

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Accelerometry as a measure of modifiable physical activity in high risk elderly preoperative patients, a prospective observational pilot study.
AUTHORS	Grimes, Lisa; Outtrim, Joanne; Griffin, Simon; Ercole, Ari

VERSION 1 – REVIEW

REVIEWER	Cynthia Olotu University Medical Centre Hamburg Centre of Anaesthesiology and Intensive Care Medicine Martinistreet 52 20251 Hamburg Germany
REVIEW RETURNED	15-Aug-2019

GENERAL COMMENTS	<p>The authors describe an interesting approach to validate elderly patients physical activity prior to surgery using an accelerometer. Apart from measuring the effect of a preoperative intervention on patients mobility, the authors intention is to gather data about physical activity in an elderly frail population, to correlate the findings to the patients self-reported degree of activity and to assess the acceptability of the wrist-worn device. The idea of using accelerometry as an easy-to-use, objective method to determine everyday activity is charming and the study is valuable, however, there are some minor aspects that still need to be addressed.</p> <ol style="list-style-type: none">1. There seems to be a contradiction within the introduction: in ll.17 ff the authors mention the evidence for the (positive, I assume) impact of PA and prehabilitation on perioperative outcomes. In ll. 26ff they state that it is unclear whether prehabilitation reduces postoperative morbidity and mortality. There is, however, quite some evidence (among them a cochrane review) showing the protective effect of preoperative exercise on postoperative outcomes, esp. pulmonary complications. This sentence should be re-considered.2. In Methods, it is not described where the patients were initially enrolled in the trial. This should be added. This is especially of interest for readers not familiar with the British hospital system. Where was the frailty screening performed, in the surgery or anaesthesia department? In an in- or out-patient setting?3. In Methods, ll. 51 ff it is stated that the intervention was "tailored to each participant" but it remains unclear how this was done. This should be described. It is especially important as they authors show that the intervention was somehow not as "successful" for orthopedic patients compared to others.4. Methods, l. 57: which adaptive equipment was delivered? Why and when was this needed?5. A figure explaining the composition of the intervention should be added.
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	<p>6. The authors mention that participant-reported PASE and accelerometer-measured PA are not correlated. It should be shown how the threshold was defined and how this was calculated, a figure would be preferable. This finding and possible explanations for it should be discussed by the authors.</p> <p>7. It would be interesting and facilitate understanding to know to which extend accelerometry is correlated to physical activity in general. This could be performed by some kind of "calibration line" correlating typical activities of elderly persons with accelerometer-measured milli-gravitational units.</p> <p>8. From the information available, it does not seem admissible to equalise an increase in accelerometer-measured mg with a successful intervention (Il 26ff, discussion) as the clinical meaningful effect (of increase in mg) on patients outcome is not yet known.</p> <p>9. Data interpretation and comparison to other trials could be facilitated by addition of a matched healthy (i.e. not scheduled for surgery) control group exposed to the same intervention.</p> <p>10. Figure 1: significant results should be indicated in the graph.</p>
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REVIEWER	Dr David MacLeod Department of Anesthesiology Duke University Hospital Durham, NC 27710 USA
REVIEW RETURNED	26-Aug-2019

GENERAL COMMENTS	<p>This is a prospective study to determine if the use of wrist worn accelerometers can measure physical activity in a surgical population of elderly patients undergoing high risk surgery. The authors should be commended for presenting a well designed study that was reported in a clear manner. The methods and results sections clearly articulated the process by which they identified the study population within their institution and subsequently obtained the data parameters. The discussion and conclusion are appropriate based upon the data presented.</p>
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REVIEWER	Elena Gimeno-Santos Respiratory Clinic Institute, Hospital Clinic of Barcelona, Barcelona, Spain. Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS)-Hospital Clínic, University of Barcelona, Barcelona, Spain
REVIEW RETURNED	26-Aug-2019

GENERAL COMMENTS	<p>This is a manuscript that presents data from a prospective observational pilot study related to the assessment and modification of physical activity in elderly and high-risk patients with elective surgery. The present data suggest that the triaxial accelerometer AX3 is well accepted by the patients and it could be feasible to assess before and after a physical activity intervention to this specific population. Although the manuscript is very interesting and the results may help to design future studies, there are some concerns that may need further discussion.</p> <p>MAJOR ISSUES</p> <p>- Authors should follow the journal instructions before the submission of the manuscript (https://authors.bmj.com/writing-and-formatting/formatting-your-paper/). References should not be included in the abstract, please, remove references number 1 and 2.</p>
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On the same way, please check the reference list and cite with the accuracy that corresponds using the BMJ reference style.

