Title: Effectiveness of exercise therapy and self-management education to improve physical activity levels in patients with acute exacerbations of chronic obstructive pulmonary disease: protocol of a systematic review and meta-analysis

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1. Introduction

Chronic Obstructive Lung Disease (COPD) is a preventable and treatable disease characterized by persistent respiratory symptoms and airflow limitation due to abnormalities of the airways and alveoli (1). The most common respiratory symptoms are dyspnea, cough, and sputum, but these symptoms are not always present (1). Decreased physical activity (PA) in COPD occurs even before symptoms such as dyspnea or the diagnosis is made (2), and PA is lower than in diseases with obstructive ventilation disorders such as bronchial asthma and bronchiectasis (3). Previous cohort studies have shown that low PA is the greatest risk factor for death in COPD patients and is more strongly associated with prognosis than exercise tolerance (4). In addition, because of the association with mortality and acute exacerbations (5), the Japanese Respiratory Society guidelines include "improvement and maintenance of exercise tolerance and physical activity" as one of the six goals (6).

A previous study reported that patients with acute exacerbation of COPD (AECOPD) had significantly lower PA during hospitalization and after discharge compared to patients with stable COPD, and patients with lower PA after

discharge were more likely to be readmitted (7). Respiratory rehabilitation for patients with COPD can be started as early as possible after hospitalization and has been reported to be safe and effective (8,9). Therefore, we believe that therapeutic management to promote PA is necessary during hospitalization and after acute exacerbations. Exercise therapy and self-management education, when used in combination, have been mentioned in previous studies (10,11) as possible ways to improve PA. In two systematic reviews of patients with stable COPD (12,13), the methodological and evidence quality was very low to moderate, although there was an effect on PA improvement, and the evidence for exercise therapy and self-management education in improving PA was limited.

Although Pitta et al. (7) suggest that "improving PA should be a part of disease management for AECOPD patients," the evidence for improving PA in AECOPD patients is still sparse, and there is no strong evidence of a positive impact on PA. The present review aims to evaluate the effectiveness of exercise therapy and self-management education in improving PA in patients with AECOPD. And to provide directions for future research.

2. Research question

To evaluate the effectiveness of exercise therapy and self-management education in improving PA in patients with AECOPD. And to provide directions for future research.

P: AECOPD patients

I: 1) Exercise therapy

2) Self-management education

3) Exercise therapy and self-management education

C: usual care

O: steps per day, moderate to vigorous physical activity (MVPA), sedentary behavior (SB)

3. Method

3.1 Protocol

We have followed the preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 in preparing this protocol. We plan to publish this protocol on protocols.io (https://www.protocols.io/).

3.2 Inclusion criteria for articles in the review

3.2.1 Study type

We plan to include all randomized controlled trials (RCTs) of exercise therapy and self-management education, or intervention alone, designed to improve PA in patients with AECOPD. As for the assessment tools for PA, if we use subjective tools such as the International Physical Activity Questionnaire (IPAQ), recall bias may affect the results (14). Therefore, we will only include studies using objective tools such as pedometers and accelerometers.

Include studies reported as full-text, studies published as abstracts only, and unpublished data. We will not include Crossover RCTs, cluster RCTs, and non-RCTs. Any language, country, or follow-up period is acceptable.

3.2.2 Study Participants

We define the target population as those diagnosed with COPD according to established criteria (GOLD guidelines (1) and expert consensus) and with COPD after hospitalization or outpatient treatment for an acute exacerbation. In addition, age, gender, race, and severity of the disease are irrelevant. We plan to include studies with a mix of patients with multiple diseases when data are available for AECOPD patients individually or when many study participants are eligible.

