Online Data Supplement

Pulmonary Rehabilitation for Chronic Obstructive Pulmonary Disease Patients With Underlying Alpha-1 Antitrypsin Deficiency: A Systematic Review and Practical Recommendations

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Table 1: Search concepts for the systematic review

Concept 1: alpha 1-Antitrypsin	*Concept 2: Pulmonary Rehabilitation*	*Concept 3: Skeletal Muscle morphology*
1 alpha 1-Antitrypsin/ 2 alpha-1 antitrypsin.ti,ab. 3 alpha 1 antitrypsin.ti,ab. 4 alpha1 antitrypsin.ti,ab. 5 alpha-1-at.ti,ab. 6 alpha-1-antitrypsin.ti,ab. 7 alpha one antitrypsin.ti,ab. 8 alpha one antitrypsin.ti,ab. 9 AAT.ti,ab. 10 A1AT.ti,ab. 11 AATD.ti,ab. 12 deficien$ or lack$.ti,ab. 13 alpha 1-Antitrypsin Deficiency/ 14 alpha 1-Antitrypsin Deficiency.mp 15 AATD.mp. 16 Augmentation therapy/ 17 Augmentation therap$.ti,ab. 18 or/ 1 to 11 19 12 and 18 20 13 or 14 or 15 21 16 or 17 22. 19 or 20 or 21	1 Pulmonary Rehabilitation/ 2 Pulmonary rehab$.ti,ab. 3 Telerehabilitation/ 4 telerehab$.ti,ab. 5 tele-rehab$.ti,ab. 6 virtual rehab$.ti,ab 6 distance rehab$.ti,ab. 7 remote rehab$.ti,ab. 8 online rehab$.ti,ab. 9 Conventional rehab$.ti,ab. 10 face to face rehab$.ti,ab. 11 face-to-face rehab$.ta,ab. 12 Supervised rehab$.ti,ab. 13 exercise therapy/ 14 exercise therap$.ti,ab. 15 exercise training/ 16 exercise train$.ti,ab. 17 Exercise$.mp 18 aerobic exercise$.ti,ab. 19 strength exercise$.ti,ab. 20. endurance exercise$.ti,ab. 21. resistance exercise$.ti,ab. 22. aerobic train$.ti,ab. 23 strength train$.ti,ab 24. endurance train$.ti,ab. 25 or/ 1 to 12 26 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 24 25 or 26	1 Skeletal muscle$/ 2 Skeletal muscle$.ti,ab. 3 Myofiber$.ti,ab. 4 Myofibre$.ti,ab. 5 Sarcomere$/ 6 Muscle fibre$/ 7 Muscle fiber$/ 8 Muscle fiber$.ti,ab. 9 Muscle fibre$.ti,ab. 10 Fast twitch.ti,ab. 11 Fast-twitch.ti,ab. 12 Slow twitch.ti,ab. 13 Slow-twitch.ti,ab. 14 Muscle Fiber$ Type I.ti,ab. 15 Muscle Fiber$ Type II.ti,ab. 16 Slow oxidative.ti,ab. 17 Slow-oxidative.ti,ab. 19 Fast glycolytic.ti,ab. 20 Fast-glycolytic.ti,ab. 21 hybrid fibre$.ti,ab. 22 hybrid fiber$.ti,ab. 23 hybrid-fiber$.ti,ab. 24 hybrid-fibre$.ti,ab. 23 or 1 to 24 24 Muscle biopsy/ 25 Muscle biops$.mp. 26 24 or 25 27 23 or 26

Table 2: Quality assessment using the Cochrane Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) assessment tool

Risk of basis	**Bias due to confounding**	**Bias in selection of participants**	**Bias of classification of interventions**	**Bias due to deviation from intended intervention**	**Bias due to missing data**	**Bias in measurement of outcomes**	**Bias in selection of the reported result**	**Overall**
Jarosch et al 2017	Serious	No information	N/A	No information	No information	Low/moderate	No information	Serious risk
Support for judgment	Many baseline characteristics show no significant difference. Where there is difference, propensity score matching ensured evenly matched groups. No information reported as to co-morbidities	More information needed: Cant find exclusion criteria listed- although referenced. No details as to start/finish of patient contact- can't confirm overlap. Not enough information onto selection/recruitment criteria.	Interventional status is well defined; however, each group received the same intervention.	Intervention described in referenced paper (3). More information needed on adherence to program.	No information given as to the potential for missing data.	Measurements comparable across groups, unlikely to be impacted by knowledge of intervention from participant. As only one intervention, assessors likely to know intervention.	No information given as to registration of study and initial full data set.	Serious risk in one domain, no information in several. Some information missing.

Kenn et al 2015	Low	Low	N/A	Low	Moderate	Low/moderate	Low	Moderate risk
Support for judgment	No information as to co-morbidities- SF-36 used to understand baseline.	Consecutive patients recruited. No exclusion criteria (other than not able to complete baseline measurements).	All participants undertook same program. Some individually structured strength training.	No data as to number of participants who did not complete. Reference to 10% of participants not having a final evauation.	Large amounts of missing data points: 91 missing data points for 6MWT, and 345 missing data points for the SF36, and participants with missing data were removed from the analysis. 902 start 466 included in analysis.	Objective outcome measures, not likely to have been influenced. As only one intervention, assessors likely to know intervention.	The outcome measures were consistent for both groups, and different regression models were used to identify covariates that influence the regression coefficient. The final analysis included covariates that significantly contributed to the model	Mostly low, with one moderate
Jarosch et al 2016	Serious	Serious	N/A	No information	Serious	Low/moderate	Moderate	Serious risk
Support for judgment	No information reported as to co-morbidities, or no substitute reporting used.. Referene given to matched baseline groups.	Study registered prior to starting- however exclusion criteria changed from registered. 20 reported as enrolled on clinicaltrials.gov, only 19 discussed- 1 missing.	All participants undertook the same structured training program.	No data as to completion rates	No information given as to missing data/drop out of participants. 20 reported as enrolled on clinicaltrials.gov, only 19 discussed- 1 missing.	Outcome measure not influenced- as only one intervention, assessors likely to know intervention.	Reported results not all registered prior to study. Outcome measures same for both groups.	Some serious risk. Some missing information

Olfert et al 2014	Low	Low/moderate	N/A	No information	No information	Low	Low	Moderate
Support for judgment	No details as to co-morbidities, but large amount of exclusion criteria which will results in mostly cohesive groups.	No reference made to study registration. Participants recruited through advertising campaign.	All participants undertook the same structured training program.	No data as to completion rates	No information on amount of people who completed. No registration information.	The protocol of outcomes measurement was unified across all groups	No evidence of selective reporting, though no published protocol was identified for this study	One moderate risk, some missing information.

Table 3: Quality assessment using the Cochrane risk-of-bias tool for randomized trials (RoB) assessment tool

Risk of Bias	**Bias arising from the randomization process**	**Bias arising from the intended intervention**	**Bias arising from missing outcome data**	**Bias arising from measurement of the outcome**	**Bias arising from the selection of reported result**	**Overall risk**
Choate et al 2021	Low risk	Low risk	Low risk	Low risk	Some concerns	Some concerns
Support for judgment	Double blind randomized-Randomization methods explained.	Double blind	500 enrolled, 429 submitted 2 minimum data levels. Dropout rates similar for both groups	Data analysis workers randomized. Same methods of analysis used for each group.	No prespecified plan of analysis	Mostly low risk, but one area with some concerns.