Author's response to reviews

Title: Combined effects of functionally-oriented exercise regimens and nutritional supplementation on both the institutionalised and free-living frail elderly (double-blind, randomised clinical trial)

Authors:

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Author's response to reviews: see over
RE: Peer review of the MS: 8923208701823219

Combined effects of functionally-oriented exercise regimens and nutritional supplementation on both the institutionalised and free-living frail elderly (double-blind, randomised clinical trial)
Marek M Zak, Christian Ch Swine and Tomasz T Grodzicki

Dear Professor Stanhope,

To begin with, we are very much indebted to you for all your perceptive comments, as we feel that your critical appraisal has tangibly helped us revise the MS in the way that successfully purged it of all its obvious deficiencies, whilst at the same time highlighting its true merits.

Please kindly note that in structuring our response we took the liberty of quoting verbatim your remarks (converted into MS WORD from the original PDF files) and then had them juxtaposed with our own comments (set in blue font for contrast and greater clarity), so that the discourse is easier to follow. It is our sincere hope you will find all the revisions in the amended MS to your satisfaction. We are also hopeful that in some instances where our respective views still seem to remain at odds, we have nevertheless managed to make our arguments persuasive enough to alleviate your concerns.

With the very best regards,

Marek Zak, PhD

_____________________________________________________________

MINOR ESSENTIAL REVISIONS
1) Change the number of study participants to the number that completed the study. Eliminate statements that the four groups were of equal size.
   Response:
   Both Figure 1 and the MS have been amended accordingly to accommodate this requirement.

2) The conclusion that only multi-factorial interventions have clear potential for appreciably improving overall functional status of elderly is not supported by the reported effort. Develop a conclusion that relates to the findings of the reported study such as task specificity (strength training increased strength but not function, Functionally-oriented exercises increased functional scores and not strength).
   Response:
   The authors concede the point and so the MS has been amended accordingly to accommodate this requirement.

3) The description of the effort to double-blind the study should be restated. While there was an adequate attempt to blind staff to the interventions, it is certainly feasible that staff within any facility or region may communicate and share the nature of the intervention being delivered. Thus, inferences could have been made.
Response:
The authors concede the point and so the MS has been amended accordingly, i.e.
Section: METHODS
Sub-section: Study design
Page: 6
Paragraph: 2

4) Clarify the list of subject inclusion (numbers 2 and 6) and exclusion criteria (numbers 1 and 6).

Response:
The authors concede the point and so the MS has been amended accordingly, i.e.
Section: METHODS
Sub-section: Study population
Page: 7 – 8

5) Eliminate the redundant information (inclusion criteria) under overall assessment of physical function.

Response:
Please kindly note that Table 1 (Baseline characteristics of the study population) merely provides the median values of the respective groups with regard to age, body weight, BMI and BBS, whereas the authors insisted on having the population precisely defined in terms of individual eligibility, hence the deliberate use of the first 4 items in the inclusion criteria as clear cut-off points during the preliminary screening procedure to facilitate precise determination. It is perhaps also worth noting that through providing median values of the above the authors effectively demonstrated homogeneity of the respective groups, which – as the authors felt - was a fairly important methodological consideration, since upon the commencement of the study regimen there were no statistically significant differences between the groups, so an “even platform”, so to speak, was ensured for all participants at the very start.

6) Describe how the dynamometer (a force measuring instrument) was used to measure joint moments in (N.m). Correct any discrepancies that may exist in the force units.

Response:
In order to measure the torque value, maximal isometric strength was multiplied by the length of the arm of force, i.e. the distance from the axis of the dynamometer to the axis of the joint, whose flexion/extension was tested. The yielded torque value was then expressed in N/m. Here, for example, is how the testing procedure with the aid of a hand-held HOGGAN dynamometer was applied to the knee extensors:

E.g. Measurement of the isometric strength - knee extension
Start position
The subjects were seated upright in a rigid chair with the knee flexed to an angle of 90° with the hand-held HOGGAN dynamometer placed by the physiotherapist on the lower leg proximally to the ankle joint just above the ankle.
Testing
The subject was then asked to lift the lower leg, i.e. push against the dynamometer held in place by the physiotherapist. The subjects were strongly encouraged to gradually increase the force to the greatest possible level, while the tester was opposing, until the maximal isometric strength was achieved. To begin with, the subject was allowed two or three practice trials, so as to familiarize himself with the actual procedure. Three formal measurements were then performed and recorded with 1-minute rest periods between the respective trials, whereas the best trial was ultimately accepted as the final result. All measurements with the aid of a hand-held HOGGAN dynamometer were carried out by the same physiotherapist, so as to ensure that there were no idiosyncratic differences in the actual application of the procedure. The authors strongly believe that in view of the already substantial size of the MS, the inclusion of the detailed descriptions of the isometric strength measurements with regard to all 4 muscle groups would make its size non-manageable, whilst not really adding to the overall clarity of the discourse.

7) Describe the selection criteria and characteristics of the four exercise bands.

Response:
In view of the above query it would appear that this particular passage manifestly lacked in clarity and so the authors decided to have it revised to demonstrate that it all actually adds up. The following breakdown should illustrate clearly enough how the PRE regimen was pursued by the study subjects.
RE: PRE
Four series of resistance exercises (stretches of Thera-Band®) broken down into the following sequential components:
3 x 10 stretches of a band per each discrete muscle group (Cf. Tables 1, 3 and 3A) performed within 1.5 min., followed by 1 min. rest period (used by the therapist to move the band to the other leg). Then the same set of exercises was repeated for the same muscle group on the other leg.

In terms of the time scale, it works out as follows:
4 x 1.5 min. (left leg) + 4 x 1.5 min. (right leg) = 12 min (exercises)
+ 4 x 1 min. x 2 legs - rest interval per leg
(inclusive of repositioning of the band) = 8 min.
= 20 min. - sequence completion
Please kindly refer to the following amended sections of the MS, i.e.
Section: METHODS
Sub-sections: Progressive resistance exercises
Individual allocation of the Thera-Band®
Page: 14

8) Describe the resistance exercises and lower limb positions. Consider providing a figure depicting the exercise elements.

Response:
In view of the fact that the MS is already 30 pages long and the presently
recommended revisions might still contribute to having it extend further, the authors feel that incorporation of the detailed descriptions of all exercise regimens followed by the subjects throughout the study would make the overall length of the MS simply non-manageable, not least for the Editors. Therefore the only amendment presently contemplated for the MS is the specific reference that the actual scope of the PRE regimen was closely based on the recommendations put forward by Thera-Band® Academy (Cf. weblink: http://www.thera-bandacademy.com). The MS has been supplemented with two new references, i.e. Section: METHODS Sub-sections: Progressive resistance exercises Page: 14 and so the REFERENCES section has also been amended accordingly.

9) Eliminate the excessive justification material under the structured exercise regimens and replace the material with a detailed description or table containing information on the actual exercises.

Response:
The MS have been amended accordingly to accommodate this requirement, i.e. i.e. Section: METHODS Sub-sections: Exercise regimens Progressive resistance exercises Individual allocation of the Thera-Band® Pages: 11, 14

10) Repeat the request under number 9 above for the methods section related to Functionally-oriented exercise and standard exercises.

Response:
This particular suggestion has been addressed in some detail in the DISCUSSION section of the MS, i.e. Section: DISCUSSION Page: 23

11) Eliminate the excessive justification related to the use of NUTRICIA. State a brief summary of this delimitation in the discussion section.

Response:
In view of the fact that the trial was actually funded by NUTRICIA RESEARCH FOUNDATION (Grant Ref. No CEBK180/2000) the authors are simply not at liberty to accommodate the Reviewer’s suggestion for contractual reasons.

12) Eliminate the first paragraph in the results section.

Response:
The entire paragraph has obviously been misplaced in the MS, as given its clearly interpretative nature it most certainly belongs in the DISCUSSION section, where it has been moved since, following necessary modification.

13) Eliminate Figure 1. It provides redundant summary information.
Response:

The authors sought specific guidance on the subject from the editors and were told that the MS must be CONSORT-compliant.
Please kindly look up the following weblinks:
http://www.consort-statement.org/?o=1011;
http://www.biomedcentral.com/1471-2288/1/2

14) On page 20, the reference to gait speed studied by others is in fact relevant to the focus of the manuscript since the 6MW test is a measure of average velocity (distance/time=average rate) and may be compared.

Response:
The authors concede the point and so the MS have been amended accordingly to accommodate this requirement, i.e. this paragraph has been deleted.

15) The last paragraph on page 20 provides little insight into the results of the study and should be eliminated.

Response:
In view of the fact that core data presentation with regard to the respective muscle groups at issue has been substantially reshuffled in the revised version of the MS (Cf. Table 3 and 3A), the authors are unable to accommodate the Reviewer’s suggestion, as otherwise the discourse would lack in consistency.

16) References to “flawed” methodology must be eliminated. Certainly, methodologies of other studies (much like the one being reported) may be limited in their scope.
Response:
The authors concede the point and the DISCUSSION section in the MS has been amended accordingly, i.e. the incriminated sentence has been deleted.