3.2.3 Intervention

We plan to compare exercise therapy and self-management education designed to improve PA, or intervention alone, with usual care. Exercise therapy may include either total body endurance training or strength (resistance) training. We will also include studies conducted as part of a comprehensive respiratory rehabilitation program that includes exercise therapy and other components. Self-management education includes goal setting and action-planning practices, educational

programs, coaching, activity counseling, diaries, feedback, self-monitoring, and telemonitoring using the Web and smartphones. These could be supervised or unsupervised. These interventions must have been initiated within 3 weeks of the onset of AECOPD or within 2 weeks of hospital discharge (1,9,15,16) and can be of any intensity, duration, or frequency.

3.2.4 Control

We will assign usual care as the control. We will also treat expressions such as "no intervention," "placebo," and "control" as identical when we integrate them.

3.3 Types of outcomes

3.3.1 Primary outcomes

Include outcomes that reflect PA objectively measured using a pedometer (e.g., StepWatch) or accelerometer (e.g., ActiGraph, ActivPAL).

1. steps per day
2. MVPA
3. SB

We plan to measure the main outcome at baseline (before the start of the intervention) and the end of the intervention and will use the change in PA from baseline in our analysis whenever possible. For outcomes measured in multiple periods, we will use the one closest to the end of the intervention. In addition, outcomes reported at the end of the intervention will be categorized as short-term (within 3 months), medium-term (3-6 months), or long-term (>6 months). If the outcome of interest is inadequately reported, we plan to ask the study authors to provide the raw data whenever possible.

3.3.2 Secondary outcomes

1. Quality of life (QOL): SF-36® (MOS Short-Form 36-Item Health Survey), COPD Assessment Test (CAT), St. George's Respiratory Questionnaire (SGRQ)
2. Dyspnea: Modified Borg Scale, Baseline Dyspnea Index (BDI)
3. Exercise capacity: 6-minute walk test, shuttle walking test
4. Adverse events (e.g., musculoskeletal injuries, falls, re-exacerbations,

rehospitalizations, etc.) that occurred during the study period

We plan to measure secondary outcomes at baseline (before the start of the intervention) and the end of the intervention and will use the change in PA from baseline in our analysis whenever possible. For outcomes measured in multiple periods, we will use the one closest to the end of the intervention. In addition, outcomes reported at the end of the intervention will be categorized as short-term (within 3 months), medium-term (3-6 months), or long-term (>6 months). If the outcome of interest is inadequately reported, we plan to ask the study authors to provide the raw data whenever possible.

3.4 Search method

3.4.1 Electronic search

Search the following databases:

1. Cochrane Central Register of Controlled Trials (CENTRAL) via Cochrane Library;
2. MEDLINE via PubMed;
3. Cumulative Index to Nursing and Allied Health Literature (CHINAHL) via EBSCOhost;
4. Web of Science;
5. Physiotherapy Evidence Database (PEDro).

As for the search formula for participants, we used the one in the previous Cochrane review (12) as a reference. We used the RCT filter described in the Cochrane Handbook (17) to narrow the search to studies with high comparability. Refer to Appendixes 1, 2, 3, 4, and 5 for search methods.

3.4.2 Other resources

We will search for unpublished and ongoing clinical trials on ClinicalTrials.gov (www.clinicaltrials.gov) and the International Clinical Trials Registry Platform (ICTRP, http://apps.who.int/trialsearch/). We will also review the reference lists of all major studies and search for additional references. In addition, we will search for references in the following guidelines (Guidelines for COPD and Guidelines

for PA).
Guidelines for COPD: COPD (Chronic Obstructive Pulmonary Disease) no sinndann to tiryou notameno gaidorain 2018 (in Japanese), rigakuryouhou gaidorainn, Second Edition (in Japanese), GOLD Report, COPD Exacerbations: An Official ERS/ATS Clinical Practice Guideline Implementation Tools, Pulmonary rehabilitation: joint ACCP/AACVPR evidence-based clinical practice guidelines.
Guidelines for PA: WHO Guidelines for Physical Activity and Sedentary Behavior (Japanese version), Physical Activity Guidelines for Americans 2nd edition.
We will be contacting each researcher to obtain the necessary data.

