Evidence on Pulmonary Rehabilitation and the Challenges Faced in Low- and Middle-Income Countries: A Systematic Qualitative Review

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Abstract

Background

In low-income countries (LIC) and low-middle-income countries (LMIC), the burden of chronic obstructive pulmonary disease (COPD) has increased due to the lack of prevention and the presence of barriers to enter rehabilitation programs. The aim of this systematic review is to analyze the evidence on pulmonary rehabilitation (PR) in LIC and LMIC.

Methods

A systematic literature review was conducted. Four electronic databases were searched for qualitative and quantitative studies that documented the presence of PR in LIC and LMIC. We report our findings following the Prisma guidelines. In addition, grey literature was also searched. Articles not in English, presenting a point of view and/or not treating an adult population (< 18 years old) were excluded from the review. Data were extracted by one reviewer and synthesized in the form of tables. Tables present individual characteristics of the PR reported within countries, including country of origin, study design, population attending, intervention (kind of program setting), frequency and duration of a program established (if available), with health outcomes. The PICO framework was used for every country with reported PR to assess population, intervention, comparison and outcomes found. This systematic review is registered on Prospero: CRD42020141655.

Results

In total, 47 publications were included in the review. In LIC, PR for HIV-infected patients was most frequently reported, while in LMIC, PR for COPD patients was most frequent. Duration and frequency of treatments reported were also different in LIC and LMIC. Health outcomes on cardiopulmonary function were established in all publications. Results found that the implementation of PR in LMIC is ongoing. The most important barriers to access are the lack of funds and know-how among professional healthcare givers.

Conclusion

Findings suggest that the literature on PR is scarce in LIC and LMIC. Structured or non-structured rehabilitation programs for patients suffering from COPD, HIV and Tuberculosis, are infrequently available. Strategic policy initiatives to diminish barriers and challenges are needed to implement more PR programs in LIC and LMIC.

Background

Low-income countries (LIC) and low-middle-income countries (LMIC) are facing limitations in their healthcare sector funding. Subsequently, pulmonary rehabilitation (PR) is either absent or lacks resources. Studies conducted have found that a cost-effective pulmonary rehabilitation program (PRP) is a multidisciplinary and non-pharmacological approach that decreases hospitalization rates, infection, depression and even mortality. PR has also shown to have benefits in treating diseases other than chronic obstructive pulmonary disease (COPD).

According to the World Health Organization, barriers to access to PR are an important feature of healthcare systems in many countries. Of the 56.4 million deaths worldwide, COPD claimed 3.2 million lives in 2015. To reduce the burden of this disease, PR must be implemented and leading causes of deaths worldwide due to pulmonary diseases must be addressed. The availability of rehabilitation care in pulmonary areas is well described for high-income countries (HIC). In LIC and LMIC, this is still limited and scattered.

The aim of this systematic review is first to identify the evidence on PR availability in LIC and LMIC, and second, to explore the differences between programs’ settings, health outcomes, patients who participated as well as the duration and frequency of PR. Third, to address the different challenges to overcome in implementing PR in LIC and LMIC.

Methods

To identify PR in LIC and LMIC and the barriers to access to such programs, we conducted a systematic literature review. We conducted this review in accordance with PRISMA statement. This protocol for this systematic review was registered on Prospero: CRD42020141655.

Keywords and combinations of keywords (component) were used for the literature search. Search terms included “pulmonary rehabilitation “ or one of its synonyms, namely “pulmonary physiotherapy” and “rehabilitation treatment”; as well as synonyms of “barriers to access pulmonary rehabilitation treatment”; and “LIC” and “LMIC”. Components with the name of each country listed in the new ATLAS' World Bank 2019-2020 fiscal list (Appendix A), were used independently along with the above search components.
We used the above combinations of search terms in each of the following databases: EMBASE, Medline, PubMed, and ScienceDirect. Only research reported in English was included. Articles were selected if published in the period starting from January 2000 till December 2019 (the date of the final search). Abstracts and clinical-case studies were not included. The initial screening was based on article titles and abstracts. The second screening was based on the full text. Articles were categorized as eligible for the review if they reported the presence and features of PR, or access to such programs in LIC and LMIC. If the same author(s) reported the study in different forms, e.g. as abstract or point of view, we only consider the form that presented the most complete information on the study.

