25-Jan-2021

BMJ-2020-063155 entitled "E-HEALTH "STANDINGTALL" BALANCE EXERCISE FOR FALL PREVENTION IN OLDER PEOPLE: RESULTS OF A TWO-YEAR RANDOMISED CONTROLLED TRIAL"

Dear Ms. Delbaere,

Thank you for sending us your paper. We sent it for external peer review and discussed it at our manuscript committee meeting. We recognise its potential importance and relevance to general medical readers, but I am afraid that we have not yet been able to reach a final decision on it because several important aspects of the work still need clarifying.

We hope very much that you will be willing and able to revise your paper as explained below in the report from the manuscript meeting, so that we will be in a better position to understand your study and decide whether the BMJ is the right journal for it. We are looking forward to reading the revised version and, we hope, reaching a decision.

Please remember that the author list and order were finalised upon initial submission, and reviewers and editors judged the paper in light of this information, particularly regarding any competing interests. If authors are later added to a paper this process is subverted. In that case, we reserve the right to rescind any previous decision or return the paper to the review process. Please also remember that we reserve the right to require formation of an authorship group when there are a large number of authors.

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Dr Wim Weber
Dep. Head of Research
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Report from The BMJ's manuscript committee meeting

These comments are an attempt to summarise the discussions at the manuscript meeting. They are not an exact transcript.

Members of the committee were: Joseph Ross (Chair), Gary Collins (Statistical advisor), Timothy Feeney, John Fletcher, Nazrul Islam, Elizabeth Loder, David Ludwig,Tiago Villanueva, Wim Weber.

Decision: Put points

Detailed comments from the meeting:

We thought your study addresses an important and interesting research question. We had the following concerns.

Outcomes seem to match between the various documents (paper, protocol, registry and SAP). Having said that, there are a considerable number of outcomes at 4 post baseline time points (e.g., 56 comparisons in Table 2, 32 in Table 3, 24 in Appendix 2, 72 in Appendix 3). You state a-priori that no adjustment for multiple testing – and ultimately most findings are non-significant.

Abstract: "Both groups had a similar rate of falls and proportion of fallers at 12-months (p=0.071 107 and p=0.461 respectively)"; we would like to see this quantified and not just p-values – what was the rate of falls in both arms or the number of falls per arm?

We would appreciate a comment on the switch of analysis from negative binomial (specified in the protocol) to a poisson model (in the SAP and paper) - the switch conveniently changes the finding at 2 years. Furthermore, the results in Figure 2 are based on a mixture of poisson and negative binomial (e.g., rate of falls at 12m 0.72; 95% CI 0.66 to 1.02 is NB, whilst rate of falls at 24m is 0.84; 95% CI 0.72 to 0.98 is poisson).

The sample size – as reported in the paper – is not reproducible nor particularly informative. The protocol provides much more detail, including assumptions, effect size (based on the primary outcome IRR) etc, but still not fully reproducible. So this needs addressing and inserting into the manuscript. Please describe the sample size calculation using an outcome and effect that have intuitive meanings to a clinician. This will help put in context the formal result of failure to detect this difference. The present "33% effect" will mean little to most people.

Might you provide more detail about the intervention, so that others could reproduce it if they wanted to.

Most authors (including corresponding) are affiliated with Neuroscience Research Australia which commercially markets "the PPA (NeuRA FallScreen)". This seems to be an assessment tool, not the intervention app (https://www.neura.edu.au/research-clinic/fbrg/). We would like some clarification whether the organization has rights and plans to commercial the app itself. Along these lines, is "Standing Tall" a trademark for a commercial program? If so, we would like to ask you to remove it from the title of the paper.

First, please revise your paper to respond to all of the comments by the reviewers. Their reports are available at the end of this letter, below.

In your response please provide, point by point, your replies to the comments made by the reviewers and the editors, explaining how you have dealt with them in the paper.

