Reviewer’s report

Title: Association of physical activity with lung function in lung-healthy German adults: Results from the KORA FF4 study

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Reviewer: Janos Porszasz

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Reviewer's comments to PULM-D-17-00115

This manuscript using apparently lung-healthy subpopulation of 48-68 yrs age group of the KORA FF4 population to study the potential association of spirometrically determined lung function and activity level quadrant categories. It was shown that although there is a weak association, most of the association was found in the ever or current smokers population but not in the never smoking cohort. It is concluded that preserved activity might contribute to preserve the lung function by affecting the low-grade systemic inflammatory influence on lung function.

The study population of n=341 out of the total 1043 subjects' who were scheduled for follow up for spirometry and activity monitoring seems to be unfortunate, but there is nothing that can be done about this at this time. I mention this as the statistical power of this kind of analysis is dramatically affected by this kind of loss in subject number and might lead to weak conclusions as it happened in this case. Regardless, I have a few questions that authors might consider while considering improving their manuscript.

Since there was a weak, although on occasion significant association between the activity level and the spirometric values (especially FEV1) of the ever/current smokers, it would be potentially beneficial to isolated the so-called PRISm population (Preserved Ratio Impaired Spirometry, i.e. FEV1/FVC>0.7 & FEV1%predicted<80%), which is probably the sign of the early (or mild) obstruction due to the effect of smoking. If this sub-population shows stronger associations, the conclusions might be more meaningful.

On the other hand, if the effect of the extent of the obstruction on the activity level is in question, it would have been better not to exclude those with poorer spirometric results. I find it puzzling, since the study was not an interventional but purely observational study, why authors excluded those with worse pulmonary function to 'minimize the potential risk'? The study itself did not carry any potential induced risk!

The main conclusion is purely speculative: in this study there were no inflammatory markers studied, yet the authors make a relatively strong conclusion that the higher level activity might have a beneficial effect on the lung function. Had the logic been reverse in that poorer lung
function is usually associated with lower daily physical activity, authors would not have to find this indirect conclusion without material basis.

Further, it is known that PA decline is manifest mainly beyond GOLD 2 groups in COPD in larger than these populations studied. The referred studies in the 'Introduction' and the current one may not have enough statistical power to detect the possible difference.

Further minor comments:

1.) Why only MIP and not MEP was measured? What justifies the selection of inspiratory pressures in the studied population as opposed to both inspiratory and expiratory maximal pressures?

2.) Line 135: Please specify the time of the day when the subjects were instructed to wear the activity monitor (e.g. 6 AM to 10 PM or 8 AM to 8 PM)

3.) Line 138: What criteria were used to judge if a recording was valid? 3 valid weekday and 1 valid weekend day is a minimalistic approach. The current recommendation is to have at least 5 valid days (8 hours/day) over a 7-day observation/recording period.

4.) Line 158: The use of MEF 25-75 should be avoided, particularly, if the expiratory time was not standardized for measuring it. Does MasterScope provide this timed standardized number or it is always considered at the end of expiration on the FVC maneuver? The problem is that if the forced expiratory time (FET) is not standardized for reporting FEF 25-75, the blows with different FET are not comparable and if included in the data base, this increases the coefficient of variation and decreases the detection power. You probably should drop the analysis of FEF25-75 as it does not seem to be practically important in any of the relationships you studied.

5.) Line 160: DLCO (TLCO) measurement should be standardized for a breath hold time of about 10 seconds but no longer than 12 seconds.

6.) Line 162: State the acceptability criteria that were considered for spirometry and to TLCO (DL)

7.) Line 182: Because of the 'data cleaning' how many subjects' data were excluded from the analysis?

8.) Line 185: What is the rationale of using these education times? In Europe, as everywhere else, middle school (or high school) is up to 12 years of schooling. (8 years elementary + 4 years high school).

9.) Line 186: Why hay fever and not 'asthma'? Or any allergic diagnosis?
10.) Lines 240 - 242: This would suggest that smokers who are more active have worse lung function by FVC than their sedentary counterparts? What can explain this controversy? One would think that in real life, those with worse lung function are less active because of activity-related symptoms. These data do not support this view. Although it is also true that this can be false positive finding as the level of significance is around 0.05 - what is the chance of a Type I error in this case; what is the power of this P value? Apparently, the absolute value of FVC and not it's z-score is significant. Therefore, I would not make this statement, or weaken the wording. Not to mention that it is NOT the FVC that matters most in obstruction, but FEV1. The next section invalidates this result also as both FEV1 and FVC is significantly higher in the high activity class (supported by a higher z-score as well).

11.) Line 262: It would have been interesting to leave those with impaired lung function in the analysis and compare them to these results. Apparently, the activity level is not decreasing in COPD compared to normal controls (sedentary) until low GOLD 2 - GOLD 3 stages have been reached. Therefore, it is not surprising that there is no association between lung function and physical activity in this cohort of apparently lung-healthy subjects.

12.) Line 281: I am sorry, but I see this differently, because it has been shown that - apart from inspiratory muscle training affecting MIP - physical training in general is not affecting lung function. Therefore, simply from the finding that specific athletic groups have higher lung function because of the training itself is false. Rather, athletes with higher lung function are self-selected for that specific athletic activity.

13.) Line 295: A discussion of the possible effect of the PRISM (Preserved Ratio Impaired Spirometry) population (i.e. FEV1/FVC>0.7 AND FEV1%predicted<80%) could be mentioned here, which is found in the ever or current smoker population. It would be important to see how much of this sub-cohort meet the criteria of PRISm and whether the studied associations with PA can be found.

14.) Line 307: This would be another reason to look at the PRISm population.

15.) Line 331: Since this was not an interventional study, it does not seem to be warranted to exclude anybody because of the lower lung function. The study itself, as it was an observational study, did not present any risk on its own to these patients. If you wanted to study the lung-healthy population by classic spirometric criteria only, then you should state it so. Do not pull another, unjustified reason to explain your selection.

16.) Table A2: List FEV1 also as it is listed everywhere else - regardless if it has any significant association or not. In the rest of the Table it is listed.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.
Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
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No

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