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Letter in Reply: A Promising Intervention for Comprehensive Pulmonary Rehabilitation for Asthma COPD Overlap Syndrome

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Dear Editor,

We acknowledge the inclination of the authors for the investigation conducted by us.[1] We appreciate their scrutiny of our investigation[2] and would like to address the issues raised by them with a holistic approach.

The point raised by the authors regarding the exclusion of the control group from educational intervention, seems misinterpreted. As per the American Thoracic Society/European Respiratory Society,[3] pulmonary rehabilitation (PR) is a comprehensive approach in which structured program educating on self-management is considered one of the key components of comprehensive PR. Our randomized control trial aimed to assess the effect of a comprehensive PR program in asthma-chronic obstructive pulmonary disease (COPD) overlap syndrome (ACOS);[2] therefore, it became imperative that the control group should be excluded from receiving any form of intervention (either exercise/education) that is a part of comprehensive PR.[3] This is also in accordance with a previously conducted investigation[4] else this inclusion might have made the study design less rigorous and could have affected the outcomes of the investigation.[1] Furthermore, studies[5,6] highlighted by the authors did not aim to evaluate the effect of educational intervention on mortality rate.

We disagree with the author's claim regarding questionable ethics pertaining to the exclusion of the control group from receiving educational intervention. Ethical issues arise when refraining certain intervention in the control group poses a risk to the participant. As per the ethical principle of 'risk-benefit balance', the rule of thumb is that a control intervention should commensurate to the best available treatment or provided with the best usual care.[7] Keeping this balance into consideration, none of the participants in our study[2] were deprived of receiving the standard medical care along with usual strategies similar to previously conducted studies.[4,5] The control group was further enrolled in the PR-program after completion of the investigation.

Another concern of the authors was the utilization of a parametric test if the data set was not normally distributed. This is a long-standing controversy: whether parametric tests are applicable to non-normally distributed continuous data.[8] Basically, the robustness of the parametric test to small deviation and estimation of the confidence intervals[8] favors the applicability of parametric statistics in most scenarios, even non-normally distributed continuous data. The authors are right to point out that within-group comparisons can be incorporated as our investigation aimed to elucidate the effect between the groups, so we were less inclined regarding within-group significance, but we have depicted mean and standard deviation for both the groups at baseline as well as after six-weeks in Table 2.[2]

To sum up, our findings[2] were strengthened with the rigorous study design, and the entire investigation was conducted in accordance with ethical considerations. The results will pave the way for clinicians to optimize PR's effectiveness

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Table 2: Standardized mean difference of outcome variables after six weeks between the groups.[2]

Outcome variables	PR group (n = 14)		Control group (n = 14)		PR group vs. control group Standardized mean difference Random (95% CI), *p*-value
	Baseline	Six weeks	Baseline	Six weeks	
6MWD, m	305.4 ± 74.0	401.9 ± 63.5	313.0 ± 48.1	321.2 ± 43.4	1.44 (0.60,2.29), 0.001*
6MWD, % Pred	64.2 ± 13.6	83.2 ± 11.4	69.4 ± 12.7	71.1 ± 12.6	0.98 (0.19,1.77), 0.014*
SGRQ					
Symptoms, %	63.1 ± 17.8	42.3 ± 12.4	65.4 ± 20.6	61.5 ± 19.8	-1.49 (-2.34,-0.64), 0.005*
Impact, %	59.9 ± 17.2	44.4 ± 13.0	68.1 ± 19.5	63.3 ± 16.9	-1.22 (-2.03,-0.40), 0.003*
Activity, %	60.0 ± 16.5	43.7 ± 12.0	65.0 ± 18.3	63.3 ± 18.3	-1.22 (-2.03,-0.40), 0.003*
Total, %	62.3 ± 17.9	45.5 ± 13.1	65.9 ± 19.5	64.3 ± 20.0	-1.15 (-1.96,-0.34), 0.007*
PFT					
FEV_1, L	1.4 ± 0.4	1.5 ± 0.5	1.2 ± 0.2	1.2 ± 0.2	0.51 (-0.25,1.26), 0.182
%Δ in FEV_1	65.1 ± 26.7	69.3 ± 31	62.8 ± 15.6	64.7 ± 16.4	0.18 (-0.56,0.92), 0.630
FVC, L	2.2 ± 0.2	2.3 ± 0.3	2.0 ± 0.3	2.1 ± 0.3	0.02 (-0.72,0.76), 0.105
% Δ in FVC	71.9 ± 20.9	74.4 ± 20.2	69.2 ± 14.7	70.4 ± 20.2	0.27 (-0.47,1.02), 0.720
FEV_1/FVC	47.3 ± 17.9	49.7 ± 18.1	45.5 ± 17.5	47.0 ± 17.2	0.14 (-0.61,0.88), 0.697
Bode index	9.3 ± 1.3	6.3 ± 1.6	8.2 ± 1.9	8.5 ± 1.9	-1.22 (-2.03,-0.40), < 0.001*

Values are presented as mean±standard deviation.
**Significant difference between groups following six weeks.*
PR: pulmonary rehabilitation; CI: confidence interval; 6MWD: six minute walk distance; SGRQ: St. George's Respiratory Questionnaire; PFT: pulmonary function test; FEV_1: forced expiratory volume in 1 second; %Δ in FEV_1: percentage change in forced expiratory volume in 1 second; FVC: forced vital capacity; %Δ in FVC: percentage change in forced vital capacity.

in patients with ACOS. However, we do agree that a multi-centered trial with blinding should be considered to reach comprehensive inferences in the future.

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