

## SAFETY AND EFFICACY OF PULMONARY REHABILITATION FOR INDIVIDUALS IN HOSPITAL WITH AN ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

### PODCAST SCRIPT

---

Hi everyone and welcome to another episode of LungFIT. Today I want to talk about a paper that we recently published in the Annals of the American Thoracic Society. This paper was a very long time in the making, it was an idea that I had probably, I don't know, about 5 or 6 years ago, when the Puhan's Cochrane review of pulmonary rehab at the time of an acute exacerbation was published. I realized that *that* review looked at pulmonary rehab across the, what I would call, the full spectrum of an AECOPD – during an admission, during recovery, and then the time after. That was interesting and certainly set the stage for pulmonary rehab as a treatment during this very unstable part of a patient's natural history. Of course historically pulmonary rehab was seen as a necessary treatment but a requirement was often that patients had to be stable to get rehab. The Cochrane review provided some clarity on the outcomes and safety, but because it focused on the full spectrum of an AECOPD, from initial flareup to recovery and beyond, it was hard to have an appreciation for its safety and effectiveness at each stage of that exacerbation.

I have always had a little dream of establishing widespread acute care pulmonary rehabilitation in Canadian hospitals. I think it would offer an amazing educational experience for clinical trainees and potentially have an enormous impact on patient outcomes. So it was important to me to explore and look at the evidence regarding safety and effectiveness of pulmonary rehab for people with COPD whose exacerbation was so severe it warranted hospital admission. Of course the Puhan paper provided some information but didn't provide results specifically for the inpatient period. So I decided to do a systematic review that would do just that, look at both efficacy and safety of pulmonary rehab during the hospital stay period of an AECOPD.

So the idea percolated for awhile, and some students got started on it but weren't able to continue, and we ran into some technical problems, and of course it wasn't funded so we had to limp along with it, even considered abandoning it several times! But I wanted to persevere, because it was a good idea, it hadn't yet been done by others so the need was still there, and I guess we had already invested so much time and energy into it it was just too difficult for me to walk away 😊

We had a few new staff and students come into the lab, which provided the people power we needed. Debora Petry Moecke is a physical therapist and PhD candidate in my lab, and she took up the challenge of providing the day-to-day involvement and analysis for this project, and is the first author of this paper.

So what did we do? We first conducted a systematic search of the literature for randomized controlled trials or RCTs and for this we cast a very wide net. We focused on RCTs because we are looking at both efficacy (or, did it work?) and safety (is there a risk of harm?). And RCTs are the studies which have less risk of bias so they are appropriate for this type of review. And why did we cast a wide net, using a very broad search strategy? The reason is that there was a question of safety we needed to answer. These patients are very sick, sick enough to be hospitalized for an AECOPD. And the intervention is, in part, exercise, so we need to know what the exercise was, and confirm it did not result in adverse events. So

we really wanted to look at as many RCTs on exercise during hospitalization for an AECOPD as we could. Our inclusion criteria was: patients greater than 19 years hospitalized with an AECOPD, and capable of initiating any form of active movement (even if this was bed mobility exercises). So not patients sedated or not able to independently, at least partly, move their arms or legs. And what did we can pulmonary rehab? We considered any intervention that involved mobilization, exercise, or ambulation, of at least 2 sessions. We included studies that continued the rehab after discharge, as long as there was a baseline measure and a hospital discharge measure of outcomes. So we are really just looking at the outcomes of a rehab intervention provided during the hospital stay. We didn't look at studies that focused solely on respiratory muscle training, or neuromuscular stimulation as the only rehab intervention.

There needed to be a control group of usual care, and we were interested in any outcomes that were measured.

So we conducted the search, then two people reviewed titles and abstracts with a third person making the decision if there was a lack of agreement. Two people then reviewed the full texts, with the third person making the final decision if there was lack of agreement. Often there was a discussion about any paper where there was difficulty making the decision. Then we abstracted data from each paper, as well as evaluated each study for risk of bias. We did seek out abstracts and contacted the authors for more information if there was not enough detail to conduct the analysis. We also contacted authors of published papers for further information when warranted. The studies were described in narrative format, and we also conducted a meta-analysis of data where we could, to be able to make statements regarding efficacy and different outcome measures.