3.5 Data collection and analysis

3.5.1 Selection of studies

Two reviewers (K.Y. and M.T.) will independently select titles and abstracts for all studies identified because of the search and code them as either "eligible" (eligible or possibly eligible/unknown) or "exclude". Two reviewers (K.Y. and M.T.) will obtain the full text of the research articles, screen each independently, identify studies to be included, and identify and record reasons for excluding ineligible studies. We plan to resolve any disagreements through discussion or, if necessary, consultation with a third reviewer (TN). We plan to identify and exclude duplicate studies and to collate multiple articles of the same study so that each study, rather than each article, is the unit of review. We will ensure that the selection process is documented in sufficient detail to complete the PRISMA flow diagram and the "Characteristics of excluded studies" table (17).

3.5.2 Data extraction and management

We will record study characteristics and outcome data using a data extraction form (Windows Excel) that has been piloted in at least one of the included studies in this review. Two reviewers (K. Y. and M. T.) will independently extract the following study characteristics from the included studies:

・method: author, journal (or research source if unpublished), year of publication, research design, and research setting;

・Participants: number, mean age, age range, gender, disease severity, baseline lung function, smoking history, inclusion criteria, exclusion criteria, and withdrawals;
・Intervention: intervention (type, frequency, intensity, duration), comparison;
・Evaluation method;
・ outcomes: change in daily steps, MVPA, and SB before and after the intervention.
We plan to resolve any disagreements through discussion or by consulting with a third reviewer (T.N.). We plan to note in the table of the data extraction form if the studies collected do not report outcome data in a usable manner. We will contact the authors of the papers to verify the extracted data where appropriate and will provide details of missing data where possible. One of the reviewers (K.Y.) will transfer the data to the Review Manager file (RevMan 5.4). We will compare the data in the data extraction form with the data in the paper to double-check that the reviewer has entered the data correctly. A second reviewer (M.T.) will check the study topically against the paper to see if the features of the study are accurate.

3.6 Assessment of risk of bias in included studies
Two reviewers (K.Y. and Y.K.) will independently assess the risk of bias for each RCT included, using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions (18). We plan to resolve any disagreements through discussion and the involvement of a third reviewer (T.N.). We will assess the risk of bias in the following areas:
(1) bias arising from the randomization process;
(2) bias due to deviations from intended interventions;
(3) bias due to missing outcome data;
(4) bias in measurement of the outcome;
(5) bias in selection of the reported result.
We will categorize potential sources of bias as either "high risk of bias," "low risk of bias," or "some concerns," and provide excerpts from the articles along with the rationale for the judgments. We will summarize the "risk of bias" judgments across

studies for each of the areas listed and summarize the results in a "risk of bias" table. We will consider blinding separately for different main outcomes (e.g., patient-reported outcome measures may differ significantly in the assessment of unblinded outcomes). When examining treatment effects, we will consider the risk of bias in studies that contribute to this outcome.

We will conduct our review according to the protocol and report any deviations in the "protocol and review differences" section of the systematic review.

3.7 Measures of treatment effects

We will analyze the data for each outcome regardless of reported participant dropout (intention-to-treat analysis).

We will combine data using meta-analysis if the data within an intervention are sufficiently clinically similar in terms of the nature of the intervention, outcome, and measurement time point. We will analyze binary data as odds ratios and 95% confidence intervals (hereafter CI). We will calculate the mean difference (MD) or standardized mean difference (SMD) and 95%CI for continuous data and use median and interquartile ranges to describe the others.

We will only list the relevant intervention group if there are multiple intervention groups in a single study. If we combine two comparisons (e.g., intervention A vs usual care, intervention B vs usual care) in the same meta-analysis, we will halve the control group to avoid double-counting.

We plan to relate the estimates and 95%CI to the Minimal Clinically Important Difference (MCID) for each outcome whenever possible. We will assess whether the estimates and 95%CI of the difference between the study groups exceed the MCID or represent an important effect (e.g., the MCID for steps is 600 steps/day (19)).