RE: Peer review of the MS: 8923208701823219

Combined effects of functionally-oriented exercise regimens and nutritional supplementation on both the institutionalised and free-living frail elderly(double-blind, randomised clinical trial)
Marek M Zak, Christian Ch Swine and Tomasz T Grodzicki

Dear Doctor Skelton,

To begin with, we are very much indebted to you for all your perceptive comments, as we feel that your critical appraisal has tangibly helped us revise the MS in the way that successfully purged it of all its obvious deficiencies, whilst at the same time highlighting its true merits.

Please kindly note that in structuring our response we took the liberty of quoting verbatim your remarks (converted into MS WORD from the original PDF files) and then had them juxtaposed with our own comments (set in blue font for contrast and greater clarity), so that the discourse is easier to follow.
It is our sincere hope you will find all the revisions in the amended MS to your satisfaction. We are also hopeful that in some instances where our respective views still seem to remain at odds, we have nevertheless managed to make our arguments persuasive enough to alleviate your concerns.

With the very best regards,

Marek Zak, PhD

MAJOR COMPULSORY REVISIONS:
MAJOR
1) Abstract:
The main question posed in the Background seems to concern the ease to apply and the cost effectiveness of an exercise intervention that could be applied nationally. The data does not support this question, it asks which of two combined exercise interventions (standard exercise and functional exercise vs. strength exercise and functional exercise) is most effective and whether nutritional supplementation enhanced the effects. The abstract and the introduction sections need amending.

Response:
The authors freely concede the point and the MS has been amended accordingly to make the conclusions fully consistent with the actual findings of the study. To begin with, the authors never expected “cost-effectiveness” to become an issue in the first place, especially given a fairly simple context in which it is referenced. Since it seems to have given rise to some queries, whose legitimacy is nevertheless fully appreciated here, the authors volunteered the following brief highlights on how geriatric rehabilitation is presently managed by the public health care sector in Poland, very much in the hope that it might throw enough light on the issue and consequently convince the Reviewer that the authors’ claim of overall cost-effectiveness of the proposed solution is indeed a legitimate one, even though the authors have now happily enough settled for “overall economic viability” in their effort to address the Reviewer’s concerns.

Average pension: PLN 1,237 (ca. EUR 364)
Incidentally, no more than ca. 40% of old age pensioners (OAPs) actually benefit from the above referenced amount, as a vast majority of them receive a monthly amount approximating PLN 700 (ca. EUR 206). For the sake of greater clarity in presentation, this does not take any account of the corresponding disability pension scales. Average costs of hospitalisation (prompted by a minor injurious incident whose successful treatment would not require a period in excess of 14 days) in geriatric wards per day: PLN 150 (ca. EUR 44). This translates into PLN 2,100 (c.a. EUR 618) for a fortnight. Average costs of hospitalisation per day in a surgical ward (prompted by a major injurious incident, e.g. fracture, whose successful treatment would require a period of at least 10 days, followed by a discharge either back into the nursing facility or into the community care (i.e. family fold), with the following
spell of statutorily due physical rehabilitation being subject to local availability of such services, distance to patient’s permanent place of residence, multiple bureaucratic constraints, etc.) PLN 7,710 (ca. EUR 2,268)

It should perhaps be noted at this juncture that if common practice be anything to go by, most regrettably a vast majority of such cases are not actually followed by physical rehabilitation (for multiple reasons), so in effect the patients never return to their pre-incident physical status, even though hardly due to their own fault.

Average costs of individually delivered (i.e. out of hospital facility) physical rehabilitation. Public health care system one-off allowance (i.e. a single series of ten 45 min. sessions following hospitalisation after a single incident): PLN 40/per session + reimbursement for travel costs = PLN 400 (i.e. EUR 12 x 10 = EUR 120).

Average monthly remuneration of a licensed physiotherapist, when on contract with the National Health Fund (NFZ): PLN 2,000 (ca. EUR 588). On average a physiotherapist may service 6 - 7 persons daily (i.e. community dwellers), allowing for a 5-day working week.

In the case of being employed full time by a nursing home facility, a single physiotherapist would be expected to attend to 40 elderly persons, which practically translates into repeating a session with any single person once every 7 - 8 days on average, which speaks for itself in terms of its expected effectiveness.

Average costs of simple rehabilitation equipment (i.e. the props actually used in the study), broken down into purchase prices and rental rates, respectively:

<table>
<thead>
<tr>
<th>Retail purchase price</th>
<th>Rental rate (per month)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ball cushion EUR 18.00 - 36.00</td>
<td>EUR 3.00 - 4.50</td>
</tr>
<tr>
<td>Pedal exerciser EUR 36.00 - 44.00</td>
<td>EUR 4.50 - 6.00</td>
</tr>
<tr>
<td>Thera-Band®</td>
<td></td>
</tr>
<tr>
<td>- Yellow code (ca. 2 m)</td>
<td>EUR ca. 4.50</td>
</tr>
<tr>
<td>- Red code (ca. 2 m)</td>
<td>EUR ca. 5.50</td>
</tr>
</tbody>
</table>

With regard to individual nutritional supplementation (i.e. NUTRIDRINK®) the issue becomes even more complex in terms of financial considerations, i.e. public health care system in Poland simply does not provide for it!

Average cost per 200 ml of NUTRIDRINK® is PLN 6 (ca. EUR 1.76)

Assuming that an elderly person should consume at least 2 x 200 ml daily x 7 days a week (Cf. NUTRICIA recommendations) to offset any possible energy deficit during the pursuit of any of the above referenced exercise regimens, this would work out as 14 NUTRIDRINKS® per week and ultimately translate into PLN 84/week (ca. EUR 25), which would ultimately work out ca. EUR 100/month.

Given the fact that a vast majority of OAPs receive ca. EUR 206/month worth of pension, the issue becomes a moot point really, to put it mildly. Please also kindly note that there are no positions of either “health assistant” or “dietary assistant” in Polish public health care system.

And finally, although the above highlights might give some insight into the specifics of Poland’s public health care services, the question of respective national affluence has altogether been left out of this argument, whereas only a viable comparison in those terms might effectively put the entire issue within truly credible context. The authors feel the Reviewer might also find the perusal of The
Economist Intelligence Unit Report on Poland
http://www.economist.com/countries/Poland/) of some additional benefit here.

MAJOR
2) Abstract: The conclusions need addressing. I do not feel that the conclusions address the results. You state that only multifactorial intervention (FOE plus supplementation) has clear potential for appreciably improving overall functional status in the frail elderly in terms of individual walking capacity and muscle strength, yet the data as I see it do not give that impression. Below is a simplified table of the results:

Exercise Regimen and nutritional supplement

<table>
<thead>
<tr>
<th>Strength Outcomes</th>
<th>Functional Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>I PRE+FOE+ NS</td>
<td>No change</td>
</tr>
<tr>
<td>II PRE+FOE+ Placebo</td>
<td>No change</td>
</tr>
<tr>
<td>III SE +FOE+ NS</td>
<td>No change</td>
</tr>
<tr>
<td>IV SE +FOE+ Placebo</td>
<td>No change</td>
</tr>
</tbody>
</table>

In fact, balance improved more in the placebo group of the SE+FOE. So I feel you need to revisit and rewrite the conclusions of this study. Perhaps a clearer explanation of the main differences between SE and FOE would help the reader, but the role of nutrition is less clear.

Response:
The authors believe that following a major revision of the tables (i.e. Table No 3 and 3A, No 4 and 4A, respectively) the results are now truly allowed to speak for themselves, so this is certainly not the case of 4 times “no change”. For more details please refer to the authors' response to Items 9 and 12 MINOR further below.
The authors do concede, however, that a clearer explanation of the main differences between SE and FOE would indeed be helpful at this juncture and so the MS has been amended accordingly, i.e. Section: DISCUSSION
Page: 23 – 24

MINOR ESSENTIAL REVISIONS:
1) MINOR
Abstract: Methods section rather than giving the test equipment information, it is more important to the reader to know the muscle groups tested (1RM). It is also necessary to add the length of the intervention and frequency of delivery.
Response:
The authors concede the point and the Abstract section has been amended accordingly.

2) MINOR
Abstract: Results section, please add number of subjects completing the intervention/study.
Response:
The authors concede the point and the Abstract has been amended accordingly. Figure 1 has also been revised.
3) MINOR
Background: This section has many very long sentences (over 6 lines long) which make clarity difficult. Please shorten sentences in this section. Suggest the second paragraph becomes the first paragraph.
Response:
The authors concede the point and the MS has been amended accordingly, i.e.
Section: BACKGROUND
Page: 4 - 5

4) MINOR
Methods: Study Population: please give an indication of “recent” when considering fractures as an exclusion criteria and whether people were excluded if they had EVER had a cerebral incident. In the UK, this would mean this intervention would be unavailable to a very large proportion of the oldest population.
Response:
The MS has been amended accordingly to take account of this issue. In fact, the authors were primarily concerned with the lasting after-effects only, as those would actually make the subjects’ participation in the study regimens non-feasible.
Section: METHODS
Sub-section: Study population
Page: 7
Please break down the n=80 to show numbers in nursing home and in community.
Response:
Out of 91 potential participants originally admitted into the study 80 subjects completed it (n = 80). Out of those 80 subjects, 38 had been recruited from the nursing home and 42 were the community-dwellers.
The authors do not think this information should actually be reflected in Figure 1, though, as no stratification of the subjects in respect of their settings was allowed for in the study design. Both Figure 1 and the MS has been amended accordingly, i.e.
Section: METHODS
Sub-section: Study population
Page: 8

5) MINOR
Methods: If the subjects were randomly assigned into the four groups why do you state “as far as it was deemed practicable/practical”? Please explain.
Response:
The authors freely concede the point. This obviously unnecessary embellishment has now been deleted from the MS. The only numerical differences in the actual allocation into the study groups resulted from the fact that “91” was an odd number.