- Authors should define if they are interested in analysing the physical activity as a part of the daily routine of the patient or if they are more interested in exercise interventions that are focused in the improvement of the functional capacity of the patient (more related to physical fitness). The introduction is not clear enough and some sentences may mix different concepts. Since you can offer an intensive (supervised or non-supervised) exercise training but not a promotion of the increasing of the daily physical activity. Hence those patients could improve their oxygen consumption values but they did not increase physical activity on a daily basis. Please, try to be concise when presenting the background of the study.

- One important concern is the use of a the Axivity AX3 as activity monitor. Nowadays there is a big amount of activity monitors available and their selection has to be justified by the objective of the assessment, the population to measure and, obviously, it is highly recommended to use validated tools. In this specific case, the AX3 is not used frequently and the physical activity outcomes (at least that the authors show throughout the manuscript) are difficult to interpret if someone tries to follow the physical activity guidelines (e.g. ENMO milli-gravitational units). That falls in the difficulty of generating interventions based on that measure. Although (as authors justify) the group of patient assessed did not represent the cut-offs for mild/moderate/vigorous intensity published for healthy people there is a lot of evidence of cut-off in similar populations (e.g. COPD, diabetes, cancer, or even elderly with chronic conditions). I would suggest to authors to use common variables for physical activity measure. Please, find some references related to this point (Matthews CE, et al. Best practices for using physical activity monitors in population-based research. *Med Sci Sports Exerc.* 2012;44(1 Suppl 1):S68–S76. / Schrack JA, et al. Assessing Daily Physical Activity in Older Adults: Unraveling the Complexity of Monitors, Measures, and Methods. *J Gerontol A Biol Sci Med Sci.* 2016;71(8):1039–1048.).

MINOR ISSUES

Abstract:

- Please, include the name and brand of the accelerometer used in the abstract.
- Do not use acronyms without previous definition (e.g. NHS, although almost everybody knows what NHS does it mean)

Introduction:

- Start the number of the first reference with 1.
- Do not use acronyms without previous definition (e.g. PA, although is used in the abstract authors should define when using for the first time in the main text).
- Page 5, line 3, provide reference for the statement “typically seen in an elderly cohort”).

Methods:

- Page 5, line 15, I strongly recommend using published data for reference purposes. Clarke CL, et al. Validation of the AX3 triaxial accelerometer in older functionally impaired people. *Aging Clin Exp Res.* 2017 Jun;29(3):451-457.

	<p>- Page 9, line 11: data processing should be move to “accelerometer and data collection” section. Keep the statistical analysis section only with the methods for analysing data (not for management of that).</p> <p>Results: - Table 1. Since high-risk surgical population is characterised by multiple comorbidities, authors should add a measure of comorbidities (some index) or state the number of comorbidities that the patients presented.</p> <p>Discussion: - Page 14, line 28. Although is very logical to think that the preoperative period is a unique period to implement an effective behavioural intervention, authors should avoid interpreting the results in that way because the desing of the study (and the small sample size) do not support that conclusion.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Please leave your comments for the authors below

The authors describe an interesting approach to validate elderly patients physical activity prior to surgery using an accelerometer. Apart from measuring the effect of a preoperative intervention on patients mobility, the authors intention is to gather data about physical activity in an elderly frail population, to correlate the findings to the patients self-reported degree of activity and to assess the acceptability of the wrist-worn device. The idea of using accelerometry as an easy-to-use, objective method to determine everyday activity is charming and the study is valuable, however, there are some minor aspects that still need to be addressed.