Unpublished literature (grey literature) was included and limited to the two first pages on google that cover more recent grey literature for each country.

An additional electronic search was done on selected local websites for countries where literature was unavailable. Specifically, local associations and international organization websites were visited to find records on PR availability in the selected countries, where we found reports on the presence of PR according to the initial databases search. The content selected for the review was analyzed qualitatively following the directed content analysis method. Results were organized in the form of tables complemented by a narrative description of the results. The main themes used in the directed content analysis were: research designs, PR features and access-related challenges in LIC and LMIC. Characteristics of the programs were presented based on the PICO tool. The PICO acronym refers to the population, intervention, comparison and outcomes of a (usually quantitative) article. It is commonly used to identify components of clinical evidence for systematic reviews in evidence-based medicine and is endorsed by the Cochrane Collaboration.

We assessed the research designs of the studies included in the review and their findings in qualitative terms only. We checked the quality of our review using the PRISMA 2009 Checklist (Appendix B).

**Results**

The initial search in the databases provided 21,694 hits for global access to rehabilitation in addition to a set of 7 records for LIC and 50 for LMIC identified through the grey literature search among sources like local organizations of rehabilitation. Hits were then reduced to 351 articles by limiting the search to access to PR specifically. All articles not in English, published before the year 2000 and not related to PR – which added up to 184 articles – were excluded. Thus, 167 records were used in the screening. Of the aforementioned, 84 articles were excluded. Namely, 62 did not cover access, 18 were about tele-rehabilitation, and 4 were excluded for other reasons. Thus, 83 full-text articles remained in the review.

Of the 83 articles assessed for eligibility, we found 47 research articles on PR, which we included in the review and 36 articles were excluded for not covering pulmonary rehabilitation. Of these studies, 20 articles were related to access to PR, 3 articles were related to home-based PR, and 24 articles were related to PR health outcomes. These articles have been selected for this review.

Figure 1 shows the flow diagram of the selection of the studies.

**Study designs reported in the publications reviewed**

The articles in the review showed several methodological issues with small sampling along with poor descriptions of PR data collection and analysis. For example, the PRP was not at a multidisciplinary level, or risk of bias appeared during data gathering.

**Programs reported in the publications reviewed**

All key data gathered through our review have been summarized in two tables. Table 1 presents results for LIC and Table 2 presents results for LMIC. For every country included in these tables, we found studies reporting the absence or presence of PR, including education sessions for healthcare professionals or awareness campaigns about PR for the population.

| Number of studies found | Number of studies selected | References |
|-------------------------|---------------------------|------------|
| Congo, Dem. Republic    | 1                         | 1          | 20         |
| Nepal                   | 7                         | 3          | 21-23      |
| Tanzania                | 1                         | 1          | 24         |
| Uganda                  | 10                        | 3          | 24-26      |

As shown in Table 1, for four LIC – Congo, Nepal, Tanzania and Uganda we found studies that reported on the presence or project of PR. The programs are in outpatients setting in Congo, Nepal and Uganda. A PR program is under implementation in Tanzania as well as in Nepal for...
inpatients. The patients treated are COPD, asthma and post TB in Congo and Tanzania. The duration of the PR is about 12 weeks in outpatient cafe and the frequency of the sessions are 3 times a week in Congo. Three studies (2 RCTs and one qualitative study) report a duration of the program of twice a week during 6 weeks in Uganda. In addition, workshops on the future development of PR have been conducted among physicians in Nepal.