6) MINOR
Methods: Baseline characteristics “EKG” should read ECG? The last sentence saying there were no differences should be at the start of results section?
Response:
An obvious, if most unwelcome mistake. The MS has been amended accordingly.
7) MINOR
Methods: Overall assessment of physical function: please state how many times the functional tests were done and whether an average or best result was used in analysis. Same for the strength measures.

Response:
Each subject was allowed two or three practice trials, so as to familiarize himself with the actual procedure. Three formal measurements were then performed and recorded with 1-minute rest periods between the respective trials, whereas the best trial was ultimately accepted as the final result.
Please kindly refer to the revised version of the MS, i.e. Section: METHODS
Sub-section: Muscle strength assessment Page: 9

On the last sentence of muscle strength assessment you discuss muscle strength was assessed in four different lower limb positions, how was this done (on HOGGAN?) and how was this compared to the start resistance of the bands?

Response:
Please kindly refer to the revised version of the MS, i.e.
Section: METHODS
Sub-sections: Muscle strength assessment,
Individual allocation of the Thera-Band®
Pages: 9, 10, 14

8) MINOR
Methods: Structured exercise sessions: please explain how the authors assessed the exercise to be high intensity. I can see that the strength training was (80% of 1RM) but how did they assess the functional exercise or the standard exercise? Please also explain how they kept the exercises at 80% 1RM if the HOGGAN was only used in the baseline assessments? What was their progressive resistance training protocol?

Response:
Please kindly refer to the revised version of the MS, i.e.
Section: METHODS
Sub-section: Muscle strength assessment,
Page: 9 – 10

9) MINOR
Statistical Analysis: I wonder if the use of a two way ANOVA might have been better
to assess the role of PRE vs. SE and Nutritional Supplement vs Placebo is a more sound statistical approach, particularly as then the home environment (nursing home vs community) and age could then have been considered as confounding factors.

Response:
As it is now quite clear in retrospect, the results presented in Tables No 3 and No 4 were indeed grouped in a rather confusing manner, and so this obviously gave rise
to the Reviewer’s queries. One-way ANOVA was used to accommodate the fact that there was just a single, if combined, differentiating factor that the authors were keen to analyse, i.e. diverse exercises + nutrition (as there was not a control group involved that received no supplementation at all, irrespective whether placebo was actually used or not). The tables at issue have been revised accordingly and the pertinent data are now comprised in the four paired tables, i.e. Table No 3 and 3A, No 4 and 4A, respectively, to enhance overall clarity. Very much in line with the Reviewer’s opinion, if the analysis were to accommodate additional factors like age, setting, etc., these might well be considered as the confounding factors.

The sentence “since all parameters of a 0-2 scale” confuses me, as Strength is measured on a continuous scale and so is distance walked etc? please clarify.

Response:
The scale at issue referred to the Tinetti test only and the Reviewer is quite right to point out that it has been referred to in a confusing manner. The MS has been amended accordingly. Please also kindly refer to the authors’ response to Item 15 MINOR for more details.

10) MINOR
Results: The Figure shows that 11 people were excluded from the assessments after the intervention; more details about why they were excluded are necessary.

Response:
The MS (Figure 1) has been revised accordingly to accommodate the required data. Please kindly refer to the authors’ response to Item 16 MINOR below for the relevant details.

11) MINOR
Results: The second sentence of the first paragraph is not well explained as if the sentence was correct, all groups I to IV would have seen improvements.

Response:
The entire paragraph has obviously been misplaced in the MS, as given its clearly interpretative nature it most certainly belongs in the DISCUSSION section, where it has been moved since, following necessary modification.

12) MINOR
Results: Primary Outcomes section - I would want to see Group I vs Group II and Group III vs Group IV, though this would be picked up by a different statistical approach (see above).

Response:
Please kindly refer back to the authors’ response to Item 9 MINOR further above. The second paragraph states that notable improvements in mobility were seen yet there was only a change in 6MWT not Tinetti’s gait score?
Response:
The authors subscribe to the view that it all actually boils down to a more
A comprehensive approach to assessing mobility. Quite a number of investigators are happy enough to assess mobility with the aid of the 6MW test, whereas this test merely gives an indication of an improvement (if any) in the distance covered since the commencement of the intervention. It does not avail of any knowledge, though, with regard to any inherent characteristics of the gait itself. E.g. Following a few weeks long training regimen a subject is now well capable of covering a longer distance (6MW), but his walk still remains pretty wobbly and his steps are of unequal length (Tinetti POMA, as subsequently modified), which only goes to show that the subject should be offered a more focused type of training in an attempt to have these deficiencies rectified to some extent at least. All in all, 6MW + Tinetti POMA approach seems to give a broader picture, as it were.

13) MINOR
Results: Secondary Outcomes section: the first sentence confuses me as there is mention of distance covered by over 35 metres yet the 6 meter walk test is used; please clarify.
Response:
The 6 Minutes Walking (6MW) test was used in the assessment, with the distance marked off by 5 meter increments.
The second paragraph of this section belongs in the discussion and needs reconsidering as FOE was in all groups anyway.
Response:
The MS has been amended accordingly, i.e. this paragraph was deleted as interpretative and therefore out of place.

14) MINOR
Table 1: Would be useful to have % in nursing home and % in the community within the table.
Response:
In view of the fact that physical homogeneity of all groups was assured at the very start through the recruitment procedure (Cf. Baseline characteristics), the authors did not think that volunteering such an information would have any bearing whatsoever on the subsequent analysis of the results yielded by the study. Besides, the study was never designed to investigate any differences between the community dwellers and nursing home residents in the first place, hence all study groups were made up of a similar number of both.

15) MINOR
In all Tables: Tinetti Total Score, Tinetti Balance Score and Tinetti Gait Score is used, but in the text there is reference to Tinetti’s Performance Oriented Mobility assessment Test (POMA); this is confusing to the reader.
Response:
To clarify the confusion: although the authors make a direct reference to Tinetti POMA test in the MS and reflect this in the References section, the test actually used was the modified version of the Tinetti original test (hence the different scale). This is an obvious oversight on the authors’ part and so the MS has been amended accordingly.

Section: METHODS
Sub-sections: Overall assessment of physical function
Statistical analyses
Pages: 9, 16
Discussion: Please discuss the 12% drop out rate (80 out of 91 starting) during the relatively short intervention of 7 weeks compared to other interventions of longer duration but less frequency that have similar drop out rates.

Response: Although 12% may indeed look an alarming rate, the reasons actually proved trivial enough and were not related in any way to the pursuit of the exercise regimens. Here is a more detailed breakdown of all the drop-outs:

To begin with, there were 4 drop-outs from the nursing home and 7 community dwellers. 1 serious adverse event (The subject developed an acute skin rash, promptly, although erroneously, as it later transpired, attributed by his GP to the ingestion of NUTRIDRINK supplement. The rash was actually caused by an ointment used by the subject’s personal masseuse, to which fact the investigators were not privy. Although the situation was rectified after 2 weeks, the subject was not re-admitted into the study for procedural reasons). 4 adverse events (All nursing home residents. In all cases subjects developed acute respiratory infections that required 2 weeks to cure thus effectively rendering them unfit for the pursuit of the study regimens).

6 voluntary withdrawals (All six subjects, following recent discharge from hospital care were granted 3-week long recuperation leaves in the sanitoria and since the rescheduling was not feasible they had to report to those facilities, which coincided with the timing of the study). All cases were duly reported to the Independent Ethics Committee and Research Monitoring Officer and the investigators were subsequently released from any professional liability. Finally, the authors did not deem such detailed information to be of sufficient importance (as there was no linkage whatsoever between the above reported dropout cases and the study regimens) to be included in the MS and would rather retain this information in its present form.

Please also discuss why the authors chose 5 days a week for the intervention (and wanted to do 7 days a week) when most exercise interventions have been shown to be effective in this aged population when done 3 times a week and in fact ACSM guidelines (not referenced) suggest that older people need rest between exercise for the body to be allowed to repair and ready itself for the next bout of exercise? It would be useful to reference the ACSM guidelines on exercise for older people as this discussed adequate warm up and components of fitness suggested to be part of a structured exercise programme for seniors. The general prescription of moderate physical activity for health is a recommended 30 mins of moderate physical activity on at least 5 days of the week so perhaps this is what the authors were aiming at with the intervention, but if so, why choose high intensity strength training (which is above moderate) and why aim for 45 mins per session?