We would like to thank reviewer 1 for their supportive comments. We respond to these minor aspects that they raise.

1. There seems to be a contradiction within the introduction: in ll.17 ff the authors mention the evidence for the (positive, I assume) impact of PA and prehabilitation on perioperative outcomes. In ll. 26ff they state that it is unclear whether prehabilitation reduces postoperative morbidity and mortality. There is, however, quite some evidence (among them a cochrane review) showing the protective effect of preoperative exercise on postoperative outcomes, esp. pulmonary complications. This sentence should be re-considered.

Apologies for this confusion. The conceptual difficulty here which we have perhaps not articulated sufficiently clearly is that we are specifically addressing physical activity (PA) rather than physical fitness (which as the reviewer states there is significant evidence for). Whilst these are clearly likely to be related, there is less evidence for PA and, specifically, for whether an intervention to improve PA is feasible or associated with an outcome benefit.

Crucially however before such studies can be undertaken to study such an intervention in this group of high-risk patients, it is necessary to establish tolerability and normative PA data in order to design such a trial. In this sense our work is needed before any discussion of whether there is a link between increasing PA and outcome and therefore whether such an intervention could be a part of

prehabilitation (although of course this is highly plausible). We have re-structured the introduction to hopefully make this clearer. We hope this new introduction makes this clearer.

2. In Methods, it is not described where the patients were initially enrolled in the trial. This should be added. This is especially of interest for readers not familiar with the British hospital system. Where was the frailty screening performed, in the surgery or anaesthesia department? In an in- or out-patient setting?

Apologies for this we have updated the methods with a description of where patients were enrolled:

“All patients awaiting high-risk surgery are seen in a nurse-led preoperative assessment clinic (outpatient setting) as part of routine care, at which point they undergo frailty screening and may be referred to the ‘Perioperative Review Informing Management of Elderly patients’ (PRIME) clinic (a multidisciplinary clinic specifically designed to optimise frail elderly patients preoperatively).

3. In Methods, ll. 51 ff it is stated that the intervention was "tailored to each participant" but it remains unclear how this was done. This should be described. It is especially important as the authors show that the intervention was somehow not as "successful" for orthopaedic patients compared to others.

This was not an intervention study and thus advice given to participants was decided by the experienced clinicians in the PRIME clinic and not by the research team. Advice was based upon clinical judgement following a comprehensive assessment focusing on aspects of function that patients report as difficult. By way of an example if a patient reported falls due to their knees giving way, the PT would provide a knee strengthening programme. This would also be the situation if the patient were awaiting a total knee replacement. If the patient were awaiting a laparotomy advice may be more targeted upon breathing exercises and the importance of early mobilisation. Because this was not an intervention study we were unable to control the particular advice given, furthermore it was not protocolised. We have added the following text to the Methods section;

“Advice given was decided by experienced clinicians in the PRIME clinic and was based upon their clinical judgement following a comprehensive assessment.”

4. Methods, l. 57: which adaptive equipment was delivered? Why and when was this needed?

In that version we referred to adaptive equipment meaning equipment that may be pre-emptively put into a patients home preoperatively to facilitate a timely discharge from hospital. The majority of equipment was to aid toileting e.g. installing commodes, or handrails to prevent patients struggling to stand from the toilet and pulling themselves up on sinks which is dangerous. We included this in an attempt to be comprehensive but on reflection it detracts from the key focus of the paper and is a source of confusion. We have removed this statement.

5. A figure explaining the composition of the intervention should be added.

Since (1) the interventions were not in any way structured or protocolised in our institution and (2) we do not seek to focus on the interventions specifically in this study (but instead gain normative data and perhaps see if our current interventions, with their limitations, were effective) we are afraid that it is not really possible to construct such a figure. Instead we describe the interventions, as far as is possible, using the TIDieR checklist which has been previously described. We hope that the reviewer will find this sufficient- clearly we agree that in a subsequent trial aimed at intervention design, such a

Careful evaluation of the intervention content would be crucial. However, it falls outside the scope of this study.