Table 2

| Countries          | N research found | N selected | References |
|--------------------|------------------|------------|------------|
| Bangladesh         | 4                | 3          | 27-30      |
| Egypt, Arab Rep    | 72               | 4          | 31-34      |
| India              | 23               | 8          | 61-69      |
| Kyrgyz Republic   | 3                | 3          | 35-37      |
| Nigeria            | 6                | 2          | 40-41      |
| Pakistan           | 28               | 78-88      | 42-46      |
| Philippines        | 3                | 89-112     | 57-60      |
| Tunisia            | 26               | 113-119    | 52-55      |
| Ukraine            | 39               | 120-125    | 47-51      |
| Vietnam            | 4                | 126-129    | 24,38      |
| Zimbabwe           | 4                | 130        | 24,56      |

Table 2 shows the presence of PR reported in 11 LMIC, namely Bangladesh, Egypt, India, Kyrgyz Republic, Nigeria, Pakistan, Philippines, Tunisia, Ukraine, Vietnam and Zimbabwe. We found 3 types of PR: outpatients, inpatients and home-based. The population treated are mild to severe COPD and post TB patients. Characteristics of the programs presented in Table 1 and 2 are described in the subsequent sub-sections (see Table 3 and 4). We used the PICO framework for every country with the presence of PR to assess the population, intervention, comparison and outcomes of the study found.

Table 3 and 4 also present the individual characteristics of PR reported, including country of origin, pathology of patients attending, program setting type, frequency and duration of a program established with health outcomes.
### Table 3
Review Findings in the Low-Income Courtiers according to PICO's schemas.

| Country   | Reference | Types of setting | Population       | Intervention | Comparison             | Outcomes                                | Study design      |
|-----------|-----------|------------------|------------------|--------------|------------------------|-----------------------------------------|------------------|
| Congo     | 20        | Outpatients      | Asthma + COPD    | PR 12 weeks  | Asthma/COPD            | FEV, QoL, walking distance              | RCT              |
| Nepal     | 21        | inpatient PR project development | Physicians | workshop on future PR development | moderate-severe COPD/CG | dyspnea, QMS, SpO2                       | workshop         |
|           | 22        | Outpatients      | COPD             | 3 weeks PR   | moderate-severe COPD/CG | dyspnea, QMS, SpO2                       | RCT              |
|           | 23        | Outpatients      | COPD             | PR during 12 weeks | moderate-severe COPD | 6MWT, FEV1                             | RCT              |
| Tanzania  | 24        | project of implementation of PR design | TBD (CLD & p-TB) | TBD and implemented | moderate-severe COPD | 6MWT, FEV1                             | project of implementation |
| Uganda    | 24        | Outpatients      | post-TB          | 6 weeks PR, twice weekly PR | TBD and implemented | 6MWD, QoL, sit to stand test            | RCT              |
|           | 25        | Outpatients      | p-TBLD           | 6 weeks-twice weekly PR | p-TBLD | QoL, exercises capacity, respiratory outcomes | RCT              |
|           | 26        | Outpatients      | CLD (=post-TB, HIV, smoking) | 6 weeks, twice weekly PR | qualitative study (interview at baseline) | improvement in functional ability, social and | qualitative study |

- RCT: Randomized Controlled Trial
- Workshop
Table 4
Review Finding in the Low-Middle Income Countries according to PICOs schemas.

