, the access rates are around 20%.

PR, even when in person, is already one of the most cost-effective interventions for chronic diseases. The triad of cost-effective interventions includes smoking cessation, vaccination, and PR. Digital PR is even more cost-effective.

In an LMIC context, PR may be even more effective because patients are lacking access to other management strategies like inhalers, pneumonia vaccines, etc.

The GOLD COPD categories are outdated and should be phased out. They measure a physiological metric but don't track patient-experienced quality of life. For this, the CAAT score and the walk tests are much more accurate. Studies should correlate CAAT scores with DALYs/QALYS.

In the long term, digital diabetes management is very exciting and cost-effective.

6 Geographic assessment

The geographic assessment was done in two stages. First, we looked at where existing organizations are working or have worked. This information was used as input in the formal geographic assessment to measure how much attention an issue is being paid. Second, we conducted a formal geographic assessment to find the top priority countries for starting a new charity.

6.1 Where existing organizations work

PR programs are usually managed by governments or local private practices. COPD patients are usually referred by their general practitioner or specialist to do PR. Therefore, the needs and availability are largely country-context-dependent.

Below are the organizations we found that work on COPD or PR.

COPD Foundation

 It is unclear where exactly they operate. They have a so-called "COPD Global" program, which seems to be an online community for people to join to meet others also suffering from COPD.

Global Initiative for Chronic Obstructive Lung Disease (GOLD)

- "GOLD works with healthcare professionals and public health officials around the world to raise awareness of COPD and to improve prevention and treatment of this lung disease."
 - Their exact activities are also vague. They produce reports and organize conferences.
- "GOLD is working to improve the lives of people with COPD in every corner of the globe."

The International Primary Care Respiratory Group (IPCRG)

- They are a clinically-led charity that works locally in primary care and collaborates globally to improve respiratory health. They comprise an alliance of 38 national primary care respiratory organizations, reaching over 155,000 GPs and other primary care professionals worldwide.
- Their ToC is focused on research and education: "Our scope is research and education on improved primary prevention, recognition, diagnosis, treatment

and palliation of non-communicable respiratory diseases, such as asthma and COPD, and respiratory infection in community and primary care settings."

• They have a <u>catalog of literature on the cost-effectiveness of PR.</u>

RECHARGE-IPCRG - teach the teacher program

- A collaboration between the National Institute for Health and Care Research (NIHR) funded the Global RECHARGE Group for PR and IPCRG.
- They operate in India (Pune and Delhi), Sri Lanka, Kyrgyzstan and Uganda
- Due to the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2)
 pandemic, the program was adapted to a digital environment using online
 platforms such as Zoom video conferencing and Google Classroom.

Chest Research Foundation (CRF), India

 Since its inception, the Chest Research Foundation has addressed this huge burden of obstructive airway diseases in India through Research, Education, and Advocacy.

There are several organizations that are focused on COPD in the US

- <u>American Lung Association</u> Not just focused on COPD or PR. They also focus on other diseases like Asthma, pneumonia, smoking, etc.
- <u>USCOPD coalition</u>

In regards to Digital PR, an expert has said that most of the work is currently being done in high-income countries like the USA and Europe. We did a quick search for organizations in the space. In addition to myCOPD, there are:

- Kaia Health has a COPD app that brings elements of PR to Germany.
- <u>Propeller Health</u> has an app that provides symptom management but not PR.
- Care TRx by Gecko Health Innovations: a smart inhaler device with no PR.
- <u>PinkTree</u>: an app that tracks symptoms but not PR in India.

This paper also lists a few other apps that have been tested in the space (Chung et al., 2024):

- Fitbug app (Belgium)
- Efil breath (South Korea)

Based on this, we think digital PR is highly neglected and underresourced in LMICs.

6.2 Geographic assessment

The <u>geographic assessment</u> was conducted with weighted considerations of many factors, including the scale (50%), neglectedness (30%) and tractability (20%). We note that we were unable to find many COPD-specific metrics.

