

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Increase in physical activity and cardio-metabolic risk profile change during lifestyle intervention in primary healthcare: one-year follow-up study among individuals at high risk for type 2 diabetes
AUTHORS	Urho M. Kujala, Jari Jokelainen, Heikki Oksa, Timo Saaristo, Nina Rautio, Leena Moilanen, Eeva Korpi-Hyövält, Juha Saltevo, Mauno Vanhala, Leo Niskanen, Markku Peltonen, Jaakko Tuomilehto, Matti Uusitupa, Sirkka Keinänen - Kiukaanniemi

VERSION 1 - REVIEW

REVIEWER	Richard Weiler Specialist in Sport & Exercise Medicine NHS, London
REVIEW RETURNED	16/08/2011

THE STUDY	<p>This is a well written paper addressing the importance of translational and practical research.</p> <p>Major comments:</p> <p>It may be helpful for readers to include brief comments or results on the excluded group (those patients who developed diabetes). What proportion developed diabetes despite lifestyle interventions? This is a relevant addition and would be interesting.</p> <p>The authors discuss limitations of physical activity assessment by questionnaire, however, perhaps more important is the validity of the LTPA to measure change in physical activity. Additional references and brief discussion on this topic would be helpful.</p> <p>Some more detail about the type of interventions would be helpful for readers (LTPA assessing leisure activity only) - it is not possible to fully consider reasons for the findings as a result of leisure time activity behaviour change if non-leisure changes were also being addressed and unmeasured.</p>
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REVIEWER	Knut Borch-Johnsen Professor Research Centre for Quality in Health Care Inst. Publ. Health Univ. Southern Denmark
REVIEW RETURNED	I have no conflict of interest relevant for the present study/review 20/09/2011

THE STUDY	<p>The study is a post hoc analysis of data from the FIN-D2D diabetes prevention programme. This paper aims at analysing the impact of increased physical activity on progression in cardio-metabolic risk. The aim is reasonably clear, but a clear answer is difficult to obtain. The intervention is complex, and involves dietary recommendations as well as physical activity. There are no data on whether adherence to nutritional recommendations is correlated to physical activity. This is important as the observed differences in cardiometabolic risk could as well be a consequence of dietary changes.</p> <p>The study is an observational study in the way that intervention was provided to all interested individuals. They are therefore self-recruited, and may only represent the most highly motivated fraction of the population.</p> <p>For the same reasons the study outcome is difficult to interpret and this is not fully reflected in the abstract and discussion</p>
RESULTS & CONCLUSIONS	<p>The problem again relates to the potential (and very likely) intercorrelation between different interventions. The comment resembles those above.</p>

REVIEWER	Jason Gill, University of Glasgow
REVIEW RETURNED	27/09/2011

THE STUDY	<p>1) It would be helpful if an explicit research question for the analysis undertaken in the paper was described in the introduction. The question about how to apply knowledge from clinical trials to clinical settings refers to the wider FIN-D2D programme and not specifically to the post-hoc analysis comparing those who did or did not increase physical activity levels which is the focus of this of this paper.</p> <p>2) More detail is required in the methods about how waist and blood pressure were measured (were there SOPs for this?) and biochemical analysis methods. At baseline 20% of blood samples were from capillary blood and 80% from venous blood. At 1 year the figures were 15% and 85%. Did some individuals have an initial capillary sample and a venous sample at 1 year? It was mentioned in the discussion that there were some changes in the methodology for glucose measurements over the course of the study. This should be fully described in the methods.</p> <p>3) More detail is needed about the nature of the intervention visits and the range of frequencies for the intervention visits.</p>
RESULTS & CONCLUSIONS	<p>1) Page 6, lines 33-35. Please rephrase sentence stating that levels of serum cardio-metabolic risk factor levels were near the upper limit of the recommended range. This is not the case for all of these factors, for example HDL concentrations were reasonably high (i.e. healthy) for both men and women.</p> <p>2) Please report baseline data for the individuals who increased and did not increase physical activity levels (and those who had always been physically active) separately. Were there any baseline differences between groups?</p> <p>3) It would be helpful if data for the 181 participants who reported that they were always highly physically active were also presented.</p> <p>4) Page 7, lines 55-57. Please provide a reference/evidence to support the comment that self-reported change in physical activity is a reliable measure. There are well-reported limitations to the use of</p>