6. The authors mention that participant-reported PASE and accelerometer-measured PA are not correlated. It

should be shown how the threshold was defined and how this was calculated, a figure would be preferable. This finding and possible explanations for it should be discussed by the authors.

We deliberately did not use any thresholds since, as the reviewer correctly states, this would be difficult to define. Furthermore, it is better to treat PA as a continuous variable as measured as this is likely to be statistically more powerful and less prone to bias from threshold choice. We simply looked for statistical correlation between the measures (as we stated- we use a Pearson correlation coefficient). We have added the text to the methods section:

“Since accelerometry and self-reported PA are continuous variables, we analysed correlation using the Pearson correlation coefficient”

7. It would be interesting and facilitate understanding to know to which extent accelerometry is correlated to physical activity in general. This could be performed by some kind of "calibration line" correlating typical activities of elderly persons with accelerometer-measured milli-gravitational units.

We agree that this would be very interesting, and the Reviewer is absolutely correct that we do not know, from the literature, what these mg units correlate to- they are likely to be very different from other populations. We hope that this will be the subject of a future study but we (deliberately) did not design our study to look in detail at activity profiles as we felt this might influence (reduce) tolerability / acceptability. We have modified the statement in the discussion to read;

“One further limitation was that we did not attempt to relate ENMO measurements to specific activities of daily living. This will be an important subsequent study but was outside the scope of this work as it might have reduced tolerability.”

8. From the information available, it does not seem admissible to equalise an increase in accelerometer-measured mg with a successful intervention (ll 26ff, discussion) as the clinical meaningful effect (of increase in mg) on patients outcome is not yet known.

We did not mean to imply a clinically meaningful effect- the reviewer is quite right that we do not know this: This will be the subject of a future study (which the present work will be critical in powering the design for). However the fact that (non-orthopaedic) PA was increased to levels comparable to age matched controls from Biobank we feel is a signal that the effect might be meaningful. We have made the following changes to the text to make this point clearer:

“The fact that the unoptimised intervention was successful is a remarkable and somewhat unexpected finding...” has been changed to “The fact that physical activity levels increased to this extent following the unoptimized intervention is a remarkable and somewhat unexpected finding...”

9. Data interpretation and comparison to other trials could be facilitated by addition of a matched healthy (i.e. not scheduled for surgery) control group exposed to the same intervention.

We designed our study to obtain normative data for the high risk population in question (rather than the non-surgical population) since such data is lacking in the literature and will be required

should a randomised intervention study be conducted in the future (as such data would be needed for a power calculation). For that reason, we do not have access to such a cohort of 'healthy' individuals. However, such results have been previously published in the Biobank study which we reference in the text. We have modified the discussion:

“By way of comparison, the UK Biobank study reported...” to “We do not have access to a ‘control’ group as such a group would be difficult to define. However, by way of comparison the UK Biobank study reported...”

10. Figure 1: significant results should be indicated in the graph. We have addressed this.

Reviewer: 2

Please leave your comments for the authors below

This is a prospective study to determine if the use of wrist worn accelerometers can measure physical activity in a surgical population of elderly patients undergoing high risk surgery.

The authors should be commended for presenting a well designed study that was reported in a clear manner. The methods and results sections clearly articulated the process by which they identified the study population within their institution and subsequently obtained the data parameters. The discussion and conclusion are appropriate based upon the data presented.

We would like to thank Reviewer 2 for these comments.

Reviewer: 3

Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below

This is a manuscript that presents data from a prospective observational pilot study related to the assessment and modification of physical activity in elderly and high-risk patients with elective surgery. The present data suggest that the triaxial accelerometer AX3 is well accepted by the patients and it could be feasible to assess before and after a physical activity intervention to this specific population. Although the manuscript is very interesting and the results may help to design future studies, there are some concerns that may need further discussion.

MAJOR ISSUES

- Authors should follow the journal instructions before the submission of the manuscript

(<https://authors.bmj.com/writing-and-formatting/formatting-your-paper/>). References should not be included in the abstract, please, remove references number 1 and 2. On the same way, please check the reference list and cite with the accuracy that corresponds using the BMJ reference style.