Scale

The scale is made up of:

- The total DALY burden taken from the Global Burden of Disease (GBD).
- The DALY rate of each country taken from GBD.
- The population of the country.

Neglectedness

Countries were scored for neglectedness using:

- Number of organizations working in those countries (see <u>where existing</u> organizations work).
- the inverse of Gross National Income (GNI) per capita was used to indicate a country's resource limitations.
- The current health expenditure as a percentage of GDP.
- The domestic government health expenditure as a percentage of GDP.
- The domestic government health expenditure as a percentage of total health expenditure.
- Health Access and Quality Index from 2015.

Tractability

Tractability was gauged using four key indexes:

- Mobile Cellular subscriptions per 100 people (2021/2022).
- Fragile States Index (2022).
- Corruption Perceptions Index (2022).
- World Justice Project (WJP) Rule of Law Index (2022).
- Freedom in the World Index (2022).

We excluded countries that we considered extremely intractable and high-income countries, such as North Korea and the United States of America.

Based on this analysis, the top most promising countries are **India**, **Nepal**, **China**, **and Indonesia**. It is mostly in middle-income countries because NCD is a bigger problem there, and there are more smokers and air pollution.

7 Cost-effectiveness analysis

Our <u>cost-effectiveness analysis</u> (CEA) is adapted from the <u>previous CEA on in-person PR</u>. It evaluates a hypothetical 10-year program in Nepal, India, and Thailand where the charity provides digital PR by partnering with myCOPD and targeting COPD patients with recent hospitalizations.

The charity is modeled to advocate for national policy and hire program officers to educate and train hospital staff on the importance of PR. We modeled for the charity to cover the costs of PR for patients.

Partnering with myCOPD to roll out unsupervised digital PR is extremely cost-effective.

Assuming the charity reaches 20% of the severe COPD patients in India, adjusted by smartphone usage, the model estimates that the intervention could avert a DALY for every \$9 spent or 108 DALYs per \$1000 spent (Table 2).

Table 2: Cost-effectiveness of myCOPD partnership model in India

	India
The number of people reached in total, NPV	353,289
DALY total, NPV	259,862
Cost total, NPV	\$2,403,046
Cost-effectiveness (\$/DALY)	\$9
Cost-effectiveness (DALY/\$1000)	108.14

Modelled for Nepal, the intervention could avert a DALY for every \$84 spent or ~11.94 DALYs for every \$1000 spent (Table 3).

Table 3: Cost-effectiveness of myCOPD partnership model in Nepal

	Nepal
The number of people reached in total, NPV	38,251
DALY total, NPV	28,135
Cost total, NPV	\$2,356,345
Cost-effectiveness (\$/DALY)	\$84
Cost-effectiveness (DALY/\$1000)	11.94

Since both India and Nepal have relatively low smartphone penetration, we also modeled for the charity to reach 50% of Thailand. The cost-effectiveness is even

higher, with an estimated DALY averted for every \$3 spent or ~350 DALYs for every \$1000 spent (Table 3).

Table 4: Cost-effectiveness of myCOPD partnership model in Thailand

	Thailand
The number of people reached total, NPV	1,201,670
DALY total, NPV	883,888
Cost total, NPV	\$2,528,808
Cost-effectiveness (\$/DALY)	\$3
Cost-effectiveness (DALY/\$1000)	349.53

7.1 Effects

We calculated the net present value benefits for the interventions by applying the following discounts:

- a standard annual discount of 1.4%
- a 1.33% counterfactual discount reflective of the likelihood that the intervention would occur anyways
- a 1.82% per year adjustment to account for the trend of increasing DALYs associated with COPD (linearly extrapolated from DALY rates between 2010-2021 for Nepal).
- a 0.91% per year adjustment for increasing population (linearly extrapolated from past trends).
- we added a 2% adjustment to account for the growing % of people with smartphones.