| COUNTRY          | References | Study design | Types of setting | Population | Intervention | Comparison | Outcomes                      |
|------------------|------------|--------------|------------------|------------|--------------|------------|-------------------------------|
| Bangladesh       | 27         | RCT          | Outpatients      | moderate COPD | PR during 2 months (30 min HB), twice daily | PR group/CG group FVC and FEV1 of PR group |                       |
|                  | 28         | RCT          | Outpatients      | moderate COPD | PR during 2 months (30 min HB), twice daily | PR group/CG group FVC and FEV1 of PR group | 6MWD, SpO2%, dyspnea and fatigue |
|                  | 29         | Systematic review | Syst Review | LMICs |                       |            |                               |
| Egypt            | 31         | RCT          | Outpatients      | stable ILD | PR 2 months, twice weekly | PR group / CG | dyspnea, HRQoL, exercises |
|                  | 32         | RCT          | Outpatients      | IPF        | PR 2 months, 3x weekly | PR group | dyspnea, HRQoL, exercises |
|                  | 33         | RCT          | Home-based PR & COPD | PR 2 months with HB daily PRP | PR group / CG | 6MWD, HRQL, CRQ-SAS and SF36 scores |                                      |
| Kyrgyz Republic  | 35         | Project | project FRESH AIR | COPD in rural clinic and hospitals |                       |            |                               |
|                  | 36         | qualitative study | qualitative study interview | COPD |                       |            |                               |
|                  | 37         | Project | Adaptation of PR within music, singing, dancing | Post TBLD RCTs |                       |            |                               |
| Nigeria          | 40         | cross-sectional | Physicians Knowledge survey | Physicians | 20 items survey | / | Good Knowledge of PR and willingness to incorporate PR into their scope of care |
|                  | 41         | RCT          | Outpatients      | severe COPD | PR 6 weeks outpatient, twice weekly | PR group | HRQL, Shuttle walking distance, A, D, |
| COUNTRY   | References | Study design | Types of setting | Population | Intervention                                                                 | Comparison | Outcomes                              |
|-----------|------------|--------------|------------------|------------|-------------------------------------------------------------------------------|------------|---------------------------------------|
| Pakistan  | 42         | RCT          | inpatients       | severe COPD | Ga (O2+ medicines), GB (PR with NIPPV + O2+ medicines)                         | GA/GB      | 6MWD, HRQL, PaO2, PaCO2, dyspnea     |
|           | 43         | RCT          | outpatients      | mild to severe COPD | Ga (conventional trt) GB (conventional trt +PR during 4 months G)              | Ga/GB      | GB outcomes > GA outcomes HRQL, Borg, 6MWD, SaO2 |
|           | 44         | RCT          | outpatients      | mild to moderate COPD | HB PR during 7 weeks, 3 times a week                                           | CG (receiving weekly phone calls and PR Group with weekly phone calls) | Nurses can implement PR, encourage and follow patients |
| Tunisia   | 52         | RCT          | Outpatients      |                      | to investigate the effect of neuromuscular stimulation +PR                   | ENMS +PR =G1 and PR=G2 | better 6MWD and balance for G1       |
|           | 54         | RCT          | prospective      | COPD and healthy subjects | to examine the effect of PR on balance in COPD patients and healthy subject | Physical activity increases muscle strength | PR improves TUG, BBS, UST, TINETTI |
|           | 53         | RCT          | Outpatients      | COPD and healthy subjects | to analyze the effect of PR on the balance of anabolic/catabolic hormone | training 3 days/week for 8 weeks | 6MWD in both groups, dyspnea, HR |
|           | 55         | RCT          | Outpatients      | COPD and healthy subjects | to evaluate the impact of 12 weeks PR on 6MWT for COPD and healthy subjects | improvement for both group | PR= 3 times a week during 6 months |
| Zimbabwe  | 56         | RCT          | TB               |                      | to evaluate trt done for TB patients                                         | no PR was ordered and need to be implemented and PR induces an improvement of |
|           | 24         | Project      | project to implement | To implement PR program |                                                                                   |            |                                       |
| Vietnam   | 38         | Project      | fresh air study  |                      |                                                                                   |            |                                       |
|           | 24         | Project      | PR to be implemented |                                                                                   |            |                                       |
| Ukraine   | 47         | RCT          | Prospective study | COPD stage III and IV | analysis of medical records of COPD patients from different areas            | no PR included in the trt plan only drugs |         |
|           | 48         | RCT          |                  |                      |                                                                                   |            |                                       |
|           | 49         | RCT          | TB patients      | PR in different level of TB patients                                           | TB patients | PR need to be ordered in post TB, and during the active phase of TB |