	<p>self-report measures to assess physical activity and these should be acknowledged.</p> <p>5) Page 8, line 4. It is stated that the association between physical activity and dietary change is a topic for future analysis. Are these data available? If so, it would markedly strengthen the paper if they were included as change in diet is an important potential confounder of the results presented in this study. As the authors acknowledge, it may be that those who increased activity also changed diet more (dietary change was part of the intervention counselling) which could have influenced the findings.</p> <p>6) Page 8, lines 14-23. A little more caution is needed in the interpretation of the data made in this paragraph. An effect of differences in diet between the groups who increased or maintained their physical activity may have contributed to the difference in weight change. This needs to be acknowledged here.</p> <p>7) Page 8, lines 33-35. Please explain and/or provide a reference for the statement that increased fat oxidation due to physical activity may reduce LDL levels.</p> <p>8) Page 8, lines 41-45. While reduced fasting and 2-hour glucose concentrations are in the group who increased physical activity are likely to reflect increased insulin sensitivity, without any insulin measurements, the data presented cannot be regarded as 'proof' of increased insulin sensitivity. This paragraph should therefore be reworded.</p> <p>9) Page 8, lines 52-54. The authors state that the findings support the idea that physical activity counselling should be one part of the preventative interventions of individuals at elevated risk for type 2 diabetes. I am not sure that this can be concluded from the present data. All participants underwent physical activity counselling, but less than 20% of them increased physical activity as a result of this. To address the issue of whether physical activity counselling should be used, it would be necessary to compare a group who received counselling with a group who did not receive counselling. This paragraph should therefore be amended.</p>
REPORTING & ETHICS	<p>The participants did not provide informed consent to participate in this study. The Ministry of Social Affairs and Health in Finland gave permission to collect the data for evaluation purposes, but I am not sure whether this is sufficient for the purposes of this publication.</p>

VERSION 1 – AUTHOR RESPONSE

Reviewer: Knut Borch-Johnsen

Professor

Research Centre for Quality in Health Care Inst. Publ. Health Univ. Southern Denmark

I have no conflict of interest relevant for the present study/review

The study is a post hoc analysis of data from the FIN-D2D diabetes prevention programme. This paper aims at analysing the impact of increased physical activity on progression in cardio-metabolic risk.

The aim is reasonably clear, but a clear answer is difficult to obtain.

The intervention is complex, and involves dietary recommendations as well as physical activity. There are no data on whether adherence to nutritional recommendations is correlated to physical activity.

This is important as the observed differences in cardiometabolic risk could as well be a consequence of dietary changes.

Authors' response: We have now included in our paper questions on dietary changes and adjusted our results for dietary changes.

The study is an observational study in the way that intervention was provided to all interested individuals. They are therefore self-recruited, and may only represent the most highly motivated fraction of the population.

For the same reasons the study outcome is difficult to interpret and this is not fully reflected in the abstract and discussion

Authors' response: We have now included this limitation in the discussion (see strengths and limitations). However, exercise motivation instead of exercise itself may not be the primary reason for the association between the observed change in cardio-metabolic risk factors and observed increase in physical activity.

Reviewer: Jason Gill, University of Glasgow

1) It would be helpful if an explicit research question for the analysis undertaken in the paper was described in the introduction. The question about how to apply knowledge from clinical trials to clinical settings refers to the wider FIN-D2D programme and not specifically to the post-hoc analysis comparing those who did or did not increase physical activity levels which is the focus of this of this paper.

Authors' response: We agree. We have deleted the misleading sentence ('a major question is...') from introduction and added one more specific sentence to clarify the focus.

2) More detail is required in the methods about how waist and blood pressure were measured (were there SOPs for this?) and biochemical analysis methods. At baseline 20% of blood samples were from capillary blood and 80% from venous blood. At 1 year the figures were 15% and 85%. Did some individuals have an initial capillary sample and a venous sample at 1 year? It was mentioned in the discussion that there were some changes in the methodology for glucose measurements over the course of the study. This should be fully described in the methods.

Authors' response: We have rewritten the 'Measurements at baseline and follow-up' paragraphs as suggested (see text) and slightly modified the comment in discussion on this as the methods changed only concerning glucose values. In discussion we already clarify that we recorded the method used and did a sub-group analysis among those participants whose glucose levels had been measured with an identical method at baseline and follow-up. These results are not shown separately as the finding in the sub-group was similar to that presented in our results. Furthermore, taking into account the large sample size, it is very unlikely that some changes in methodology of OGTT glucose measurements hamper the main conclusions we have made from these results.

3) More detail is needed about the nature of the intervention visits and the range of frequencies for the intervention visits.

Authors' response: As it would take much space to explain the intervention guidelines in detail and as they are available in web in English, we have included this reference, so, more comprehensive intervention guidelines can be easily found. The reference is:

Ref: Finnish Diabetes Association. Implementation of type 2 diabetes prevention plan: Project plan 2003-2007, FIN-D2D project [article online], 2006. Available From

http://www.diabetes.fi/files/1107/Implementation_of_Type_2_Diabetes_Prevention._Project_Plan_2003-2007.pdf

In fact an even more detailed guidelines were given in Finnish.

In addition, we have added a comment on the commonly recommended physical activity modalities to the methods. Unfortunately, exact content of each intervention visit in the primary health care has until now not been collected comprehensively for evaluation purposes and due to the high proportion of missing data on this at the moment we have given only the number of visits.

1) Page 6, lines 33-35. Please rephrase sentence stating that levels of serum cardio-metabolic risk factor levels were near the upper limit of the recommended range. This is not the case for all of these factors, for example HDL concentrations were reasonably high (i.e. healthy) for both men and women.