There were two main benefits that we quantified in the model:

 The mortality reduction. This was calculated by taking the expected mortality in the two years following a hospitalization event for a severe COPD patient and multiplying that with the 42% mortality reduction reported in a meta-analysis (Ryrsø et al., 2018)¹⁰¹¹. We multiplied this by the expected DALY benefit of saving the life of a 70-year-old COPD patient, which is discounted by the disability weight of living with moderate COPD.

- 2. Improvement in quality of life. We used a weighted average of several estimates of QALY or DALY improvements. Where QALYs were reported, we assumed a 1:1 conversion ratio between QALYS and DALYs.
 - a. The QALY improvement reported from this paper on PR (weight: 50%) (Toubes-Navarro et al., 2023).
 - b. The QALY improvement reported from this paper on PR (weight: 30%) (Griffiths et al., 2001).
 - c. The QALY improvement reported from this paper on physical activity (weight 10%) (Ramos et al., 2019).
 - d. The discounted DALY benefit of going from severe to moderate COPD (Table 1).

We assumed that these QoL benefits last 6.1 years per patient, which is the average life expectancy post-hospitalization of patients with severe COPD (van Hirtum et al., 2018). However, we discounted this by 50% to adjust for the patients not maintaining the exercises.

All numbers relating to effect sizes were discounted by internal and external validity adjustments (based on intuitive guess).

7.2 Costs

Fixed costs: We modeled for the charity to have about four full-time staff members, with a fixed cost of \$280,000. We budgeted for an additional two local program officers who are receiving a physiotherapist's salary, and additional one-off costs of reaching a new jurisdiction (~\$183,000), which includes language translation, protocol adaptation, and healthcare worker training/ health minister engagement. Yearly fixed

¹⁰ This meta-analysis looks at the mortality effect from in-person PR. We assumed that the mortality benefits would be the same for digital PR as in-person PR, because of the inferiority studies (Evidence Section). Theoretically, the programs are also very similar and the difference mainly being one is in-person and one is at home.

¹¹ The studies generally measure mortality around 1 year time point. Some studies are half a year, some are two years. So we think assuming this to be the mortality rate reduction at 1 year is fair.

maintenance costs (~\$20,000) are also included for the charity to update the program according to the latest medical protocols and guidelines.

Variable costs: The incremental costs for each additional user are very minimal at \$0.2, which is made up entirely of the data storage, data curation, and data security costs.

The net present value costs were calculated by applying a 4% discount.

7.3 Reach

In modeling each country, we calculate the reach of the interventions by multiplying the following:

- For India, we discounted the population by 80% as we assume the charity would only reach 20% of the states. For Thailand, we discount the population by 50%.
- Prevalence of moderate to severe cases of COPD (around 4-7%) (<u>Viegi et al.</u>, 2000).
- Number of hospitalizations expected per patient per year (1 in 5).
- Discount by 15%, which is the percentage of patients who won't survive hospitalization (<u>Ekezie et al., 2021</u>; <u>Hoogendoorn et al., 2011</u>).
- Discount by baseline availability of PR, as those patients would receive treatment anyway.
- Discount by % of elderly using smartphones (5-83% depending on country)
- The expected uptake in digital PR in the people who are eligible but without access currently (around 40%).