**Notes:**
- RCT: Randomized Controlled Trial
- PR: Pulmonary Rehabilitation
- 6MWD: 6-Minute Walk Distance
- HRQL: Health-Related Quality of Life
- PaO2, PaCO2: Arterial Oxygen and Carbon Dioxide Partial Pressures
- TUG: Timed Up and Go Test
- BBS: Berg Balance Scale
- UST: Unity of Support Test
- TINETTI: Tinetti Balance Confidence Scale
| COUNTRY | References | Study design | Types of setting | Population | Intervention | Comparison | Outcomes |
|---------|------------|--------------|------------------|------------|--------------|------------|----------|
|         | 50         | RCT          | RCT              | CHF & COPD | Conventional trt and as yogic breathing as PR +conventional trt | CG / PR= IG | both group dyspnea, exercise tolerance |
|         | 51         | RCT          | use BODE index to determine PR effectiveness | COPD and Obesity | PR for COPD and obesity patients | diet, Physical exercises need to be added for COPD patients with obesity |
| Philippines | 57   | RCT          | RCT              | COPD <70% mild to moderate | PR (aerobic + strength training exercise) | 9 patients | 6MWD, dyspnea, HRQL |
|         | 58         | RCT          | outpatient       | COPD and Non-COPD patients | PR for 8-week PR | COPD/Non-COPD patients | 6MWD, muscle fatigue and shortness of breath |
|         |            |              | prospective cohort study | stable COPD | stable COPD | stable COPD | better improvement non-copd > copd |
|         | 59         | RCT          | outpatient       | stable COPD | PR for 4-weeks twice weekly | stable COPD | FVC, 6MWT |
|         | 60         | RCT          | RCT care program | stable COPD | PR 4-weeks with additive high-intensity muscle training in PR | stable COPD | HRQL, exercise capacity, inspiratory muscle |
| India   | 61         | RCT          | Outpatient       | CLIPTB* | PR | None | 6MWD |
|         |            |              |                  |            | *CLIPTB= chronic lung impairment post tuberculosis | |
|         | 62         | systematic review | systematic review | COPD |  |  | to stimulate enrollment to PR in India |
|         | 63         | RCT          | Outpatients      | ILD* | PR for 8-weeks | / | 6MWD, Muscle strength, HRQL, Dyspnea |
|         |            |              |                  | stable COPD | PR for 8-weeks | / | 6MWD, HRQL, Dyspnea, exercise capacity |
|         | 65         | cross sectional study | cross sectional survey | COPD | Awareness | / | to increase awareness and education of PR |
|         | 66         | RCT          | Home-based outpatient | COPD | PR for 4-weeks HB | COPD/CG | 6MWD, Dyspnea, fatigue, |
### References

| Study design | Population | Intervention | Comparison | Outcomes |
|--------------|------------|--------------|------------|----------|
| RCT          | COPD II, III level | 30 min exercises twice daily | Yoga group/CG PR | Yoga group dyspnea, fatigue, 6MWD > CG |
| RCT          | COPD       | 1 single session of education, bronchial hygiene, exercises before 6 months to 1-year HB PR | / | health status of the patient |

### Types of Setting

- **Inpatient**: Programs were reported in India and the Philippines. We did not find the exact number of PR settings and their location. It was necessary to visit the website of every rehabilitation program or medical institution to obtain the essential data for this review. India has a Lung Center as well as associations for cardiovascular treatment and PR for inpatients and outpatients. In India, we found an "Indian Association of Respiratory Care" (IARC) in Amrita Hospitals in Delhi, as well as a Lung India journal which is the official publication of the Indian Chest Society.

- **Outpatient**: Studies conducted in Uganda and Zambia have shown that the most common PR setting is outpatient care. In Congo, India, Egypt, the Philippines, Nigeria, and Tunisia, most of the programs are available in an outpatient setting. Specifically, in Kinshasa, 38 patients in two hospitals were treated who had bronchial asthma (n=14) and COPD (n=24). Patients were treated three times a week for twelve weeks. COPD patients improved their FEV1 significantly compared with asthma patients.

- **Home-based**: PR was reported in Egypt and India. In Egypt, a study evaluated the effect of a two-month, home-based program with outpatient supervision every two weeks, with tolerance exercises and health-related quality of life (HRQOL) using Arabic-translated generic and specific questionnaires in 39 COPD patients. The two-month home-based PR was found to be an effective non-pharmacological intervention for COPD patients due to health outcomes on the quality of life and better cardiopulmonary function.

An Indian study incorporating 6 weeks of home-based PR was effective in increasing exercise endurance in patients with lung infections. Another Indian study evaluated the effect of home-based PR in COPD patients in rural areas, including 40 patients who completed the PR and 20 who were excluded in PRP which composed the control group. Results showed that the 6MWT had an average increase of 75.72 meters in the study group, while an average decrease of 2.1 meters in the control group. Results were statistically significant (p<0.005).