3.8 Unit of analysis issues

We plan to consider the participant as the unit of analysis in studies in which individual participants are randomly assigned to intervention groups.

3.9 Dealing with missing data

We will contact the principal investigator when data are missing, confirm key study characteristics, and obtain missing numerical outcome data when possible (e.g., for studies reported only as abstracts).

3.9.1 Missing outcomes

We plan to conduct sensitivity analyses to analyze the impact of including such studies in the overall results if missing data are not available and if the missing data may be related to the intervention.

3.9.2 Missing statistics

We will calculate the standard deviation based on Altman's method when only the standard error or p-value is reported in the original paper (20). We will calculate standard deviations with t-values and CI using the methods in the Cochrane Handbook for Systematic Reviews of Interventions (18) or validated methods (21) when these values are not known after querying the authors. These methods will be validated by sensitivity analysis.

3.10 Assessment of heterogeneity

We will check for between-test heterogeneity using Cochran's Q test in each analysis. In addition, we will use the I^2 statistic to calculate the proportion of the variability in the test results that is explained by "between-test heterogeneity" and will consider $I^2 \geq 50\%$ as substantial heterogeneity. If statistically significant heterogeneity is found, we will report it and investigate the cause by pre-specified subgroup analysis.

3.11 Assessment of reporting bias

We plan to conduct an extensive literature search for unpublished clinical trials by accessing clinical trial registries (ClinicalTrials.gov and ICTRP). When we have

gathered more than 10 eligible trials, we will create funnel plots and analyze them for small trials and possible publication bias.

3.12 Meta-analysis

We plan to conduct the meta-analysis using Review Manager software (RevMan 5.4) with a random-effects model.

3.13 Subgroup analysis

We plan to conduct subgroup analyses of the primary outcome based on the following factors once sufficient data are collected to illustrate the effect of effect modifiers on the outcome:

1. Age (< 64 years vs. 65 years or older) (22).
2. Duration of intervention (< 3 months vs. > 3 months) (10).
3. Disease severity (mild disease (defined as %FEV1 ≥ 80%) vs. moderate to most severe disease) (23).

3.14 Sensitivity analysis

We plan to examine the effect of methodological quality on outcomes by excluding studies with a high risk of bias in the areas of bias due to the randomization process and bias due to missing outcome data, given sufficient data for the main outcome. We defined "high risk" as studies with inadequate allocation concealment or random allocation and missing data of more than 20% (24). We also plan to examine the effect of excluding studies in which patients with multiple diseases are included.

4. Summary of findings table

We will create a "Summary of findings" table using the following outcomes:

1. PA: steps per day, MVPA, SB;
2. QOL: SF-36®, CAT, SGRQ;
3. Dyspnea: Modified Borg Scale, BDI;
4. Exercise capacity: 6-minute walk test, shuttle walk test;
4. Adverse events (e.g., musculoskeletal injuries, falls, re-exacerbations,

rehospitalizations, etc.) that occurred during the study period.

We will use the five GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) considerations (risk of bias, inconsistency, imprecision, nondirective, and publication bias) to assess the certainty of evidence associated with studies that provided data for a meta-analysis of prespecified outcomes. We plan to use the GRADEpro Guideline Development Tool software (GRADEpro GDT 2014) with the methods and recommendations described in the Cochrane Handbook for Systematic Reviews of Interventions (18). We will justify any decision to downgrade against the certainty of evidence with footnotes and, where appropriate, provide comments to aid the reader's understanding of the review. We have chosen not to include studies published only in abstract form or data from clinical trial registries because of inadequate assessment of the risk of bias.

5. Conflict of interest

No conflicts of interest.

6. Support

None.