The final number represents the counterfactual number of hospitalized moderate/severe COPD patients who have smartphones and who would take up digital PR in a year. The numbers are:

Nepal: 4,057

• Thailand: 127,462

• India: 46,007

7.4 Reasons for error

Underestimate

- Reaching more people: The intervention is extremely scalable, so if we manage
 to serve more people, the cost-effectiveness could improve. Current estimated
 costs and the number of people reached are conservative. If the reach is
 increased, the scale could potentially be much larger.
- Reaching mild COPD patients: The effects modeled are for patients with severe COPD who just had an exacerbation. Once the regulatory hurdles are solved, the incremental costs of scaling to include moderate or mild COPD patients are extremely low. This could potentially have a much greater impact.
- Treatment is more effective: Tom Wilkinson, the CEO of my mhealth,
 mentioned that the head-to-head comparisons show that myCOPD is more
 favorable and effective compared to in-person or video-supervised PR.
 However, the effect sizes we use for modeling are mostly from in-person PR.
 The effectiveness of PR could be larger due to LMIC patients not having access
 to other forms of treatment.
- Externalities: We did not model externalities such as income benefits, cost savings to hospitals from reduced exacerbations, and mental health effects.

Overestimate

- The life expectancy of patients we serve could be lower, in which case the quality of life benefits would be reduced (though this has already been discounted by 50% to account for lack of maintenance).
- The reach could be overestimated if we think that patient referral is going to be challenging. This was one of our uncertainties flagged from the evidence review.
- The costs could be higher: We are not fully confident about the per-person data costs.

Next steps to model if there's more time

If there was more time, we would model the following (color-coded by whether it would improve or reduce the cost-effectiveness):

- Another way to estimate and sense check mortality via indirect measurement:
 hospitalizations prevented by PR and fatality rate of hospitalizations.
- Include estimates for cost saved for reduced hospitalization
- Include estimates for increased income gains for patients having higher mobility.
- Model the addition of moderate to mild COPD patients.
- Model mental health benefits.

8 Implementation

8.1 What does working on this idea look like?

The founders would spend a fair amount of time engaging with the stakeholders, which include myCOPD, hospitals, and government health officials, to convince them to invest resources into PR. One of the biggest barriers is achieving regulatory approval, and the founders would have to spend a significant amount of time on this.

The founders would likely work closely with the program managers to ensure the education training for health workers is going smoothly.

There would be a lot of work involved with measurement and evaluation, as well as discussing patient feedback with myCOPD to improve the program.

8.2 Key factors

This section summarizes our concerns (or lack thereof) about different aspects of a new charity putting this idea into practice.

Table 5: Implementation concerns

Factor	Assessment
Talent	Low Concern
Access to information	Low Concern
Access to relevant stakeholders	Low Concern
Feedback loops	Low Concern
Funding	Low Concern
The scale of the problem	Low Concern
Neglectedness	Low Concern
Execution difficulty/Tractability	Moderate Concern
Negative externalities	Low Concern
Positive externalities	Moderate

Talent

We think that typical generalist entrepreneurs who go through the Charity Entrepreneurship Incubation Program would have the required skills to launch this charity. However, there are qualities that are nice to have, listed in Table 6.

Table 6: Founder requirements and nice to haves

Must have	Preferable (offsets a 10% diff in incubatee strength)	Preferable, all else equal
		 Experience working with LMIC governments Experience with COPD or PR programs Global health or medical background Experience living in target countries Experience with digital health apps or telehealth interventions

Access

Information

Not very concerned. There is a lot of information on PR programs and a large body of evidence and research. We also have access to experts in COPD.

Relevant stakeholders

Not very concerned. The interventions rely on engaging hospitals and, to a lesser extent, the government. However, there are indications that governments are interested in such interventions (see evidence section).

My mhealth has already shown an interest in partnering with you.

Feedback loops

Feedback loops are not too concerning. The charity would be able to retrieve data on referral and uptake and survey patients to assess improvements in mortality and quality of life. Digital health interventions lend themselves well to monitoring.

Funding

Funding from funders in the AIM network

The broader AIM network has not looked into Pulmonary Rehabilitation. Most of the work addressing COPD has been focused on preventive measures such as tobacco taxation or research on reducing air pollution. Based on the high cost-effectiveness of the model, we are not too worried about the charity's ability to fundraise from the AIM network.

Broader funding sources

We are quite uncertain about the broader funding sources for this type of work. There tends to be a slight bias from funders towards tech and scalable ideas.