In another Indian home-based study of forty patients of stable COPD having severe airflow obstructions were divided into control and experimental groups randomly. Exercises of 30 minutes duration were performed at home twice daily for four weeks with supervision. Domiciliary PR for four weeks results in significant improvement in the quality of life and exercise tolerance, even without improvement in Force Expiratory Volume in one second (FEV1).
Patients attending PR

In Uganda, patients-participants included lung tuberculosis (TB), HIV but not COPD\textsuperscript{24–26}. Results of the studies reviewed suggest most of the patients treated are suffering from respiratory diseases like COPD in Congo, India, Philippine, Nigeria, and Tunisia\textsuperscript{20,22,23}. In Tunisia, in a study on COPD patients, the intervention group underwent balance training 3 times a week for 6 months in addition to the standard PR. The control group received 6 months of the standard PR only. Balance-training incorporated into a standard PRP significantly improved balance test score in COPD patients\textsuperscript{53,54}.

Frequency and duration of the program

In Uganda, PR duration varied from 4-8 weeks for patients who are HIV infected\textsuperscript{24–26}. The program's frequency varied from 2-4 weeks and the program length of stay diverged from 4-24 weeks.

In Ukraine, the results of a study showed that PR should be applied at all disease stages, starting at the stationary phase and continuing during the outpatient and homecare phases. A recommendation of this study was that the session's exercise duration should be no more than 30 minutes 3–5 times a week for 8–12 weeks [49].

In India, PR was available of different durations and frequencies according to the program setting, phase and medical establishment's policy\textsuperscript{60–69}. Also, in Maghreb and in Tunisia, one study done on COPD men who were clinically stable and underwent PR one session per day twice a week for eight weeks reported improvement\textsuperscript{55}.

Health outcomes

Evidence on health outcomes established in studies reviewed was based on 6MWT, FEV1, and the Quality-of-Life questionnaire. As previously mentioned in Kinshasa, after the rehabilitation program, COPD patients improved their FEV1 score significantly compared with asthma patients\textsuperscript{20}.

In Nigeria, anxiety and depression levels have been assessed, and an outpatient program for the rehabilitation of patients with severe ventilatory impairment due to COPD was conducted. Patients entered a 6-week outpatient program during which they attended twice weekly 2.5-hour sessions. There was a significant reduction in the depression and patients' anxiety levels after the program. Walking distance also improved significantly and was maintained at the improved level for six months\textsuperscript{41}. A cohort study was conducted in Philippine, a 6MWT as well as a symptom-limited exercise testing was done at baseline and at the end of the eight-week program. After an 8-week rehabilitation program, results showed an improvement in exercise tolerance, shortness of breath and muscle fatigue in patients with pulmonary diseases throughout the studied population, according to the Philippines association of cardiovascular rehabilitation\textsuperscript{58}.

Awareness campaign and education initiatives about PR

In countries where PR is not reported yet, we found awareness programs and/or education sessions for healthcare givers and for the population. Awareness campaigns aimed to increase healthcare providers' education to implement and refer patients to the program when efficient. Results showed that PR is highly recommended in Madagascar, Rwanda, Senegal, Tanzania and Zimbabwe\textsuperscript{24}. In addition, some projects on PR's are in process in Africa.

In Nepal, the internal medicine society organized a workshop on PR in August 2016 to educate professional healthcare providers and physicians about the importance and benefits of PR\textsuperscript{21}. In addition, SOLID Nepal, a community-based pulmonary health support a project for 3 years and a COPD control-Promotion of comprehensive PR was established in February 2019. This project was implemented in the Bhaktapur district and the purpose of this project was to improve quality of life of COPD patients by providing PR to the population\textsuperscript{24}.

In Bangladesh, the engagement of stakeholders can improve research prioritization, implementation, and outcomes. The organization of stakeholder engagement aimed to support the implementation of PR for patients with chronic respiratory diseases\textsuperscript{27–29}. Raising awareness of the benefits of PR between stakeholders is a step forward in the implementation of PR. Understanding the views of patients, public health officials, policymakers, politicians, religious leaders help to create support for PR.