Appendix 1: CENTRAL (via Cochrane Library) search strategy

Participant Keywords: ([mh "pulmonary disease, chronic obstructive"] OR COPD:ti,ab OR "Chronic Obstructive Pulmonary Disease":ti,ab OR "chronic obstructive lung disease":ti,ab OR COAD:ti,ab OR COBD:ti,ab OR AECB:ti,ab OR AECOPD:ti,ab OR eCOPD:ti,ab OR "chronic lung disease":ti,ab OR ([mh "pulmonary emphysema"] OR [mh emphysema] OR emphysema*:ti,ab OR "pulmonary emphysema":ti,ab) OR (("chronic bronchitis":ti,ab AND (chronic*:ti,ab AND bronchiti*:ti,ab)) OR (obstruct*:ti,ab AND (pulmonary:ti,ab OR lung*:ti,ab OR airway*:ti,ab OR bronch*:ti,ab OR respirat*:ti,ab)))) AND ([mh "symptom flare up"] OR exacerb*:ti,ab)

Intervention Keywords: ("muscle training":ti,ab OR "resistance training":ti,ab OR [mh "exercise therapy"] OR exercis*:ti,ab OR [mh exercise] OR "physical exercise training":ti,ab OR train*:ti,ab OR "pulmonary rehabilitation":ti,ab OR "cardiopulmonary rehabilitation":ti,ab OR "aerobic exercise":ti,ab OR "endurance training":ti,ab OR ([mh "distance counseling"] OR [mh "directive counseling"] OR counseling:ti,ab) OR (advise:ti,ab OR motivation*:ti,ab OR [mh mentoring] OR mentoring:ti,ab OR coaching:ti,ab) OR ([mh "cognitive behavioral therapy"] OR behavior*:ti,ab) OR (feedback:ti,ab OR [mh "formative feedback"]) OR ("patient education handout":ti,ab OR "patient education as topic":ti,ab OR "patient education":ti,ab) OR ([mh "health records, personal"] OR ("health" NEXT record*):ti,ab OR diary:ti,ab) OR "goal setting":ti,ab OR ([mh self-management] OR self-management:ti,ab OR self-management:ti,ab OR manag*:ti,ab) OR (((telephone*:ti,ab OR [mh telephone] OR [mh hotlines] OR telehealth:ti,ab OR [mh telemedicine] OR telemedicine:ti,ab OR ehealth:ti,ab OR e-health:ti,ab OR mhealth:ti,ab OR m-health:ti,ab) OR [mh "internet-based intervention"]) OR "internet-based intervention":ti,ab OR "internet-based intervention":ti,ab OR "web intervention":ti,ab OR telerehabilitation:ti,ab))

Appendix 2: MEDLINE (via PubMed) search strategy

Participant Keywords: ("pulmonary disease, chronic obstructive"[Mesh] OR COPD[tiab] OR "Chronic Obstructive Pulmonary Disease"[tiab] OR "chronic obstructive lung disease"[tiab] OR COAD[tiab] OR COBD[tiab] OR

AECB[tiab] OR AECOPD[tiab] OR eCOPD[tiab] OR "chronic lung disease"[tiab] OR ("pulmonary emphysema"[Mesh] OR emphysema[Mesh] OR emphysema*[tiab] OR "pulmonary emphysema"[tiab]) OR (("chronic bronchitis"[tiab] AND (chronic*[tiab] AND bronchiti*[tiab])) OR (obstruct*[tiab] AND (pulmonary[tiab] OR lung*[tiab] OR airway*[tiab] OR bronch*[tiab] OR respirat*[tiab])))) AND ("symptom flare up"[Mesh] OR exacerb*[tiab])