The scale of the problem

We are not concerned that this intervention will be too small. COPD is the world's third leading cause of death; though this intervention specifically targets a subset of those patients, there should still be a large enough scale.

Neglectedness

We are not concerned with neglectedness in LMICs. This seems neglected both from a governmental and nonprofit perspective. A lot of attention is rightly placed on reducing smoking; however, increasing PR could still be a cost-effective solution.

A lot of COPD nonprofits seem to focus on HICs like the US. Most of the app development in the space is also concentrated in high-income countries.

Tractability

We have some concerns about the tractability of the intervention. It seems there are multiple steps in the theory of change that require human behavior changes, including

getting healthcare workers to increase referrals and getting the patients to adhere to the PR program. This increases the failure modes and difficulty of the intervention.

Additionally, we are uncertain about how easy it is to achieve regulatory approval for the app.

Partnering with *my mhealth* would make things a lot easier, as the charity would not have to worry about app development. The fact that myCOPD is approved in the UK bodes well for their approval in other countries.

Externalities

Reducing hospital readmissions should be cost-saving for the patient or health system and free up more of the healthcare system's resources.

There is also some evidence that PR is effective at improving the mental health of COPD patients.

The PR exercises should be beneficial for other co-morbidities.

There may be income benefits as the patients' increased mobility could be more productive or spend less on support.

The negative externalities are mainly related to injuries attained during exertion and exercise. Like normal exercise, with appropriate instruction, these risks are considered minimal and outweighed by the benefits.

Remaining uncertainties

As already mentioned in the tractability section, we have some uncertainties about the ease of increasing referrals and achieving regulatory approval. We also have some uncertainties about the duration of the effects and whether patients will continue to use the app in the long term.

9 Conclusion

Overall, we think this idea is worth recommending to potential Charity

Entrepreneurship founders. We think PR is effective, neglected, and needed in LMICs. Partnerships with other organizations, such as the myCOPD app, considerably simplify implementation. Because the incremental costs of additional patients are so low, once regulatory barriers are overcome, the upside of the charity is incredibly high, with the cost-effectiveness increasing per user acquired. With the rising burden of COPD and NCDs in general and the increasing penetration of smartphone and digital health technologies, we think this charity idea is very promising.

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Annex

Evidence for home-based PR

There is weak and mixed evidence that the effectiveness of home-based PR is comparable to that of outpatient PR.

- A systematic review of 12 RCTs and two observation studies found that home-based PR was comparable in measured outcomes, such as HRQoL, functional exercise capacity, and healthcare resource utilization. However, the authors noted that the quality of the evidence was low (<u>Stafinski et al.</u>, 2022).
- Consistent with this, a separate meta-analysis found that the evidence for effectiveness was inconsistent between studies, and the pooled effect size for physical function and QoL was insignificant (<u>Shaw et al., 2020</u>).

CEA modeling TOC of developing its own digital PR platform, with video group-based rehabilitation sessions.

We also modeled for the possibility that the charity would have to develop its own digital PR platform. Since the evidence base for non-supervised digital PR is weaker, we modeled for the charity to hire physiotherapists to conduct group-based video digital PR.

In this <u>version</u>, the benefits modeled are essentially the same, but there is an increased cost associated with hired physiotherapists and their managers, software development, and maintenance costs.

Group-based PR on a self-developed platform is estimated to be cost-effective but just under our bar. The model estimates that the intervention could avert a DALY for every \$130 spent or ~8 DALYs for every \$1000 spent (Table 7).

Table 7: Cost-effectiveness of self-developed group-based PR in Nepal

	Nepal
The number of people reached in total, NPV	38,251
DALY total, NPV	28,135
Cost total, NPV	\$3,659,829
Cost-effectiveness (\$/DALY)	\$130
Cost-effectiveness (DALY/\$1000)	7.69