Comments from Reviewers

Reviewer: 1

Recommendation:

Comments:
This article is very well written and it's subject is highly relevant and appropriate to community level strategies in the prevention of falls on older people. This is especially so in light of the pandemic and reduced social mobility within communities.
Several areas could be highlighted and considered important information;

1. The recruitment of participants were based on advertisement and word of mouth. Information on how widespread in terms of locality, areas covered and medium of advertisement would allude to whether there was a wider inclusion of different types of communities into the study .
2. Were all the participants assessed for their ability or digital literacy to use the digital platform independently or otherwise ? If so how was this assessed?
3.was there a difference in sociodemographic background of subjects? This is raised as often respondents to such a trial often belong to a similar or homogeneous population. Did participants also performed other types of exercises of outdoor activities?
4. The usability and age appropriateness was tested on a group of older people ; should include further details such as sample population numbers, mean age, gender etc.

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Please enter your name: Shahrul Bahyah Kamaruzzaman

Job Title: Consultant Geriatrician

Institution: University of Malaya

Reimbursement for attending a symposium?: No

A fee for speaking?: No

A fee for organising education?: No

Funds for research?: No

Funds for a member of staff?: No

Fees for consulting?: No

Reviewer: 2

Recommendation:

Comments:
This study examined an important area of fall prevention and fall management. Using e-health
home-based programme is innovative. It has a large sample size. Please find below comments for
authors to address.

Introduction: Please add a hypothesis of the study

Methods
For randomization, elaborate which web-based randomization programme was used to implement
random allocation sequence. It is indicated in Page 8, the allocation ratio is 1:1, why the subject number
is not identical in IG and Con group (i.e. IG=254 vs CON=249)

Training protocol – when compared with con group, IG group had an additional exercise time of 120
minutes/week and was given exercise equipment. The improvement in outcomes could simply be
attributed to the great placebo effect and additional treatment time, regardless of which mode of
exercise delivery. Please comment.

How the participants registered their exercise duration?

There are many secondary outcomes. For instance, physical measurements included balance, functional
mobility and gait assessment, step performance, SPPB – why each of them is needed.

Justify the use of 3 tests to assess cognitive function - Montreal Cognitive Assessment(17), Trail-Making Tests (TMT)(18), and the Victoria Stroop task(19).

Justify the use of 3 scales to measure Health-related quality of life - 12-item WHO Disability Assessment Schedule(23), 5-level EuroQol- 5 Dimension (EQ-5D-5L)(24), and 20-item Assessment of Quality of Life 6-Dimensions (AQoL-6D) questionnaires(25).

Why lab re-asst was only performed in 226 participants? How to determine that 226 participants for the lab re-asst, who did the selection, blinded?

Results – are there any differences in baseline demographic between those who continued the training and follow-ups vs those who dropped out.

"We did find a small improvement of 0.03 (95% CI 0.01-0.06) on the EQ-5D-5L utility score at 6-months in IG compared to CG." Comment on clinical significance

The baseline value of TUG indicates that the participants are fit and have good mobility, why did the investigators target this group?

Discussion
The study found no significant improvement in the primary outcomes at 12-month but there was reduction of fall rate and injurious fallers at 24-month. The discussion has to be strengthened by giving some insights on why there was reduction of fall rate and injurious fallers at 24-month despite no improvement in the physical, balance and mobility outcomes. The authors cited "their 20% reduction in the proportion of injurious fallers at 24-months, may be higher than the previously reported 12% reductions (3)". Which part of training programme contributes to the positive findings? which particular aspect of e-Health makes it effective? Or Is it just because of the additional exercise time of the IG when compared to the CON group?

In the conclusion, the investigators claimed that this is a "low resources and low-cost intervention". However, each participant was given a tablet, exercise equipment and exercise mat etc. And human resources are needed to registered the entry regularly. It seems that the cost and resource are not that low. Please comment.

More improvement for those less concerns about falls, and lower physio risk, what is the significance of these findings?

Please confirm that you understand and consent to the above terms and conditions.: I consent to the publication of this review

Please enter your name: Margaret Mak

Job Title: Professor

Institution: Department of Rehabilitation Sciences, The Hong Kong Polytechnic University

Reimbursement for attending a symposium?: No

A fee for speaking?: No

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Reviewer: 3

Recommendation:

Comments:
The present study tests the effects of a fall prevention treatment in preventing falls in older people. The intervention consists in balance exercises delivered via an App.
Results show a reduction in rate of falls two years after baseline assessment without a firm, concomitant improvement in balance.