Intervention Keywords: ("muscle training"[tiab] OR "resistance training"[tiab] OR "exercise therapy"[Mesh] OR exercis*[tiab] OR exercise[Mesh] OR "physical exercise training"[tiab] OR train*[tiab] OR "pulmonary rehabilitation"[tiab] OR "cardiopulmonary rehabilitation"[tiab] OR "aerobic exercise"[tiab] OR "endurance training"[tiab] OR ("distance counseling"[Mesh] OR "directive counseling"[Mesh] OR counseling[tiab]) OR (advise[tiab] OR motivation*[tiab] OR mentoring[Mesh] OR mentoring[tiab] OR coaching[tiab]) OR ("cognitive behavioral therapy"[Mesh] OR behavior*[tiab]) OR (feedback[tiab] OR "formative feedback"[Mesh]) OR ("patient education handout"[tiab] OR "patient education as topic"[tiab] OR "patient education"[tiab]) OR ("health records, personal"[Mesh] OR "health record*"[tiab] OR diary[tiab]) OR "goal setting"[tiab] OR (self-management[Mesh] OR self-management[tiab] OR self-management[tiab] OR manag*[tiab]) OR (((telephone*[tiab] OR telephone[Mesh] OR hotlines[Mesh] OR telehealth[tiab] OR telemedicine[Mesh] OR telemedicine[tiab] OR ehealth[tiab] OR e-health[tiab] OR mhealth[tiab] OR m-health[tiab]) OR "internet-based intervention"[Mesh]) OR "internet-based intervention"[tiab] OR "internet-based intervention"[tiab] OR "web intervention"[tiab] OR telerehabilitation[tiab]))

Study design Keywords: (("randomized controlled trial"[pt] OR "controlled clinical trial"[pt] OR randomized[tiab] OR placebo[tiab] OR "drug therapy"[sh] OR randomly[tiab] OR trial[tiab] OR groups[tiab]) NOT (animals[Mesh] NOT humans[Mesh]))

Appendix 3: CHINAHL (via EBSCOhost) search strategy

Participant Keywords: ((MH "pulmonary disease, chronic obstructive"+) OR (TI

COPD OR AB COPD) OR (TI "Chronic Obstructive Pulmonary Disease" OR AB "Chronic Obstructive Pulmonary Disease") OR (TI "chronic obstructive lung disease" OR AB "chronic obstructive lung disease") OR (TI COAD OR AB COAD) OR (TI COBD OR AB COBD) OR (TI AECB OR AB AECB) OR (TI AECOPD OR AB AECOPD) OR (TI eCOPD OR AB eCOPD) OR (TI "chronic lung disease" OR AB "chronic lung disease") OR ((MH "pulmonary emphysema"+) OR (MH emphysema+) OR (TI emphysema* OR AB emphysema*) OR (TI "pulmonary emphysema" OR AB "pulmonary emphysema")) OR (((TI "chronic bronchitis" OR AB "chronic bronchitis") AND ((TI chronic* OR AB chronic*) AND (TI bronchiti* OR AB bronchiti*))) OR ((TI obstruct* OR AB obstruct*) AND ((TI pulmonary OR AB pulmonary) OR (TI lung* OR AB lung*) OR (TI airway* OR AB airway*) OR (TI bronch* OR AB bronch*) OR (TI respirat* OR AB respirat*))))) AND ((MH "symptom flare up"+) OR (TI exacerb* OR AB exacerb*))

Intervention Keywords: ((TI "muscle training" OR AB "muscle training") OR (TI "resistance training" OR AB "resistance training") OR (MH "exercise therapy"+) OR (TI exercis* OR AB exercis*) OR (MH exercise+) OR (TI "physical exercise training" OR AB "physical exercise training") OR (TI train* OR AB train*) OR (TI "pulmonary rehabilitation" OR AB "pulmonary rehabilitation") OR (TI "cardiopulmonary rehabilitation" OR AB "cardiopulmonary rehabilitation") OR (TI "aerobic exercise" OR AB "aerobic exercise") OR (TI "endurance training" OR AB "endurance training") OR ((MH "distance counseling"+) OR (MH "directive counseling"+) OR (TI counseling OR AB counseling)) OR ((TI advise OR AB advise) OR (TI motivation* OR AB motivation*) OR (MH mentoring+) OR (TI mentoring OR AB mentoring) OR (TI coaching OR AB coaching)) OR ((MH "cognitive behavioral therapy"+) OR (TI behavior* OR AB behavior*)) OR ((TI feedback OR AB feedback) OR (MH "formative feedback"+)) OR ((TI "patient education handout" OR AB "patient education handout") OR (TI "patient education as topic" OR AB "patient education as topic") OR (TI "patient education" OR AB "patient education")) OR ((MH "health records, personal"+) OR (TI "health record*" OR AB "health record*") OR (TI diary OR AB diary)) OR (TI "goal setting" OR AB "goal setting") OR ((MH self-management+) OR