Response: Although the authors were aware of the ACSM Guidelines when designing the study, they deliberately opted for an altogether different approach, even though the main precepts were obviously taken on board. The high-intensity exercise regimen designated by the authors was not without precedent in the available literature, either (Cf. de Vreede et al. 2005 JAGS; Bonnefoy et al. 2003 Br J Nutr; Chin A Paw et al. 2002 Br J Sports Med), even though it did differ in the actual frequency.
None of the subjects reported any undue fatigue during the study, nor were any dropouts related to the pursuit of the respective regimens. All subjects were actually quite enthusiastic about performing the various exercises and they seemed to understand well enough that a consistent and diligent pursuit of the prescribed regimens was supposed to offer them tangible benefits in terms of helping them restore any already impaired functional capabilities, as well as help them sustain them long-term, once restored. Besides, all subjects were strictly monitored on a daily basis with regard to their blood pressure, pulse rate, muscle fatigue, etc. (CRFs), so as to make sure that their bodies were up for the task throughout. On the other hand, however, the authors did want to focus specifically on assessing the actual effects of the referenced exercise regimens on possible enhancement of individual functional capabilities (muscle strength and mobility being construed here as the principal terms of reference) and therefore deliberately favoured a nondiscriminatory approach (i.e. no tailoring of the respective exercise regimens to individual functional deficits), to ensure that all study outcomes would ultimately lend themselves to unequivocal interpretation. Apart from the individualised approaches being fairly well documented to date (e.g. Rosendahl et al 2006), the authors in principle intended to design some sort of a viable structured exercise programme that might prospectively be used as a groundwork for a nationwide rehabilitation scheme for the frail elderly, initially for nursing home residents, and possibly with a view to having it subsequently extended to the community dwellers, subject to sufficient availability of public health care funding. As far as the actual design of the study is concerned, the authors aimed to focus on establishing whether specifically structured, higher intensity training might actually make some appreciable difference to the subjects’ ability to pursue their tasks of daily living more effectively rather than follow the already well beaten track. The authors were firmly guided by their belief that as long as the subjects tolerated the regimens well (i.e. there were no complaints of any fatigue), there was indeed some hope that some new inroads might possibly be made into this issue. And if not for the budgetary limitations of the study, more achievements of more quantifiable nature could reasonably have been hoped for; the openly speculative character of this opinion notwithstanding.

Please also kindly note that none of the exercises were of the endurance type and substantial diversity was allowed for during each 45-min. session. Surely this will make the intervention more costly (in terms of 1 to 1 delivery) and mean that the population are less likely to adhere to the programme. Please kindly refer back to the authors’ response to Items 1 MAJOR and 18 MINOR.

Within the discussion perhaps the authors could also explain why the exercise warm up started in the recumbent position and whether there was any incidence of postural hypotension following and also whether there was any cool-down at the end of the session?

Response:
The “cool-down” are actually called “relaxation exercises” in the MS, please kindly refer to the relevant passage, i.e.

Section: METHODS
Sub-section: Structured exercise session
Page: 13
Blood pressure was regularly monitored during the actual execution of the exercise regimen, whereas not a single case of hypotension was ever reported throughout the study. There needs to be some discussion about chances of long term behaviour change and adherence to exercise following such a short intervention (7 wks) when most studies have shown behaviour change takes longer in terms of exercise.

Response:
The authors concede the point and the MS has been amended accordingly, i.e.

Section: DISCUSSION
Page: 23
Paragraph: 2

Finally, considering the exercise intervention was aimed at improving mobility and consisted of functional exercises, why were the exercises performed seated?

Response:
As evidenced by our own clinical experience, a vast majority of frail elderly find it particularly hard to initiate the exercise regimen for reasons of impaired balance even in a sitting position, let alone effectively initiating a postural shift (sit-to-stand). In view of the above, the authors concluded that in order to overcome these difficulties and get ready to initiate the exercise sequence in the right way it would by far be best to commence the task seated. Since the issue of basic instability (impaired balance) had to be addressed first and foremost to pave the way for the core part of the sequence, the patient was seated on a ball cushion to simulate an uneven surface and then asked to keep his balance, whilst at the same time trying to initiate the sit-to-stand sequence. This was obviously the very first step and the other parts of the sequence followed, once this initial challenge has successfully been overcome. Some clarity as to the decisions made as to the type/frequency/duration/intensity will make this study easier to understand.

Response:
In line with the Reviewer’s suggestion this issue has now been addressed in more detail in the revised version of the MS, i.e.

Section: METHODS
Sub-sections: Exercise regimens
Progressive Resistance Exercises (PRE)
Individual allocation of the Thera-Band®
Pages: 12, 14

17) MINOR
Discussion: There is again mention of easy applied and cost-effective solutions yet there is no time/staff or cost data in this paper; perhaps remove and discuss effective interventions.

Response:
Please kindly refer back to the authors’ response to Item 1 MAJOR (i.e. highlights on Polish public health care system).
The authors most definitely did not want to get involved in addressing at length the “cost-effectiveness” of the proposed solutions, primarily for fear of getting bogged down in the attendant complexities of bona fide economic analysis. On the other hand, the authors believe the lack of such an economic analysis to determine overall cost-effectiveness does not actually constitute a legitimate study limitation,
since (a) it was never the focus of the study itself, (b) even a cursory attempt at comparing disparate national health care systems (even within the EU countries) in terms of the actual expenditure allocated to geriatric rehabilitation would require a comprehensive economic study very much within its own right, (c) a few simple props used in the present study, combined with personal attendance of trained physiotherapists (its time scale remaining well within the scope allowed by the public health care system in Poland) may reasonably be construed as being both a financially sound and feasible proposition in terms of its prospective application in Polish public health care system.

18) MINOR
Discussion: In the UK and in the USA there are exercise on prescription schemes that GPs can refer people into, this is a practical way of ensuring there is a way of physicians helping to slow the functional decline in older people, perhaps some reference to these published schemes? Particularly as there has been some costings against such schemes.

Response:
Please kindly refer back to the authors’ response to Item 1 MAJOR (i.e. highlights on Polish public health care system) for the basic information. Although the authors fully appreciate the Reviewer’s concerns here, offering a comprehensive explanation (let alone contemplating the actual revision of the MS in this respect) would by far exceed the allocated space. Apart from the above, the Reviewer may perhaps find useful the following pointers regarding the specifics of everyday practice in Polish public health care system:

1. Exercises on prescription (to use this terms for greater clarity) may only be ordered by a specialist consultant (i.e. not a GP), to whom a referral is required, however, from a GP.
2. In line with the applicable procedural constraints of the public health care system (funding being drawn from the National Health Fund (NFZ), a specialist consultant is allowed to order just a single series of physical rehabilitation exercises (i.e. ten 45 min. long sessions) at any one time only.
3. Should there be a legitimate need for such a series of exercises to be repeated, the procedure would effectively take the patient back to square one; the most obvious disadvantage consisting in the fact that there is a long waiting list to every specialist consultant and there are no shortcuts (loopholes) in the system to overcome the bureaucracy.

19) MINOR
Discussion: The authors note the daunting task of trying to quantify approaches that discuss the tailoring of exercise to the individual, yet in falls prevention exercise interventions we know that the ONLY ones that work are ones that are tailored to the individuals ability and progressed to suit the individual (Cochrane Review). Perhaps some further discussion on this to clarify the authors’ position?

Response:
The authors are fully in agreement with the Reviewer that individualized approaches are always by far the best, however the authors’ principal intention was to focus specifically on assessing the actual effects of the referenced exercise regimens on possible enhancement of individual functional capabilities (muscle strength and mobility being construed here as the principal terms of reference) and therefore deliberately favoured a non-discriminatory approach (i.e. no tailoring of the
respective exercise regimens to individual functional deficits), to ensure that all study outcomes would ultimately lend themselves to unequivocal interpretation. Apart from the individualised approaches being fairly well documented to date (e.g. Rosendahl et al 2006), the authors were very keen on designing some sort of a viable, structured exercise programme that might prospectively be used as a groundwork for a nationwide rehabilitation scheme for the frail elderly, initially for nursing home residents, and possibly with a view to having it subsequently extended to the community dwellers, subject to sufficient availability of public health care funding. Given the already substantial size of the paper, however, the authors feel unable to expand on this issue, if not entirely without some misgivings.

20) MINOR
Discussion: Much of the discussion reads a bit critically of other studies methods and approaches, I am sure this was not intentional but perhaps the contents of the discussion could be reviewed?
Response:
To begin with, the authors never intended to be disrespectful of other work in this area, nor indeed did they ever contemplate overestimating the quality of their own efforts. They do nevertheless strongly feel they have legitimate right to be critical of other work as long as they can actually argue it all out on merit, which they can in every single instance. On the other hand, the authors are indeed quite appreciative of the Reviewer’s perceptive suggestion in this regard, so the incriminated sections of the MS have been slightly toned down in terms of style, whilst upholding the authors’ original opinions in terms of the actual merit.