Introduction
The introduction nicely reports evidences from literature on fall prevention in this population and overall, the research questions are clearly defined.
A brief overview on treatment related changes after balance rehabilitation would improve readers understanding of methods and results of the present paper.
Methods
The design of the study is appropriate. Prospective RCT is a typical study design to assess fall prevention interventions.
In this section authors should state whether this intervention incorporates international recommendations for fall prevention in this population.
In addition, authors should add an extra appendix to better explain treatment provided. Is it possible to better explain how balance exercises were tailored? For example providing an algorithm to link subjects' impairments and functional deficits to treatments provided. Likewise, is it possible to explain how exercise difficulty increased over time? This would improve reproducibility.

Linear models using generalized least squares are adequate to assess the impact of interventions in longitudinal study since the errors are allowed to be correlated. Negative binomial and poisson distributions have been used to this purpose.
Appendix 1 reports results comparing negative binominal vs Poisson distribution. Results are inconsistent, this suggests results are not so conclusive. A larger sample size is probably needed to get firmer conclusions. Please, provide a comment.
The sample size statement is unclear. What does 33% reduction in incidence rate mean? Is it a 33% reduction compared to the control group or an absolute change? Assuming it is the between group difference 33% seems a quite high percentage. Please comment.

Moreover, I do not understand why missing data were not imputed for primary outcome. In general this approach is not recommended (see for example Little et al. The Prevention and Treatment of Missing Data in Clinical Trials. doi:10.1056/NEJMsr1203730.)
Authors stated data were missing at random. Chained equations are usually preferred to means single imputation to avoid biased standard errors. Please comment

Results
Table 1 reports baseline characteristics. Time to a first fall should be reported.

In addition, please clearly report % of subjects who did not fill in the falls diary and proportion of injurious fallers in both groups at 24-month FU.

Discussion
Discussion could be improved.
In specific results do not clearly show the effects of intervention in reducing falls or improving balance.
For example between groups differences in rate of falls at 24monts vanished simply using a negative binomial model.
Several hypotheses could be explored and mentioned in this section.
Is it possible that treatment was provided to subjects not in need of a balance prevention program?

Is it possible that better results would be observed recruiting subjects having balance disorders and experiencing 1 or more falls before be beginning of the study?

Additionally, is a two hour/week training enough to foster balance changes? This is of importance since results show that only 40% of participants achieved the prescribed dose at 6 months follow up. Only 34% of participants received the prescribed dose at 12 months. This does not reflect trends seen in the results where improvements more evident after 12 months.

I think these three elements may be better addressed in the discussion section to suggest improvements for further studies.

Again, in the discussion authors stated that "Adherence was good [...]". However, 60% of participants did not receive adequate dose of the intervention. Additionally, the following statement "The high adherence and zero serious adverse events support the feasibility and safety [...] intervention to a population level" seems overreaching. The same is for "Standing tall is a scalable intervention and can be easily implemented into clinical practice". Feasibility is not the aim of this study.

I am concerned on the lack balance improvements. This makes difficult to explain the main outcome and suggests that expectation bias may have distorted the results. Authors should compare their treatment protocol with already published protocols to highlight differences. They should also provide evidences to readers that this protocol complies with published recommendations.

Finally, authors stated "This trial might have been underpowered for detecting differences in fall risk factors, as our sample had a lower fall risk than anticipated." It seems that lower fall risk, an overoptimistic expected reduction in rate of falls and a lower than expected dosage may have caused lack of balance improvements. Please, elaborate on this issue in the discussion

Dr. Wim Weber

I have read and reviewed the manuscript. In my opinion, the article addresses an important topic and is interesting for readers. Falls matter to clinicians and patients and fall prevention has been addressed in many trials. However, few of them included unsupervised, home-based, e-Health balance exercises. This is intriguing in light of the COVID-19 pandemic.

In this perspective, I think this study adds enough to existing knowledge and will be cited.

Strength of this study is the large sample size and and the extensive clinical assessment. Also, methodology is fine and results are clearly presented.

