**Author's response to reviews**

**Title:** An impaired health related muscular fitness contributes to a reduced walking capacity in patients with schizophrenia: a cross-sectional study

**Authors:**

Davy Vancampfort (Davy.Vancampfort@uc-kortenberg.be)
Michel Probst (Michel.Probst@faber.kuleuven.be)
Amber De Herdt (Amber.De.Herdt@faber.kuleuven.be)
Rui Corredeira (Rui.Cordeire@fade.up.pt)
Attilio Carraro (Attilio.Carraro@unipd.it)
Dirk De Wachter (Dirk.De.Wachter@uc-kortenberg.be)
Marc De Hert (Marc.De.Hert@uc-kortenberg.be)

**Version:** 2 **Date:** 28 December 2012

**Author's response to reviews:** see over
Dear Editorial Office of BMC Psychiatry,

Please reconsider our manuscript ‘An impaired health related muscular fitness contributes to a reduced walking capacity in patients with schizophrenia: a cross-sectional study’. We would like to thank the editor and the four reviewers for giving us the opportunity to rework and resubmit our manuscript. The authors also wish to express their gratitude for the great efforts of the reviewers and the editor in directing the manuscript towards a more acceptable form for publication. The authors hope that the added revisions adequately address the comments of the reviewers and the editor, and hope that this resubmission could be considered for possible publication in BMC Psychiatry.

Sincerely,

Davy Vancampfort
Marc De Hert
University Psychiatric Centre K.U.Leuven, Campus Kortenberg
Leuvenesesteenweg 517, B-3070 Kortenberg, Belgium
Tel.: +32 2 758 05 79
Fax: +32 2 759 9879
E-mail: Davy.Vancampfort@uc-kortenberg.be
Reviewer's report 1

The subject examined by the authors is a very interesting and relevant one, especially in view of the growing emphasis on physical health of people with schizophrenia. The procedures they used, though simple, are replicable under clinical situations. The paper will do better with some revisions. The following are some issues I noted that the authors could address in their revision:

The authors would like to thank reviewer 1 for his positive feedback and valuable comments and suggestions.

1. Major

1.1 In finding a relationship of overall MET to walking capacity one needs to be aware that calculation of the MET/week from the IPAQ includes component of walking as well. Hence I feel it is better not to include this variable in the regression or exclude MET calculated from the walking activity.

Thank you very much for this suggestion. Nevertheless, we do believe that walking is a very important and relevant physical activity modus for patients with schizophrenia. We do believe that it is justified to include it in the MET-analyses. While walking is situated at the physical activity level, the walking capacity can be situated at the physical fitness level.

1.2 The relevance of exercise to mental health is fairly robust with depression in contrast to schizophrenia. Hence a reference to improvement in overall mental health on page 15 may be found wanting in evidence.


2. Minor

2.1 To describe a typical patient that has all the variables found significant on regression (older patient with long duration of illness and high BMI) may tend to dilute the significant effect of the individual variable (Second sentence in Discussion and the Conclusion)
We do agree with reviewer 1 that describing a typical patient that has all the variables found significant on regression tends to dilute the significant effect of the individual variable. Both sentences were deleted. In the discussion the sentence was replaced by: “Especially older age, a longer illness duration, a higher BMI and physically activity level were identified as independent predictors of the health related muscular fitness.”

2.2 The discussion on IGF 1 could be bit more streamlined and shortened relating it directly to the findings of this study.

We agree that the discussion on IGF-1 should be related to the present findings. After reconsidering this we chose to delete this paragraph. Thanks for the comment.

2.3 The reason why OGTT was done as this was not discussed though insulin resistance was discussed in relation to IGF 1

The OGTT assessed fasting glucose which is one of the metabolic syndrome criteria. The IGF-1 part was deleted, see also our answer on comment 2.2.

2.4 Some sentences looked incomplete-lines 1 and 6 of paragraph 2 of page 11, line 14 of page 13

We completed these sentences.

2.5 The term ‘first episode and chronic patients’ needs change. The duration refers to illness and not the nature of the person affected.

We referred to Flickt et al. (reference 33). The terms are used in accordance with the terms used by Flickt et al. We therefore do believe that its use is justified here.