Discussion of gait speed vs. distance covered is not really appropriate as older people need both to be optimal to maintain independence?
Response:
The authors appreciate the Reviewer’s advice and so the MS has been modified accordingly, i.e. this paragraph has been deleted.

There is discussion about compliance to nutritional supplementation being better, is this just because the physiotherapists were more directive and were in the patients homes telling them to drink the supplement whereas in other trials people had to take the supplement undirected?
Response:
Yes, indeed, this was precisely the reason why the authors insisted on maintaining strict supervision of both regimens (i.e. exercises and nutritional supplementation), as they simply do not believe that a 100% adherence rate could ever be achieved (especially with regard to exercises) without personally delivered encouragement combined with strict monitoring, even given a relatively simple regimen to pursue. The Reviewer might perhaps be interested to know that there was also a number of fail-safe procedural guidelines in place (study design) to ensure 100% compliance rates.

E.g. All NUTRIDRINK® packaging was subject to strict accountability, i.e. all used up packages had to be obligatorily surrendered by the staff/attending physiotherapists to the Project Supervisory Officer periodically, so that the number of the originally signed-off NUTRIDRINK® packages fully balanced out with the number of empty packages returned. And last but not least, the CRFs were also amended accordingly on a daily basis.
There is no need to criticise other authors only giving data on one leg following training, if the training was using both limbs there is no real need to give both, many trials give average of both legs and not both legs separately.

**Response:**

The authors appreciate the Reviewer’s advice and so the MS has been modified accordingly in the relevant section to accommodate it, i.e. this paragraph has been deleted.

**21) MINOR**

Discussion - Some relevant studies are not included (eg Skelton 1995 strength training programme that did not improve function and Skelton 1996 strength and functional exercise that did improve function; ACSM guidelines and recent metaanalysis of exercise to improve balance (Howe 2007, Cochrane review).

**Response:**

The authors freely concede the point and the MS has been amended accordingly, i.e.

**Sections: METHODS**

**DISCUSSION**

**Pages: 12, 19, 23**

**22) MINOR**

Conclusions: Need revision considering above comments.

**Response:**

The authors freely concede the point and so the MS has been amended accordingly.

**Discretionary Revisions:**

1) **Abstract:** Methods section suggest replace “embraced” with “included”.

**Response:**

The authors concede the point, but since the Abstract has been structurally revised this particular suggestion has lost its relevance since.

2) **Background:** It would be useful to have a reference next to the comment that functional deficiency is expected to take a significant portion of medical practice time. It would also be useful to have a reference for the sentence that loss of strength and function with advancing age is reversible.

**Response:**

The authors concede the point and the MS has been amended accordingly, i.e.

**Section: BACKGROUND**

**Page: 5**

The term “a sense of balance” is misleading, perhaps should just say “balance”.

**Response:**

The authors concede the point and the MS has been amended accordingly, i.e.

**Section: METHODS**

**Sub-sections: Exercise regimens**

**Functionally-oriented exercises**

**Pages: 12 – 13**
RE: Peer review of the MS: 8923208701823219

Combined effects of functionally-oriented exercise regimens and nutritional supplementation on both the institutionalised and free-living frail elderly (double-blind, randomised clinical trial) Marek M Zak, Christian Ch Swine and Tomasz T Grodzicki

Dear Doctor Miller,

To begin with, we are very much indebted to you for all your perceptive comments, as we feel that your critical appraisal has tangibly helped us revise the MS in the way that successfully purged it of all its obvious deficiencies, whilst at the same time highlighting its true merits. Please kindly note that in structuring our response we took the liberty of quoting verbatim your remarks (converted into MS WORD from the original PDF files) and then had them juxtaposed with our own comments (set in blue font for contrast and greater clarity), so that the discourse is easier to follow. It is our sincere hope you will find all the revisions in the amended MS to your satisfaction. We are also hopeful that in some instances where our respective views still seem to remain at odds, we have nevertheless managed to make our arguments persuasive enough to alleviate your concerns.

With the very best regards,
Marek Zak, PhD

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MAJOR COMPULSORY REVISIONS

1. (MAJOR)
The tone of the article is disrespectful of other work in this area while overestimating the quality of the study reported. In particular the authors are encouraged to revise sections describing the work of Rosendahl and Bunout.

Response:
To begin with, the authors never intended to be disrespectful of other work in this area, nor indeed did they ever contemplate overestimating the quality of their own efforts. They do nevertheless strongly feel they have legitimate right to be critical of other work as long as they can actually argue it all out on merit, which they can in every single instance. Since the Reviewer seems to be particularly sensitive to any “against” remarks at large (and with regard to a select few investigators in particular), the authors have slightly toned down the incriminated sections of the MS in terms of style, whilst upholding their original opinions in terms of the actual merit.

In addition the authors should acknowledge the limitations of the study reported, namely lack of economic analysis to determine cost effectiveness, a one dose fits all approach to nutrition supplementation, non intention to treat analysis and apparent lack of a power calculation.

Response:
Also, the authors never expected "cost-effectiveness" to become an issue in the first place, especially given a fairly simple context in which it has been referenced. Since it seems to have given rise to some queries, whose legitimacy is
nevertheless fully appreciated here, the authors decided to “play safe” and refrain from making any direct references to this term, replacing it with the innocuously enough sounding “overall economic viability”. The above notwithstanding, the authors most definitely do not consider “the lack of economic analysis to determine cost effectiveness” a legitimate study limitation, since (a) it was never the focus of the study itself, (b) even a cursory attempt at comparing disparate national health care systems (even within the EU countries) in terms of the actual expenditure allocated to geriatric rehabilitation would require a comprehensive economic study very much within its own right, (c) a few simple props used in the present study, combined with personal attendance of trained physiotherapists (its time scale remaining well within the scope allowed by the public health care system in Poland) cannot reasonably be construed as giving sufficient grounds to any possible allegations of financial extravagance within the project framework. Since the Reviewer is obviously not familiar with Polish specifics in this respect, the authors volunteered the following brief highlights on how geriatric rehabilitation is presently managed by the public health care sector in the country, very much in the hope that it might throw enough light on the issue and consequently convince the Reviewer that the authors’ claim of overall cost-effectiveness of the proposed solution is indeed a legitimate one, even though the authors have now happily enough settled for “overall economic viability” in their effort to address the Reviewer’s concerns.

Average pension: PLN 1,237 (ca. EUR 364)
Incidentally, no more than ca. 40% of old age pensioners (OAPs) actually benefit from the above referenced amount, as a vast majority of them receive a monthly amount approximating PLN 700 (ca. EUR 206).
For the sake of greater clarity in presentation, this does not take any account of the corresponding disability pension scales. Average costs of hospitalisation (prompted by a minor injurious incident whose successful treatment would not require a period in excess of 14 days) in geriatric wards per day: PLN 150 (ca. EUR 44). This translates into PLN 2,100 (c.a. EUR 618) for a fortnight.
Average costs of hospitalisation per day in a surgical ward (prompted by a major injurious incident, e.g. fracture, whose successful treatment would require a period of at least 10 days, followed by a discharge either back into the nursing facility or into the community care (i.e. family fold), with the following spell of statutorily due physical rehabilitation being subject to local availability of such services, distance to patient’s permanent place of residence, multiple bureaucratic constraints, etc.) PLN 7,710 (ca. EUR 2,268) It should perhaps be noted at this juncture that if common practice be anything to go by, most regrettably a vast majority of such cases are not actually followed by physical rehabilitation (for multiple reasons), so in effect the patients never return to their pre-incident physical status, even though hardly due to their own fault. Average costs of individually delivered (i.e. out of hospital facility) physical rehabilitation. Public health care system one-off allowance (i.e. a single series of ten 45 min. sessions following hospitalisation after a single incident): PLN 40/per session + reimbursement for travel costs = PLN 400 (i.e. EUR 12 x 10 = EUR 120). Average monthly remuneration of a licensed physiotherapist, when on contract with the National Health Fund (NFZ): PLN 2,000 (ca. EUR 588).
On average a physiotherapist may service 6 - 7 persons daily (i.e. community dwellers), allowing for a 5-day working week. In the case of being employed full time by a nursing home facility, a single physiotherapist would be expected to attend to 40 elderly persons, which practically translates into repeating a session with any single person every 7 - 8 days on average, which speaks for itself in terms of its expected effectiveness. Average costs of simple rehabilitation equipment (i.e. the props actually used in the study), broken down into purchase prices and rental rates, respectively:

<table>
<thead>
<tr>
<th>Retail purchase price</th>
<th>Rental rate (per month)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ball cushion EUR 18.00 - 36.00</td>
<td>EUR 3.00 - 4.50</td>
</tr>
<tr>
<td>Pedal exerciser EUR 36.00 - 44.00</td>
<td>EUR 4.50 - 6.00</td>
</tr>
<tr>
<td>Thera-Band® - Yellow code (ca. 2 m)</td>
<td>EUR ca. 4.50</td>
</tr>
<tr>
<td>- Red code (ca. 2 m)</td>
<td>EUR ca. 5.50</td>
</tr>
</tbody>
</table>

With regard to individual nutritional supplementation (i.e. NUTRIDRINK®) the issue becomes even more complex in terms of financial considerations, i.e. public health care system in Poland simply does not provide for it!