Authors' response: Table 1 has been modified (see next point) and the sentence has been rephrased.

2) Please report baseline data for the individuals who increased and did not increase physical activity levels (and those who had always been physically active) separately. Were there any baseline differences between groups?

Authors' response: Table 1 has been changed to include baseline data for the individuals who increased and did not increase physical activity levels with p values for statistical difference. Our primary analysis strategy did not include adjustment for baseline values as baseline levels may have an influence on how intensively the intervention guidelines are given. However, as the baseline values are given in table 1, we have now added results adjusted for sex, baseline age and baseline values to table 3 and added a comment on this to discussion. After adjustment for baseline values other results persisted but the borderline difference in systolic blood pressure was no more statistically significant after the adjustment, but on the other hand the difference in triglyceride levels became statistically significant the adjusted p value for group difference being 0.007.

3) It would be helpful if data for the 181 participants who reported that they were always highly physically active were also presented.

Authors' response: We think that presenting this interesting data in the current report may make the presentation of the results more complicated and the main message of our paper would be more difficult to follow. However, we give here the results of changes in the main risk factors in the group who reported that they were always highly physically active. The mean (SD) changes during the one-year follow-up for this subgroup were -1.55 (3.63) kg for weight, -0.59 (1.34) kg/m² for BMI, -1.91 (5.38) cm for waist, -0.16 (0.74) mmol/L for total cholesterol, 0.06 (0.22) mmol/L for HDL cholesterol, -0.19 (0.70) mmol/L for LDL cholesterol, -0.02 (1.08) mmol/L for triglycerides, -0.08 (0.49) mmol/L for fasting glucose. Expectedly, the changes during the one-year intervention in this sub-group were more similar to those who did not change their exercise habits than to those who changed (please, compare to the values shown in the paper table 3). Exceptions to this rule were the increase in HDL cholesterol (persistent physical activity is known to increase large HDL particles) and change in fasting glucose (dietary changes may have influenced this). We have now slightly modified our discussion in this respect as our results may be best generalized to those individuals who are formerly sedentary.

4) Page 7, lines 55-57. Please provide a reference/evidence to support the comment that self-reported change in physical activity is a reliable measure. There are well-reported limitations to the use of self-report measures to assess physical activity and these should be acknowledged.

Authors' response: This has now been modified and discussed in more detail and additional data on physical activity has been given in the paper.

5) Page 8, line 4. It is stated that the association between physical activity and dietary change is a topic for future analysis. Are these data available? If so, it would markedly strengthen the paper if they were included as change in diet is an important potential confounder of the results presented in this study. As the authors acknowledge, it may be that those who increased activity also changed diet more (dietary change was part of the intervention counselling) which could have influenced the findings.

Authors' response: The dietary changes have been included and adjusted for in our revised version.

6) Page 8, lines 14-23. A little more caution is needed in the interpretation of the data made in this paragraph. An effect of differences in diet between the groups who increased or maintained their physical activity may have contributed to the difference in weight change. This needs to be acknowledged here.

Authors' response: The dietary changes have been analyzed, adjusted for and discussed.

7) Page 8, lines 33-35. Please explain and/or provide a reference for the statement that increased fat oxidation due to physical activity may reduce LDL levels.

Authors' response: This statement has been changed to a more general statement of the mechanisms mediating the effects of physical activity and a reference on the exercise-associated novel mechanisms has been added.

8) Page 8, lines 41-45. While reduced fasting and 2-hour glucose concentrations are in the group who increased physical activity are likely to reflect increased insulin sensitivity, without any insulin measurements, the data presented cannot be regarded as 'proof' of increased insulin sensitivity. This paragraph should therefore be reworded.

Authors' response: This is reworded by changing 'proof of' to 'in accordance with the finding of'

9) Page 8, lines 52-54. The authors state that the findings support the idea that physical activity counselling should be one part of the preventative interventions of individuals at elevated risk for type 2 diabetes. I am not sure that this can be concluded from the present data. All participants underwent physical activity counselling, but less than 20% of them increased physical activity as a result of this. To address the issue of whether physical activity counselling should be used, it would be necessary to compare a group who received counselling with a group who did not receive counselling. This paragraph should therefore be amended.

Authors' response: The paragraph has been modified as suggested.

The participants did not provide informed consent to participate in this study. The Ministry of Social Affairs and Health in Finland gave permission to collect the data for evaluation purposes, but I am not sure whether this is sufficient for the purposes of this publication.

Authors' response: The permission also included specifically permission for scientific publication which has been included in the paper.

VERSION 2 - REVIEW

REVIEWER	Jason Gill, Senior Lecturer, University of Glasgow
REVIEW RETURNED	27/10/2011

The reviewer filled out the checklist but did not make any further comments.

REVIEWER	Knut Borch-Johnsen, Professor Research Centre for Quality in Health Care Univ. Southern Denmark
REVIEW RETURNED	31/10/2011

The reviewer filled out the checklist but did not make any further comments.