2.6 The tables esp. 1 and 2 can be presented in text

We do believe that in these tables we can offer a clear overview of the results. In order to avoid double information, we did not repeat the results in the text.
3. Discretionary

3.1 The extent of benefit accrued by people with schizophrenia on rigorous exercise is untested. The benefits of exertions by clinicians to make them engage in exercise programs as part of treatment is an issue that needs some more thinking (not necessary to discuss it in this paper).

Thank you.

We do hope that the revisions above adequately address the concerns of reviewer 1.
Reviewer's report 2
The manuscript is well written, the data seem interesting, and the references are appropriated. However, I consider that the aims and the results of the study should be reviewed in order to properly focus the discussion section.
The authors would like to thank reviewer 2 for his positive feedback and valuable comments and suggestions.

Major Compulsory Revisions
1. Title
The title must be directly related with the aims and the conclusions. Please, re-write the title.
The title now reads as follows: ‘An impaired health related muscular fitness contributes to a reduced walking capacity in patients with schizophrenia: a cross-sectional study’.

2. Abstract
The Abstract only include one of the aims of the study, and it does not fit with the conclusions. Please, check this issue.
We added the following: “Secondly, we identified variables that could explain the variability in health related muscular fitness in patients with schizophrenia.”

Please, include a brief sentence indicating how many controls were recruited for the study.
Included as requested.

3. Background
In my opinion the aims of the study were (1) to assess walking capacity and muscular fitness in a sample of patients with schizophrenia, and (2) to establish the variables that can explain the variability on walking capacity and muscular fitness. Please, rewrite the aims of the study.
This was changed as requested. The aims now read as follows: “The aim of this study was to quantify walking capacity and health related muscular fitness using easy-to-perform field tests in patients with schizophrenia compared with age-, gender and body mass index (BMI)-matched healthy controls. Secondly, we identified variables that could explain the variability in walking capacity and in health related muscular fitness in patients with schizophrenia.”
4. Methods
How did you evaluate smoking habit? How did you evaluate illness duration? Please, include these issues at methods section.
We added the following: “Demographic patients’ data (including illness duration) were obtained from medical records while age for the control participants was self-reported. All participants were asked whether they currently smoked. Those participants who responded affirmatively to this question were asked how many cigarettes they smoked per day.”

Statistical section should be clarified according the aims of the study. Some of the statistical analyses are not clearly stated at this section. At Table 2 you calculated the effect size statistics as Cohen’s d. Please, define the use of this statistical test at statistics section and at the table, and indicate the 95% confidence intervals.
We added in the statistical analyses section and in table 2 that effect sizes were calculated using Cohen’s d. We also added the 95% confidence intervals.

Please, indicate the significance of “#” at statistics section and at the table 2.
We explained that the “∆” is the difference expressed as a percentage between patients and controls. We added additional information on the statistics. See also our answers on the comments of the other reviewers.

Indicate at the end of statistical analyses the p value that you considered statistically significant (p<0.01).
We added the significance levels in tables 4 and 5.

5. Results
The sub-title of paragraph 4 indicates “associations” but you calculate “correlations”. Please, check this issue.
We changed the word “associations” to “correlations”.

Why did you create table 4?. What is the relationship of table 4 with the aims of the study? Please, clarify this issue.
We do agree that all the data in table 4 were not strictly necessary. We deleted the table in this revision. Nevertheless, we do believe that adding the metabolic syndrome as a possible
variable that can explain the variability on walking capacity and muscular fitness is of added value. For this reason some data of table 4 are now added in the text.

6. Discussion
In my opinion discussion section should be rewritten and divided into several paragraphs. A general review is necessary to fit the discussion and conclusions with the aims of the study. We added a paragraph with the heading “general findings” and one with the heading “future research”.

In my opinion, data about metabolic syndrome (Table 4) and all the comments included at discussion section are out of the aims of the study. Probably, all the speculations about the relationship between fitness and metabolic syndrome should be omitted. Table 4 was deleted and the discussion on the metabolic syndrome was shortened, although we do believe that the metabolic syndrome is of added value in the manuscript since differences in health related muscular fitness were found between patients with and without the metabolic syndrome. See also our answer on your comments above.

A high percentage of the discussion is focused on “future studies”, but I consider that this information should be briefly included at the end of the discussion. Changed as requested.

Clinical implications should be focused on the results of the study:
- Whether you did not check the recommendations of weekly physical activity, you only can state that patients with schizophrenia should improve muscular fitness in order to maintain walking capability.