Average cost per 200 ml of NUTRIDRINK® is PLN 6 (ca. EUR 1.76)

Assuming that an elderly person should consume at least 2 x 200 ml daily x 7 days a week (Cf. NUTRICIA recommendations) to offset any possible energy deficit during the pursuit of any of the above referenced exercise regimens, this would work out as 14 NUTRIDRINKS® per week and ultimately translate into PLN 84/week (ca. EUR 25), which would ultimately work out ca. EUR 100/month.

Given the fact that a vast majority of OAPs receive ca. EUR 206/month worth of pension, the issue becomes a moot point really, to put it mildly. Please also kindly note that there are no positions of either “health assistant” or “dietary assistant” in Polish public health care system. And finally, although the above highlights might give some insight into the specifics of Poland’s public health care services, the question of respective national affluence has altogether been left out of this argument, whereas only a viable comparison in those terms might effectively put the entire issue within truly credible context. The authors feel the Reviewer might also find the perusal of The Economist Intelligence Unit Report on Poland (http://www.economist.com/countries/Poland/) of some additional benefit here.

With regard to nutritional supplementation please kindly refer to the authors’ detailed response to Items 6 MAJOR and 7 MINOR.

2. (MAJOR)
The manuscript requires revision to remove ageist remarks and attend to complicated, long sentences.

Response:
The authors did their level best to accommodate the Reviewer’s suggestion with regard to a number of syntactically challenging clauses throughout the MS, specifically in the Background and Discussion sections.

3. (MAJOR)
In addition, there needs to be some discussion of the workforce implications of
requiring a physiotherapist 5 days per week to deliver what appears to be a relatively simple program. Perhaps a further recommendation might be to trial a similar regime using allied health assistants rather than physiotherapists.

Response:
Core of this issue has already comprehensively been addressed in the authors’ response to Item 1 MAJOR further above. Incidentally, the authors simply do not believe that a 100% adherence (compliance) rate could ever be achieved (especially with regard to the exercises) without personally delivered encouragement combined with strict monitoring, even given a relatively simple regimen to pursue.

4. (MAJOR)
Further consideration should be given to the nutritional status of frail older adults and assessment/prescription/monitoring by qualified staff e.g. Dieticians or dietetic assistants. The nutritional needs of older frail adults is poorly understood and best practice would suggest more attention be given than a one dose fits all approach.

Response:
Although the authors fully agree with the Reviewer that “nutritional needs of older frail adults are poorly understood”, neither the available study resources (budgetary limitations), nor the relatively straightforward design of the study itself with the principal focus resting firmly on the structured exercise regimens made it actually possible to expand its scope into individualised approaches to nutritional needs. The authors merely had to resign themselves to relying on the originally assured homogeneity of the respective study groups (Cf. baseline characteristics) in terms of nutritional intake. It might also be of possible interest to the Reviewer that before the actual commencement of the study the authors had to face up to a pretty stark choice (well anchored in the inherent budgetary limitations): either admit less participants and allocate 2 NUTRIDRINKS® daily per head, or admit more subjects and allocate 1 NUTRIDRINK® daily per head only, with a view to offsetting any potential energy deficit that might possibly be caused by an extra energy expenditure required during an execution of the exercise regimens. Since the principal focus of the study was on determining the actual effectiveness of the respective exercise regimens, the authors obviously opted for the latter. Please kindly refer to the authors’ response to Item 4 MINOR.

5. (MAJOR)
Adherence needs to be more comprehensively described for both the exercise and nutrition interventions. How was nutrition adherence measured and confirmed in freeliving participants?

Response:
Please kindly refer to the authors’ response to Item 7 MINOR.

6. (MAJOR)
Description of the assessment of nutritional intake requires revision. Appears as though a 7 day food record was completed for caloric intake initially but there are no details on why these data were collected. It also appears as though daily food records were completed for the duration of the study. This is a highly burdensome method and the data have not been sufficiently utilised. It is unclear why it was collected as the nutrition supplementation was a one dose fits all approach.

Response:
The reason why the initial 7-day assessment of individual caloric intake was completed by a dietician (and continued throughout the duration of the study) was to ascertain whether all study subjects actually benefited from comparable food
intake, as this would then ensure their homogeneity in this respect, thus putting them on an “even platform” at the very start (i.e. no statistically significant differences among the subjects at baseline). Please kindly note this was simply intended as an additional assessment measure, apart from BMI and MNA scores. Admittedly, it was a pretty burdensome procedure (not least with regard to the physiotherapists who were also required to fill in the CRFs, when attending to the free-living subjects), and the collected data might yet be effectively utilised in the forthcoming, related studies, although the present one had an altogether different principal focus. Why the one-dose-fits-all approach? This approach was adopted in line with the principal premises of the actual study design: to develop an effective formula for nutritional supplementation in combination with a specifically structured exercise regimen for frail elderly of homogenous nutritional status (despite living in two different environments) that would both preclude potential nutritional deficit (in view of increased energy expenditure) and help them sustain the desired energy level. The composition of the supplement ensured this requirement was effectively satisfied, as all study subjects had positively been assessed as remaining on a par with regard to their respective baseline characteristics and individual dietary intake. Admittedly, the self-acknowledged study limitation (1 NUTRIDRINK®/person/day only - for budgetary reasons) did not allow the authors to establish whether an increased dosage (i.e. up to 3 NUTRIDRINKS®/person/day), as recommended by NUTRICIA, might tangibly improve the outcome with regard to muscle strength and possibly also to body weight gains. It seems only reasonable to assume, speculative as it is, that individual muscle strength might well stand a chance of even more quantifiable improvement, should a study subject pursue the progressive resistance exercise (PRE) regimen, whilst consuming 3 NUTRIDRINKS® daily.

At the very least the authors should have the capacity to comment on what % of requirements were met by the supplement vs voluntary oral intake alone and overall whether the dietary intervention resulted in participants achieving sufficient energy etc to meet or exceed estimated requirements. These data would also be useful to determine whether the supplements ‘supplemented’ the diet or replaced voluntary oral intake. What food composition database was used? How were the multiple days of intake data analysed?

Response: Please kindly note that the authors do say in the MS (page 15, Nutritional supplementation) that “[...]The nutritional supplement - a 200 ml liquid supplying 300 kcal in the form of carbohydrate (49%), lipids (35%) and protein (16%) mixture was designed to augment individual caloric intake by ca. 20%, [...] The administration of the nutritional supplement was never designed to exceed the estimated individual requirements, it was merely meant to safeguard against any potential nutritional deficit in view of the need for an increased energy expenditure (pursuit of individually diversified exercise regimens). Although the authors ensured 100% compliance rates in both environments (strictly supervised administration of the supplement), they had no means of verifying whether the study subjects actually consumed their daily dietary allowances in sufficient volume to cover their daily energy requirement and therefore had to rely on their feedback that it was indeed so.
Since no body weight losses were recorded at the conclusion of the study (there were some gains instead), the authors seemed to be right in their assumptions in this regard. To the best of the authors' knowledge, no study subjects ever attempted to replace part of their voluntary dietary intake with a NUTRIDRINK® supplement. All subjects had been initially advised that NUTRIDRINK® was meant to help them complete their respective exercise regimens without additional energy expenditure on their part. Food composition database used in the study: FAO/WHO/UNU (1985): Energy and protein requirements: Report of a joint FAO/WHO/UNU Expert Consultation. WHO Technical Report No 724. Geneva: WHO. In line with the above referenced database, basic metabolic rate (BMR) for frail elderly people (i.e. over 70 years old; average body weight up to 65 kg) is assumed to remain within the 1,250 - 1,350 kcal/24 range, for women and men, respectively. Since all study subjects were required to pursue specific exercise regimens which would then be expected to draw significantly upon their daily caloric allowance (intake) through extra energy expenditure, a 300 kcal worth of compensatory energy intake was provided (200 ml NUTRIDRINK®), so as to safeguard against any potential nutritional deficit. No analysis of multiple days of intake data was pursued as the principal focus of the study rested firmly on assessing the likely impact of structured exercise regimens on primary outcomes, with nutritional supplementation being considered merely an extra benefit designed to help the subjects with an effective pursuit of their tasks, especially in view of its rather small volume (Cf. Study limitations).

MS has been amended accordingly, i.e.
Section: METHODS
Sub-section: Study limitations
Page: 15
7. (MAJOR)
Remove all interpretative statements from the results section.
Response:
The authors concede the point and so the MS has been amended accordingly.
The data should be allowed to speak for itself. Suggest the revision of this section to
(1) describe the sample (refer to key messages from Table 1); (2) primary outcomes
– insert the data to demonstrate the magnitude of the muscle strength gains for both
resistance training groups and the lack of translation into mobility outcomes, highlight
the SE + nutrition group achieved mobility gains without gains in strength. The authors should attempt to correct this inconsistency in the discussion rather than critiquing other work. (3) secondary outcomes – the data presented here appear to highlight within group achievements. It could be considered more useful to present other between group differences such as body composition (also change in overall nutritional status – e.g. MNA), changes in mobility aids, health service utilisation outcomes, mortality etc. (4) a section on adherence to all interventions is warranted to allow the reader to place the findings within context.
Response:
The authors believe that following a major revision of data presentation in the tables (i.e. pertinent data are now comprised in the four paired tables, i.e. Table No
3 and 3A, No 4 and 4A, respectively), overall clarity has now sufficiently been enhanced. Please also kindly refer to Item 8 MINOR further below for more details.