In India, a cross-sectional survey was executed to evaluate awareness through a COPD-awareness questionnaire\textsuperscript{65}. Also, studies show that PR was going to be implemented in Rwanda, Senegal and Zimbabwe for HIV-infected patients\textsuperscript{24}.

Overall, studies concluded that patient-awareness campaigns enabled patients to acquire better self-management skills, helped reduce the severity and frequency of disease's exacerbations, prevents hospitalizations and improved the patients' HRQoL.

Barriers to access PR

In Zambia, a research team developed the international rollout of a larger evaluation trial, which incorporated centers in Uganda, Tanzania and Zambia\textsuperscript{24}. In Nigeria, a study conducted by Akinremi et al. sought to investigate physicians' knowledge and perceived barriers to PR in Nigeria. Five
top barriers to PR identified included unavailable/insufficient rehabilitation specialists, lack of rehab equipment, non-availability of institutionalized documented PR protocols, inadequate training on PR and cost of care to patients\textsuperscript{40}.

Discussion

This paper has reviewed the evidence on PRP in LIC and LMIC. Additionally, it has outlined differences in PRP in terms of duration and frequency. Barriers reported in this study are not limited to one type or context, and extend to individual, health, financial and environmental factors. PRP are most frequently established under medical supervision in an “outpatient center” design program in LMIC.

In LIC, we observed that the average duration of the programs varied from 4-8 weeks for patients treated, who were HIV infected patients. In LMIC, the frequency of PRP reported, differed from 2 to 4 weeks. A program length of stay (duration) diverges from 4 to 24 weeks in LMIC.

According to one study, PR in HIC and LMIC has a median length of 9 weeks with 2.5 sessions a week. The duration of each session is between 1-2 hours per session. Most of the programs in Europe and the USA are also outpatient\textsuperscript{70}.

According to our results depicted in Table 1 and 2, we found health outcomes on HRQOL and 6MWD in 2 LIC as well. Additionally, in LMIC, we found more health outcomes on cardiopulmonary function.

Barriers to access to pulmonary rehabilitation programs

We found that PRP reported in LIC and LMIC, vary widely in terms of duration and location\textsuperscript{71}. PR faced four major barriers, which include individual, financial, organization of healthcare and environmental barriers. Individual barriers, including cultural factors, lack of information about diseases and treatments, self-management underuse, over-reliance on pharmacological care, and use of unproven alternative therapies, act as a determinant for the patient’s adherence to the program in low and middle-income countries. In addition, no covering of the program by the local government and no funds to implement PR is a major barrier to overcome in LIC and LMIC.

Patients’ health status is a major barrier to adherence. Disease severity plays a significant role and influences attendance and adherence to PR in every country. The level of the disease (use of long-term oxygen therapy) and COPD exacerbation are important limitations to their attendance\textsuperscript{71}. Current smokers tend to be less inclined to adopt health promotion behaviors which is a strong predictor of both attendance and adherence to PR\textsuperscript{72}. In LIC, patients who lived alone were less likely to attend PR\textsuperscript{73}.

In HIC, PR benefits are correlated with smoking status (active-smoking), depression, lower levels of social support, female gender, FEV\textsubscript{1} and low HRQOL and extremes of age of patients are important determinants of joining the programs\textsuperscript{72,73}. The demographic feature of the patient, such as mobility conditions, longer traveling distance to reach hospitals and location to the rehabilitation’s clinic are the most important reasons for adherence.\textsuperscript{71} Graves et al. found that patients living further than 25 minutes from a PR center were less likely to attend a PR education session while patients were more likely to adhere to a program if they lived closer to PRP in every country\textsuperscript{74,75}.

In LIC and LMIC, the most common barriers found are at a financial level, including poverty, poor education, and infrastructure or no clinics due to a lack of public health priority, implementation costs of PR, and lack of data on morbidity and mortality for every country on pulmonary diseases. Unsustainable generalizations across cultures and healthcare systems explain why management guidelines developed in HIC are difficult to implement in LIC and LMIC. The lack of funds and ineffective governance do not support the implementation of programs and building outpatient rehabilitation programs. Also, no reimbursement is available in LIC and LMIC, which complicates the attendance and adherence to the program if a center does exist.