(TI self-management OR AB self-management) OR (TI self-management OR AB self-management) OR (TI manag* OR AB manag*)) OR ((((TI telephone* OR AB telephone*) OR (MH telephone+) OR (MH hotlines+) OR (TI telehealth OR AB telehealth) OR (MH telemedicine+) OR (TI telemedicine OR AB telemedicine) OR (TI ehealth OR AB ehealth) OR (TI e-health OR AB e-health) OR (TI mhealth OR AB mhealth) OR (TI m-health OR AB m-health)) OR (MH "internet-based intervention"+)) OR (TI "internet-based intervention" OR AB "internet-based intervention") OR (TI "internet-based intervention" OR AB "internet-based intervention") OR (TI "web intervention" OR AB "web intervention") OR (TI telerehabilitation OR AB telerehabilitation)))

Study design Keywords: (((MH randomized controlled trials) OR (MH double-blind studies) OR (MH single-blind studies) OR (MH random assignment) OR (MH pretest-posttest design) OR (MH cluster sample) OR (TI (randomised OR randomized)) OR(AB (random*)) OR (TI (trial)) OR (MH (sample size) AND AB (assigned OR allocated OR control)) OR (MH (placebos)) OR(PT (randomized controlled trial)) OR (AB (control W5 group)) OR (MH (crossover design) OR MH (comparative studies))))NOT ((((MH animals+) OR(MH (animal studies)) OR (TI (animal model*))) NOT (MH (human))))

Appendix 4: Web of Science search strategy

Participant Keywords: TS=("pulmonary disease, chronic obstructive" OR COPD OR "Chronic Obstructive Pulmonary Disease" OR "chronic obstructive lung disease" OR COAD OR COBD OR AECB OR AECOPD OR eCOPD OR "chronic lung disease" OR ("pulmonary emphysema" OR emphysema OR emphysema* OR "pulmonary emphysema") OR (("chronic bronchitis" AND (chronic* AND bronchiti*)) OR (obstruct* AND (pulmonary OR lung* OR airway* OR bronch* OR respirat*)))) AND ("symptom flare up" OR exacerb*)

Intervention Keywords: TS=("muscle training" OR "resistance training" OR "exercise therapy" OR exercis* OR exercise OR "physical exercise training" OR train* OR "pulmonary rehabilitation" OR "cardiopulmonary rehabilitation" OR "aerobic exercise" OR "endurance training" OR ("distance counseling" OR "directive counseling" OR counseling) OR (advise OR motivation* OR mentoring

OR mentoring OR coaching) OR ("cognitive behavioral therapy" OR behavior*) OR (feedback OR "formative feedback") OR ("patient education handout" OR "patient education as topic" OR "patient education") OR ("health records, personal" OR "health record*" OR diary) OR "goal setting" OR (self-management OR self-management OR self-management OR manag*) OR (((telephone* OR telephone OR hotlines OR telehealth OR telemedicine OR telemedicine OR ehealth OR e-health OR mhealth OR m-health) OR "internet-based intervention") OR "internet-based intervention" OR "internet-based intervention" OR "web intervention" OR telerehabilitation))

Study design Keywords: TS=(randomised OR randomized OR randomisation OR randomisation OR placebo* OR (random* AND (allocat* OR assign*)) OR (blind* AND (single OR double OR treble OR triple)))

Appendix 5: PEDro search strategy

Participant Keywords: "acute exacerbation of chronic obstructive pulmonary disease", "acute exacerbation of COPD", "exacerbation of COPD", AECOPD, eCOPD

Study design Keywords: clinical trial

Appendix 6: Reference

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