8. (MAJOR)
The conclusion needs revision to be consistent with actual study findings.
Response:
The authors freely concede the point, and so the MS has been amended accordingly,
i.e.
Section: CONCLUSIONS
Page: 24
MINOR ESSENTIAL REVISIONS- Miller
1. (MINOR)
The abstract should be revised to accurately report the study in sufficient detail to stand alone.
Response:
The authors concede the point. Both the Abstract and the MS and have been amended accordingly.
Was the allocation stratified for the two settings (nursing home and community)?
Response:
No stratification was considered in view of overall homogeneity of the respective
groups (Cf. Baseline - Table 1).
Methods should describe the DBRCT design of the study not the background.
Response:
The authors concede the point and so the MS has been amended accordingly, i.e.
Section: ABSTRACT
Sub-section: Methods
Page: 2
The design would be more clearly described as FOE with SE or RT and each of these groups being either nutritionally supplemented or not.
Response:
It would appear to the authors that the core study protocol comprehensively
addressing all those issues is comprised in Table 2, precisely the one that the
Reviewer postulated (Cf. Item 10 MINOR) be altogether scrapped.
Please also kindly note that the authors never used the term RT (resistance
training) but PRE (progressive resistance exercises) instead, which is not without
some significance, either.
Describe the key components of the exercise (ie. 45min program incorporating
warm up, functionally-oriented exercises and 20min of either resistance training or
standard exercises) and nutrition interventions (ie. multinutrient to provide xx% of
RDA for energy, etc). State all outcome measures. Results should report data
alone, not interpretation.
Response:
Please kindly note this issue has now comprehensively been addressed in the
authors’ response to Items: 6 MAJOR, 2 MINOR and 7 MINOR.
P=0.05 is not significant.
Response:
This is a most regretful misprint that must have occurred during the final editing
and was subsequently missed out at proofreading. Obviously enough, it should
have read: P = 0.04.
Revise the conclusion as the data does not support this statement.

Response:
The authors concede the point and so the MS has been amended accordingly.

2. (MINOR)
Define ‘all-inclusive nutritional supplementation’.

Response:
The Reviewer might perhaps like to appraise herself of the contents of the EU Directive No 1999/21/EC (Food For Special Medical Purposes), which addresses this point in some detail. Since the trial was carried out in an EU country, it had to be fully compliant with the above referenced Directive.

3. (MINOR)
There are some sections that are either unnecessary or repetitive – Methods, paragraph commencing with ‘the actual study design envisaged …..’.

Response:
The MS has been amended accordingly, i.e.

4. (MINOR)
Comment on inter-rater reliability is warranted given data was collected by both nursing staff and physiotherapists. Was the outcome assessment blind? Was the outcome assessment performed by the Project Leader? If not then what did the Project Leader do? If it was just the data management then this section of the sentence is unnecessary.

Response:
The MS has been amended accordingly in order to enhance overall clarity, i.e.

5. (MINOR)
It is not clear what criteria were used for overweight and underweight. This section implies that only overweight or underweight older adults were included however a BMI >19 suggests that the underweight would have been excluded. In addition the data presented in Table 1 suggests the participants were within the desirable BMI range for older adults.

Response:
The authors freely concede the point, as due to an apparent oversight the underweight participants were said to have been enrolled into the study, which in fact was not the case. The MS has been amended accordingly. There is actually a bit more to this particular issue, though, that the authors feel should briefly be discussed here. One of the principal self-imposed constraints in the actual study design was to ensure that no subjects had any apparent nutritional deficit at the start, hence BMI >19 was assumed as a reasonably safe cut-off point in that respect.
Admittedly, the wording of Item 2 in the Inclusion criteria is not clear enough, as what the authors actually meant by being overweight within the 20% range was the 20% difference in relation to the body weight allocated to BMI 19 score. Incidentally, Table 1 also demonstrates that in both Group III and Group IV the subjects boasted 25.2 BMI score, which in line with the NOVARTIS BMI calculator already puts them in the slightly overweight category.

MS has been amended accordingly, i.e.

Section: METHODS
Sub-section: Study population
Page: 7

6. (MINOR)
The exercise descriptions could be described more succinctly. [...] Clarify if breathing and relaxation exercises were within the 45 min period or in addition. It is not clear if the standard exercises took 10min + 3 30sec breaks, where the other 8.5min of the 20min standard exercise went. Likewise it is not clear how the 20min for the PRE was attained.

Response:
Apart from the MS having already been amended accordingly, i.e.

Section: METHODS
Sub-section: Structured exercise sessions
Page: 14

please also kindly consider the following clarification:
Both types of exercises remained indeed well within the overall 45 time-span, i.e.
RE: SE
10 simple exercises took 8.5 min to complete
Pedal exerciser - 10 min. (+ 3 x 0.30 sec. rest periods) = 11.5 min in all
8.5 min + 11.5 min = 20 min.
RE: PRE
Four series of resistance exercises (stretches of Thera-Band®) broken down into the following sequential components:
3 x 10 stretches of a band per each discrete muscle group (Cf. Tables 1, 3 and 3A) performed within 1.5 min., followed by 1 min. rest period (used by the therapist to move the band to the other leg). Then the same set of exercises was repeated for the same muscle group on the other leg.

In terms of the time scale, it works out as follows:
4 x 1.5 min. (left leg) + 4 x 1.5 min. (right leg) = 12 min (exercises)
+ 4 x 1 min. x 2 legs - rest interval per leg
(inclusive of repositioning of the band) = 8 min.
= 20 min. - sequence completion

Remove anecdotes,
Response:
(On a lighter note, if the authors really wanted to sound anecdotal here, they might well have recommended that the frail elderly watch on TV all sorts of high adrenaline-pumping sports events, e.g. Tour de France bicycle race, whilst pedalling away on their exercisers; the temptation the authors gallantly resisted...)
... justify selection of exercises in one sentence,
Response:
In line with the Reviewer’s suggestion the authors have slightly trimmed down the incriminated sections of the MS in the revised version. If they were to accommodate the Reviewer’s suggestion literally, however, the justification for this particular selection of exercises would surely be found somewhat wanting in substance.

... suggest high intensity be reserved for challenge as opposed to frequency.
Response:
The issue of high intensity training is referenced in the Discussion section (Ref. 38 - Rosendahl et al.), where the authors juxtapose the exercise regimen devised by themselves against the one proposed by Rosendahl et al., who claims his to be of high intensity. The structural differences between those two disparate regimens seem to give grounds to believe that the authors actually do have a good enough reason to label theirs as the high intensity one.
Please consider the following:
Rosendahl et al.: 45-minute exercise sessions pursued 5 times every fortnight over 13 weeks. Statistically speaking this works out that each session was performed every 2.8 day.
Ours: 45-minute exercise sessions pursued 5 times every week over 7 weeks. All exercises were of the same type for all participants (except for the between groups differences) and no individual tailoring by the attending physiotherapist was deemed admissible, so as to preclude any confounding factors.
Please also kindly note that Rosendahl et al. is rather vague in describing his regimens. Since the issue of exercise intensity seems to be giving rise to queries, however, the authors decided to supplement the MS accordingly, so that this matter may now convincingly be addressed through a detailed breakdown, thus underpinning the authors’ claim with much needed credence.
7. (MINOR)
The prescription of the nutritional supplement requires clarification. It seems that the authors believe they would increase energy intake by 20% and vitamin and mineral intake by 25% through provision of 200ml per day. The authors should declare whether the aim was to meet or exceed the daily allowances. 100% adherence is rare in previous literature, please describe how this was measured and any quality control procedures used to ensure an accurate record was kept.
Response:
Please note this issue has already been addressed above. Let us reiterate one specific point here, though: 100% compliance rate was ensured through strict supervision. There were no quality control procedures required, as the nutritional supplementation records reflected the actual facts (NUTRIDRINK® served by the nursing staff and attending physiotherapist, respectively, and consumed by the subjects prior to the commencement of the exercise session) one to one. Besides, since nutritional supplement was being administered in a rather small volume, the authors insisted upon ensuring strict supervision throughout the study. (The Reviewer might perhaps be interested to know that all NUTRIDRINK® packaging was subject to strict accountability, i.e. all used up packages had to be obligatorily surrendered by the staff/attending physiotherapists to the Project Supervisory Officer periodically, so that the number of the originally signed-off NUTRIDRINK® packages fully balanced out with the number of empty packages
returned. And last but not least, the CRFs were also amended accordingly on a daily basis).