The final inherent barrier is the organization of healthcare services. Professional healthcare providers are the main referrals and need awareness and training about PR to limit the use of basic medications and start sending patients to PRP in LIC and LMIC. Poor education of referrals on the management of COPD, non-existence of supply and distribution infrastructure are important barriers to the program.

Comparison with studies in HIC

Literature on PR in HIC is more significant and much larger compared to that in LIC and LMIC. Plenty of national surveys, international reviews, and meta-analyses have been conducted in HIC. For example, in 2014, one study reviewed differences in the content and organizational aspects of PR in HIC. A 12-question survey was completed by PR representatives of 430 centers from 40 countries from Europe (43.7%) or North America (43.5%). Findings demonstrated large differences among PR across continents in all surveyed aspects, including the setting, case-mix of individuals with a chronic respiratory disease, the composition of the PR team, completion rates, methods of referral and types of reimbursement.

In the US, there are over 230 PR (copdfoundation.org). In Canada, a report from the Canadian Thoracic society conducted an online survey in all the hospitals to identify PR, which also confirms the high availability of PRP. In HIC, HRQOL, 6MWT and dyspnea are identified as the three most important outcomes.
An important challenge to add: is the implementation of PR in LMICs during the Covid-19 pandemic. The presence of cost-effective programs will be an added value to Covid-19 survivors. A home-based PRP may overcome barriers in the treatment post coronavirus in LIC and LMIC countries. A call of action is needed to implement PR in LMICs with the help of HIC’s experts.

**Strength and limitations of the review**

Our results are bound by certain limitations as well as supported by strengths. A major limitation is that for a lot of countries, information is unavailable. For 28 LIC and 49 LMIC we were unable to find any information. Another limitation was the exclusion of non-English literature, which means that some relevant publications from non-English speaking countries and might have been excluded in this review. The financial barrier in LIC that bounds the implementation of PR centers and training of professional healthcare providers is another limitation. Additionally, PR might be implemented in some countries but not analyzed and reported in the literature. The risk of bias across studies included a lack of researches conducted in LIC, especially in LMIC.

**Conclusion**

Our review shows that only a few studies are available for LIC and LMIC on PR, especially on access to such programs. Literature is thin or nearly “absent”. Evidence on access to PR and barriers faced by patients is also sparse. There is a need for research in this area to provide evidence for policies to decrease the burden of pulmonary diseases and to prevent infections, thus, increasing quality of life and health of patients. This review shows that there is evidence on the efficacy of PR in the management of persons living with HIV and AIDS in developing countries, COPD patients and Covid-19 survivors. For other patient’s groups, these are absent, indicating gaps in research. “A call for action” and imperative invitations for funds are required to decrease the burden of diseases and increase the quality of life of suffering patients in LIC and LMIC.

**Abbreviations**

COPD: chronic obstructive pulmonary diseases
ERS: European Respiratory Society
PRP: Pulmonary Rehabilitation Program
PR: Pulmonary Rehabilitation
HRQoL: Health related Quality of life
QoL: Quality of life
LIC: Low-income country
MIC: Middle-income country
Trt: treatment
LMIC: Low-Middle-income country
HIC: High-income country
TB: Tuberculosis
CLD: Chronic Lung Disease
WHO: World Health Organization
AACVPR: American Association of Cardiovascular & Pulmonary Rehabilitation
GOLD: Global initiative for Obstructive lung disease
FEV1: FEV1 is the maximal amount of air you can forcefully exhale in one second.
6MWT: a six-minute walking test
6MWD: six-minute walking distance
SGRQ: ST GEORGE’S RESPIRATORY QUESTIONNAIRE
Declarations

a) Ethics approval and consent to participate: Not Applicable. The protocol for this systematic review was registered on Prospero: CRD42020141655.

b) Consent for publication: Not Applicable

c) Availability of data and materials: All data generated or analysed during this study are included in this published article [and its supplementary information files].

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RF conducted the analysis of the literature

RF, WG, MP prepared tables and figures

RF, WG, MP wrote the main manuscript text

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h) Authors’ information (optional)

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