We agree that we cannot conclude that the present findings offer evidence for the guidelines. We stated the following now: “The present findings indicate that patients with schizophrenia should improve their muscular fitness in order to maintain walking capability. The current International Organization of Physical Therapy in Mental Health guidelines [32] do recommend that for substantial health benefits, patients with schizophrenia should not only do at a minimum 150 minutes a week of moderate-intensity, or 75 minutes of moderate-to-vigorous-intensity aerobic activity, but should also perform muscle-strengthening exercises that are of at least moderate intensity and involve all major muscle groups on two or more days a week [32, 33].”
- As you do not evaluate the effects of muscular exercise, you can not speculate about its benefits.

Also here we agree with reviewer 2; this paragraph was deleted.

- Due to the cross sectional design of the study, you cannot state about the effects of improve fitness in patients with schizophrenia. The use of one test to evaluate muscular fitness (standing broad jump), a the small sample of control group should be included as limitations of the study.

All these aspects were included now as limitations.

Minor Essential Revisions

1. Background

Background section is well focused according the aims of the study, but I consider that it should be divided into 3 or 4 paragraphs to a easier reading.

Changed as requested.

2. Methods

Please, briefly define DSM-IV criteria first time it appears.

We wrote “DSM” when it appeared for the first time in full: “Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition” and added a reference.

Why did the authors only select 40 control people?

We agree that pair-wise matching and including an additional of 40 control people would have increased the power of our findings. The limited sample size, especially related to controls has been added as a limitation.

I would not include the name of the tests in the subtitles of methods section (e.g. 6MWT, IPAQ, PECC…). Please, simplify the subtitles.

Simplified as requested.
Please, briefly define the diagnosis of metabolic syndrome according the International Diabetes Federation criteria.

We added the following: “According to these criteria, for a patient to be defined as having the MetS they must have: central obesity (defined as waist circumference ≥94cm for European men and ≥80cm for European women, with ethnicity specific values for other groups) plus any two of the following four factors: (1) raised TG level: ≥150 mg/dL (1.7 mmol/L), or specific treatment for this lipid abnormality, (2) reduced HDL cholesterol: <40 mg/dL (1.03 mmol/L*) in males and <50 mg/dL (1.29 mmol/L*) in females, or specific treatment for this lipid abnormality, (3) raised blood pressure: systolic BP ≥130 or diastolic BP ≥85 mm Hg, or treatment of previously diagnosed hypertension, (4) raised fasting plasma glucose (FPG) ≥100 mg/dL (5.6 mmol/L), or previously diagnosed type 2 diabetes.”

How did the authors record the dosage of chlorpromazine? Please, add some information about this issue.

We added that we used Gardner’s table; a reference is available.

3. Results

The information of second paragraph about “mean duration of illness” could be stated at the first paragraph.

Changed as requested.

Please, include “IPAQ” over the corresponding results at Table 2 and Table 3, and indicate the significance at the end of the tables.

Included as requested.

Please, include “PECC” over the corresponding results at Table 3, and indicate the significance at the end of the table.

Included as requested.

Tables 5 and 6 are not self-explanatory. Please, add some information in the title about the statistical analysis, and include a brief explanation about “Cumulative r2” and “F” at the end of the tables.

The titles were changed to “Multiple stepwise regression analysis of the variables associated with the walking capacity score” and “Multiple stepwise regression analysis of the variables
associated with the health related muscular fitness score”, respectively. We added that $r^2 =$ determination coefficient. The F-values were deleted but we added the following in the index: Criteria: probability of F-to-enter $\leq 0.5$; probability of F-to-remove $\geq 0.10$.

Please, avoid to start the discussion with “to the best of our knowledge”. I consider more adequate to open the discussion section with “the main results of the study indicate that…”.

This is avoided now as requested.

Minor issues not for publication

Include a dot at the end of the first line at the limitations section.

Changed, thank you very much. We do hope that these revisions adequately address the concerns of reviewer 2.
Reviewer's report 3

The subject is of topical interest and the paper is generally well written. It comes from a group which has been working in this area.

The authors would like to thank reviewer 3 for his positive feedback and valuable comments and suggestions.

There is not enough details about the controls. The authors say that they "were recruited from among personnel of the participating centers' I assume this means health care workers, researchers, students, etc. Given that persons with schizophrenia are likely to be from a lower social class than controls drawn in this manner, needs to be discussed and justified.