However, results are not very consistent and the message is less clear than expected. Authors found reduction in rate of falls only at second baselines (24 months) without balance improvement. Moreover, improvements seem to disappear using a different statistical model.

Weakness. Although participants characteristics are adequately described, study inclusion and exclusion criteria are problematic. It seems the study enrolled subjects without balance disorders and falls. Including subjects not in need of a fall prevention program may have weakened the results.

Overall, it seems that inclusion of healthy subjects having lower fall risk, an overoptimistic expected reduction in rate of falls and a lower than planned dosage may have caused lack of balance improvements and not firm results on falls reduction.

Best Regards,
Davide Cattaneo
Dr. Davide Cattaneo, PT, PhD.
LaRiCE Lab
Research Coordinator
Fnd Don C Gnocchi I.R.C.C.S
Santa Maria Nascente (MI)
Italy

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Please enter your name: Davide Cattaneo

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Institution: IRCCS Fondazione Don Carlo Gnocchi

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Reviewer: 4

Recommendation:

Comments:
In this population-based randomized controlled trial, Delbaere and colleagues evaluate the effectiveness of an e-Health balance exercise program delivered via an App compared to health education program only. Participants were 503 individuals age 70 or above who were independent in activities of daily living and without cognitive impairment or any other major disease precluding exercise. The trial was assessor blinded and randomization done in blocks. The primary outcomes were the rate of falls and the number of fallers over 12-months. The authors further tested 18 secondary outcomes. The results indicated no statistically significant differences of the primary outcomes. About the secondary outcomes, the intervention group had a 16% lower rate of falls over 2-years compared to the controls (incidence rate ratio:0.84, 95% confidence interval, 95%CI:0.72-0.98) and a lower proportion of injuries after 2 years.

Trial on the population levels are very difficult to conduct and the authors are to be congratulated to have achieved to keep participants motivated. The trial is overall well conducted and analyzed, including the complier averaged causal effect and bootstrap analyzes. I have a few suggestions that the authors may want to consider.

Comments:

1. The conclusions in the abstract and the discussion differ and just be similar. The authors should be clearer whether they call their study a null finding study or focus on some statistically significant findings of the secondary outcomes. The authors stated in the protocol that they did not correct for multiple testing as they viewed all their 18 secondary outcomes are plausible and a priori testable outcomes. I challenge this view and rather encourage the authors to look at the consistency of some effect estimates. The incidence rate ratio of the primary outcome (rate of falls after 12 months, 0.82, 95%dary outcome (incident rate ratio of falls after 24 months, 0.84, 95% CI 0.72-0.98). This consistency can also be seen in Figure 2. Thus, one could speak of a consistent effect on falls in the trial. It is apparent that the effect in the trial was not as strong as a priori expected and as a result, the sample size was a little too small. Nevertheless, I think that the consistent effect on falls is more important than focusing on small differences of the P values, one statistically "significant" the other not.

2. The exercise program included a daily program of up to 20 min per day (provided on a tablet computer). People who did not at least exercised 100 min per week were contacted by phone and all participants in the intervention group received two home visits. I wonder how applicable this program will be outside the trial when people are only using the App also considering that, as expected, not all participants in the trial were adherent. Could the authors discuss this point in the paper?

3. I may have missed it, but I am missing a subgroup analysis by sex. I think that one cannot assume similar physiological effects of an exercise program according to sex.

4. Please report proper effect estimates in the abstract and not just P values. Please report P values to the 2 decimal when >0.10.

5. Please omit the statement that this is the first large study about this topic. While this may be correct, it is not a scientific statement and does not indicate the quality of a study.

6. The authors call the program "unsupervised." As there was a follow-up on how often and how long participants did the program plus there were calls and visits, I am not certain that "unsupervised" is the right label.

7. While not directly related to this study, the authors may want to add a reference to the study by Stensvold https://doi.org/10.1136/bmj.m3485 showing some benefit of a high intensity interval training on all cause mortality (to underscore the importance of exercise programs in elderly people).

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Please enter your name: Tobias Kurth

Job Title: Epidemiologist

Institution: Charité, Berlin

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