And, drum roll, what did we find? Our wide net search resulted in many many thousands of papers retrieved, of which 393 full text papers were reviewed and 27 records retained for analysis. Papers were published from 1998 to 2022, with almost half published within the last 5 years. The studies together recruited just over 1300 participants. Most patients started rehab by the 3<sup>rd</sup> day of their hospitalization, with 8 studies delivering an aerobic intervention, 5 a resistance training program, 10 had both, and 4 not specifying.

A common outcome used in these trials was the 6 minute walk distance. We found that inpatient PR improved 6MWD by 105 meters which far exceeds the minimally clinically important difference of 30m. The 5 repetition sit-to-stand test was also used by several studies, and the meta-analysis showed that inpatient PR improved it by 7 seconds. Interestingly though, there was no difference between groups with the studies that used the 30 second sit to stand.

What about quality of life? We found that inpatient pulm rehab improved several subscales of the EuroQoL Group-5 dimension measure, including mobility, self-care, and usual activities. However, there was no difference in quality of life when looking at the COPD Assessment Test.

When looking at length of stay, we found no difference in length of stay between those who received and those who did not. So it didn't shorten the length of stay, but didn't lengthen it either.

And one of the most important questions, was there a safety risk? This has been a concern with rehab for people with an AECOPD when they are not in the hospital – are there also safety concerns while they are in the hospital and very unstable. 15 studies reported adverse events, which was 797 people, and 1

study did report an adverse event – an episode of arrhythmia which resolved within an hour of the rehab session ending.

Why was this review important? Well, there had been a bit of a cloud over pulmonary rehab during an AECOPD, based on the results of a study done a few years back. In that study, they had no adverse events during the in-hospital period, but once patients were discharged and exercising independently, the exercise group had higher mortality. There wasn't really any supervision of the exercise group, and actually we have seen this phenomena before, of a higher mortality with patients who are self-managing. It might be that some patients who would normally seek medical attention do not do so when they are in a self-management or self-exercise research study. That's just speculation of course, I don't know the reason why, but regardless that 'cloud' of patient harm has followed pulmonary rehab for AECOPD, to the point where some papers actually warned against it.

Which I have to say, I couldn't understand. I mean, we have seen very strong evidence about early mobilization programs for ICU, and other rehab programs in acute care, such as for patients with stroke or cardiac issues. Are patients hospitalized with an AECOPD less stable than these patients? I don't know, but the highly supervised environment of acute care seemed to me to be a place where carefully assessed AECOPD patients prescribed an individualized exercise program could see improvements in their physical function and quality of life without undue risk. And this systematic review provided evidence to support the safety and efficacy of pulmonary rehab for the hospitalized AECOPD patients.

Now, what we can't do is try to say, well that means it would have the same benefits outside the hospital. As I've mentioned, hospitals are highly supervised places with excellent monitoring equipment, and highly trained staff. This is not the home or community environment. So to understand the safety and efficacy of pulmonary rehab outside of the hospital setting, we need to look at data from the hospital discharge moment onward. That work is now just being done and will be published, stay tuned on more news on that.

You might be asking why we do systematic reviews? I mean, weren't there 27 studies that basically showed these results. And the answer is – not exactly. It can be difficult to recruit patients for these studies, and as many of us know, research on COPD is woefully underfunded. We don't get big trials with 1000s of patients like other disease condition trials do. So oftentimes studies, with a small sample size, don't show differences between groups on important outcomes like physical function or quality of life. But when you take a bunch of little trials, and then using the process that I've described here, where you select them carefully, take their results, and combine them with powerful statistical tools, you can see the effect of an intervention where maybe a small trial wasn't big enough to show.

Will this study change care? Well, I hope so. At the very least I hope we can remove the 'cloud of suspicion' about the safety of pulmonary rehab during the hospitalization phase of an AECOPD. And we probably need more research for a further look at other outcomes – such as, does providing this care in hospital reduce the risk of readmission? Are people able to recover more quickly at home if this rehab was provided in hospital? Should we be focusing more on aerobic exercise, to get people ambulating easier, or should we focus on strength, knowing how much muscle mass is lost when people are on bedrest or more sedentary? And how can we work toward more inpatient rehab for AECOPD? How does this patient population compare to others who come to hospital with an acute event (such as those with stroke or myocardial infarction)? Is there an equity issue here – are AECOPD patients treated with the

same urgency? Lots of questions, but hopefully we can advocate more strongly for the need for this care, based on the results of this systematic review and the RCTs involved.

Thank you for listening to this episode, and to the many people who supported this systematic review over the years. Definitely a great team effort, and an important message for those of us in pulmonary rehab.

See you on our next episode!