We do agree with reviewer 3 that additional information on the controls is needed. We did add in this resubmission that healthy controls were indeed mainly health care workers, researchers, and students. We also do agree that since persons with schizophrenia are likely to be from a lower social class than controls and since we did not control for (parental) socio-economic status this should be mentioned as a limitation. We added the following in the limitations section: “Secondly, we also did not include parameters such as socio-economic status and educational level. Both parameters are known to be associated with the level of physical activity participation and physical fitness, also in patients with schizophrenia.” And referred to reference 13. Related to the healthy controls we also mentioned the following: “Although in the healthy controls the IPAQ scores were in agreement with several other Belgian studies, the overall smoking prevalence rate was approximately 1.5 times lower than in the corresponding general population.” We referred to:

It has already been noted by the author that smoking rates differed between patients and controls. If the argument is that the level of fitness has something to do with the illness directly, it might have been better to match the controls on characteristics which might be presumed to affect fitness.

We do agree with reviewer 3 that we should be more cautious in stating that schizophrenia related characteristics might be presumed to affect physical fitness. We added in the discussion that “...the higher rates of cigarettes smoking in patients with schizophrenia might be a confounding variable. Although smoking behaviour could not be identified as independent predictor for health related muscular fitness in patients with schizophrenia, it cannot be excluded that differences in health related muscular fitness between patients and controls might only reflect differences in smoking behaviour.”

The controls and patients were matched it is said, for age, BMI, and sex. But with only 40 controls, I am assuming that they were not matched pair-wise to the schizophrenia subjects. Given that the number of data points in the two groups is not the same, the authors should discuss why it was appropriate to use t tests for paired samples.

Thank you very much for this comment. After reconsidering your remark on the fact that controls were not pair-wise matched we chose to use the t-test for unpaired samples. The p-values were changed accordingly. No significant differences compared with the paired t-test were however found. Thank you once again for the observation. We do hope that these revisions adequately address the concerns of reviewer 3.
Reviewer's report 4

This paper presents useful data on physical fitness in people with schizophrenia, although the results are not surprising. It would be expected that people with a worse ability to walk for 6 minutes or jump from a standing start are more obese, take less exercise and (given that they are fatter) are more likely to have metabolic syndrome. The two tests selected for this study are useful, do not require specialized equipment, and are within the capabilities of people with schizophrenia, so may be more widely adopted in future clinical studies. The detail in the method is therefore necessary.

The authors would like to thank reviewer 4 for her positive feedback and valuable comments and suggestions.

Otherwise the paper could be more concise; the discussion in particular is too long given that there is nothing in the results requiring detailed exploration and explanation. Some of the results are unnecessarily repeated in the discussion. The discussion about the possible role of insulin could be rewritten so it is clearer, but this is interesting and worth including.

Thank you very much for this comment. We do agree that a better focus in the discussion was needed. The discussion was rewritten based on the comments of all the 4 reviewers. We avoided a repetition of the results and deleted also the insulin part, although interesting it was actually out of the scope of the current study. We hope that the present discussion adequately addresses your concerns.

Specific points:
Sentence for reference 12 – whose “goals”?  
Thank you for this observation. We clarified that only 25% of patients with schizophrenia meet the minimum health recommendations of 150min of at least moderate intensity physical activity per week.

The paper has many grammatical errors and the written English requires attention. Some sentences cannot be understood eg what do they mean by “An increased explanation for the relatively poor physical activity participation is the increased risk for somatic complications”? The grammar was checked. We also deleted the mentioned sentence.
The PECC appears to be for use by caregivers but was assessed by a nurse? The PECC has indeed been developed for caregivers including nurses. The PECC has been validated against the PANSS (reference presented).

P11 how is smoking behaviour related to muscular fitness? “there was no difference in smoking behaviours in smokers” – what does this mean?
Smoking was no independent predictor of the health related muscular fitness (see also our answer on the next comment and the comment on smoking of reviewer 3). We did clarify that there was no difference in the number of cigarettes smoked per day.

Smoking is liable to be quite important so it would be good to clarify the associations between smoking and the other variables e.g. do the smokers have a lower BMI? Are they more or less fit than nonsmokers?
We added that except for the fact that in schizophrenia smokers were less physically active (MET-minutes per week: 984.1±853.2 versus 1830.8±1517.2, p<0.001), no statistical differences between smokers and non-smoker were found (data not presented). We do hope that the revisions above adequately address the concerns of reviewer 4.