In addition what strategies were used in both settings to encourage consumption, how was taste fatigue overcome when only a single supplement of one flavour was available?
Response:
No encouragement for consumption of the supplement was ever needed whatsoever!
There were no cases of taste fatigue recorded, either.
(Incidentally, would not the Reviewer think that the query of how “taste fatigue was overcome” would be more appropriate with regard to the paper of Bunout et al.: The impact of nutritional supplementation and resistance training on the health functioning of free-living Chilean elders: Results of 18 months of follow-up. J Nutr 2001, 131(9) Suppl:2441–2446, (p. 2, paragraph 3), where the subjects where expected to endure some porridge concoction on a daily basis for 18 months on end and apparently a substantial number of them was indeed overcome by taste fatigue, if the cited compliance rates regarding nutritional supplementation are anything to go by?

It would appear therefore that a strawberry-flavoured NUTRIDRINK® must have been a step in the right direction at the very least. After all, it only stands to reason that a sweet treat is always welcome by just about anyone exposed long enough to dreary food routinely served in a vast majority of nursing homes).

Suggest move the section on recommendations by the company to the limitations section of the manuscript.
Response:
The authors concede the point and so the MS has been amended accordingly by way of specifically introducing the Study limitations section, i.e.

Section: METHODS
Sub-section: Study limitations
Page: 15

Indeed, it would be far better to determine how much of a shortfall remained after diet and supplement intake was determined rather than assume that participants would all have required between 1-3 servings of nutridrink.
Response:
There was no shortfall, please see above.
The 1 - 3 NUTRIDRINK® dosage comes from NUTRICIA product recommendations and the authors merely regretted that for budgetary reasons they were unable to follow them (Cf. study limitations), as then the study outcomes might reasonably have been expected to be far more promising in this particular respect.

What difference was there between participants who consumed the supplements and those who did not? More information on the placebo supplement would be beneficial – was the only difference 41kcal (or 300-41kcal)? What about differences in other nutrients, namely protein? How was the supplement administered in the community setting?
Response:
In short: those who had the benefit of a NUTRIDRINK® were getting 300 kcal extra, whereas those who did not, were getting 41 kcal worth of nutritional supplementation only (i.e. 259 kcal less).

Main composition differences between NUTRIDRINK® and placebo:
(All values are expressed per 200 ml serving)

NUTRIDRINK® Placebo
Energy: 300 kcal 41 kcal
Protein: 12.0 g 0.02 g
Fat: 11.6 g 0.0 g
Carbohydrates: 36.8 g 10.0 g

(Please kindly refer to NUTRICIA official website for further details on the subject: http://www.nutricia-clinical-care.co.uk/asp/show_subject.asp)

The authors did not deem the above breakdown to be of sufficient consequence to the main discourse to make an express reference to it in the MS.

8. (MINOR)
The statistics appear relevant however the section on the 0-2 scale is unclear, please clarify perhaps by giving some examples.
Response:
The scale at issue referred to the Tinetti test only. To clarify the ensuing confusion: although the authors made an express reference to Tinetti POMA test in the MS and reflected this in the References section, the test actually used was the modified version of the Tinetti original test (hence the different scale). This is and obvious oversight on the authors’ part and so the MS has been amended accordingly, i.e.

Section: METHODS
Sub-section: Overall assessment of physical function
Page: 9

Section: METHODS
Sub-section: Statistical analyses
Page: 16

Furthermore it is not clear whether the analysis is a 4 group comparison as Table 3 suggests that only 2 groups were compared at any one time: the 2 nutritional supplement groups and the 2 exercise groups without nutritional supplements. The primary outcome analysis should be a 4 way comparison. If the P-values in the tables are referring to the Bonferroni comparisons the overall P-value should be included somewhere in the table for completeness.
Response:
It goes without saying that the authors did in fact set out to compare four groups and not merely two. However, as it has now become quite clear in retrospect, the results presented in Tables No 3 and No 4 were indeed grouped in a rather confusing manner, and so this obviously gave rise to the Reviewer’s queries. Analysis of variance with the Bonferroni correction was used for four groups, whereas the single differentiating (combined) factor, i.e. diverse exercises + nutrition, was what actually prompted the authors to allocate the subjects into the respective study groups. The tables at issue have been revised accordingly and all pertinent data are now comprised in the four paired tables, i.e. Table No 3 and 3A, No 4 and 4A, respectively, to enhance overall clarity. Overall p value was accommodated in Tables No 3 and 4, respectively, to ensure completeness of the statistical analysis.

9. (MINOR)
The authors appear to be resistant to implementing individualized approaches to care
despite this being usual and safest practice, particularly when dealing with exercise and diet modifications amongst older adults. Please clarify your position on this issue.

Response:
The authors are fully in agreement with the Reviewer that individualized approaches are always by far the best and therefore the Reviewer’s inference to the contrary seems to be a rather long shot at best.

On the other hand, however, the authors did want to focus specifically on assessing the actual effects of the referenced exercise regimens on possible enhancement of individual functional capabilities (muscle strength and mobility being construed here as the principal terms of reference) and therefore deliberately favoured a nondiscriminatory approach (i.e. no tailoring of the respective exercise regimens to individual functional deficits), to ensure that all outcomes would ultimately lend themselves to unequivocal interpretation.

Apart from the individualised approaches being fairly well documented to date (e.g. Rosendahl et al. 2006), the authors in principle intended to design some sort of a viable structured exercise programme that might prospectively be used as a groundwork for a nationwide rehabilitation scheme for the frail elderly, initially for nursing home residents, and possibly also with a view to having it subsequently extended to the community dwellers, subject to sufficient availability of public health care funding.

10. (MINOR)
Much of Table 1 is surplus to requirements and could be removed as the authors do not make any mention of much of this content. Table 2 is unnecessary.

Only between group comparisons are justified for inclusion as Tables. Within group are for interest only and could be simply described in the text.

Figure 1 – clarify if the n-values assessed (i.e. 19, 21, 19, 21) were the n-values analyzed – non intention to treat.

Response:
1. The alleged “surplus” has been put there quite intentionally in fact, as the authors were rather keen on demonstrating overall homogeneity of the respective study groups, although at the same time they were not prepared to address all the components of the baseline listing, as only the select ones fell within the actual scope of the study design. In view of the above the authors feel the baseline listing in its present form is actually an advantage.
2. Since Table 2 rather comprehensively sets out the core of the study protocol the authors clearly fail to comprehend why this should seem unnecessary to the Reviewer.
3. The presentation of statistical data has now been reorganized and two new tables have been incorporated. (Cf. Table 3A and Table 4A). Although the authors actually do agree with the Reviewer that any within-group differences are a matter of interest only and could be described in the body of the MS, they still feel that their presentation in table form is far more conducive to a reader, unless the editors should insist that the tables at issue should be scrapped altogether as being of little value for the core data presentation.
4. Figure 1 has been revised accordingly to preclude any possible confusion.

DISCRETIONARY REVISIONS
1. (DISCRETIONARY)
Consider acknowledging the work of Breen et al – review published in 2007 in Geriatr Gerontol Int. Other references would also be beneficial – page 11 after high anxiety; page 12 after stating that functionally orientated exercises are commonly acknowledged to be universally well tolerated.

Response:
The authors are most grateful to the Reviewer for this specific pointer, even though when the work on the MS had been in progress Breen’s paper was still pending publication. Since Breen’s review is indeed relevant to the subject matter at issue, it has been referenced accordingly in the revised version of the MS, i.e.

Section: BACKGROUND
Page: 4 - 5
Paragraph: 1 on both pages

2. (DISCRETIONARY)
Consider altering the terminology used to describe the free-living elderly to recently hospitalised older adults.

Response:
The authors feel that some sort of confusion must have set in with regard to this particular issue. In order to clarify this, please consider the following explanation: To begin with, the authors looked for potential study participants amongst the patients in a geriatric ward for reasons of obvious convenience (i.e. close proximity of both facilities), but were also prompted to do so by the fact that all recently hospitalised patients were physically weaker, which made them pretty much on a par with their nursing home counterparts in terms of overall physical fitness, which consequently contributed to overall homogeneity of the study groups. Besides, once discharged from the hospital facility, those patients actually returned to the fold of the community, thus resuming their original status of free-living community dwellers. Hence the authors insist on retaining the original terms.

3. (DISCRETIONARY)
Remove ‘present’ that appears in front of the term authors throughout.

Response:
The MS has been amended accordingly throughout.

4. (DISCRETIONARY)
Consider altering 301 original volunteers to 301 potential participants.

Response:
The authors are quite happy with the term actually used, whereas their view on this issue seems to be corroborated well enough by the available literature on the subject.

5. (DISCRETIONARY)
Consider rearranging the order of the methods section, commencing with study design (including stratification if accurate), recruitment (including inclusion and exclusion criteria), baseline data collection (including description of outcome measures), randomisation, outcome assessment (including who performed and timing), statistical analyses.

Response:
The authors concede the point and the MS has been amended accordingly, i.e.

Section: METHODS

6. (DISCRETIONARY)
A table would be useful to provide examples of the exercises completed.

Response:
The revised version of the MS addresses the respective exercise regimens in more detail.
Given the existing size of the MS and the fact that two extra tables have now been incorporated in order to enhance the presentation of vital statistical data the authors are unable to accommodate the Reviewer’s suggestion for reasons of space.