We have addressed this (and the introduction has been extensively modified after Reviewer 1's comments). We believe that we are now fully in accordance with BMJ style- please let us know if we have missed anything.

- Authors should define if they are interested in analysing the physical activity as a part of the daily routine of the patient or if they are more interested in exercise interventions that are focused in the improvement of the functional capacity of the patient (more related to physical fitness). The introduction is not clear enough and some sentences may mix different concepts. Since you can offer an intensive (supervised or non-supervised) exercise training but not a promotion of the increasing of the daily physical activity. Hence those patients could improve their oxygen consumption values but they did not increase physical activity on a daily basis. Please, try to be concise when presenting the background of the study.

For the purposes of this study we were primarily interested in obtaining normative data regarding daily routine as well as assessing to some extent, the effect (or otherwise) of current clinical practice (in as much as this influences daily routine). We agree that some of the introduction could be tightened up- we have extensively re-written this (also in the light of Reviewer 1's comments) to streamline the presentation of our logical argument. We hope that this will be satisfactory.

- One important concern is the use of a the Axivity AX3 as activity monitor. Nowadays there is a big amount of activity monitors available and their selection has to be justified by the objective of the assessment, the population to measure and, obviously, it is highly recommended to use validated tools. In this specific case, the AX3 is not used frequently and the physical activity outcomes (at least that the authors show throughout the manuscript) are difficult to interpret if someone tries to follow the physical activity guidelines (e.g. ENMO milli-gravitational units). That falls in the difficulty of generating interventions based on that measure. Although (as authors justify) the group of patient assessed did not represent the cut-offs for mild/moderate/vigorous intensity published for healthy people there is a lot of evidence of cut-off in similar populations (e.g. COPD, diabetes, cancer, or even elderly with chronic conditions). I would suggest to authors to use common variables for physical activity measure. Please, find some references related to this point (Matthews CE, et al. Best practices for using physical activity monitors in population-based research. *Med Sci Sports Exerc.* 2012;44(1 Suppl 1):S68–S76. / Schrack JA, et al. Assessing Daily Physical Activity in Older Adults: Unravelling the Complexity of Monitors, Measures, and Methods. *J Gerontol A Biol Sci Med Sci.* 2016;71(8):1039–1048.).

We would respectfully disagree with this on two grounds.

Firstly, as the reference that the Reviewer cites (Schrack 2016) explicitly states, algorithms used to estimate energy expenditure are generally developed in younger healthy populations thus may not be appropriate for an older population, let alone a surgical population.

Secondly, we explicitly and deliberately seek to keep away from any potentially proprietary algorithms which might post-process the data to a different assessment of activity or step count. For this reason, we deliberately chose to use ENMO. This is the fundamental, unprocessed, physical property being measured by the triaxial accelerometer electronics (this is what is output by the silicon sensor built in to all such devices). As such, we suggest that this is the most generalisable measurement possible. Other post-processed measures may be more intuitive to readers but lack this generalisability across populations.

The silicon microelectromechanical (MEMS) technology within the AX3 is not specific to the AX3 in any way. There is no reason to think that ENMO measurements from this device would be any different to those measured by another (wrist worn) device. Furthermore, the Axivity AX3 has been used by large scale studies such as Biobank with over 100,000 participants.

Of course, data to equate ENMO to actual metabolic equivalents is still lacking- it is an area we would like to study in the future with a study specifically designed for this.

We have added the following to the discussions:

“ENMO may not be as intuitive as post-processed PA intensity metrics. However, such metrics may not generalise outside the population in which they were developed [Schrack]. Furthermore, we wanted to avoid using any potentially proprietary algorithms. Using un-processed ENMO avoids both of these problems as it is the fundamental physical quantity measured by all accelerometers and should therefore be agnostic to patient-group.”

MINOR ISSUES

Abstract:

- Please, include the name and brand of the accelerometer used in the abstract. We have added this

- Do not use acronyms without previous definition (e.g. NHS, although almost everybody knows what NHS does it mean)

We have corrected this.

Introduction:

- Start the number of the first reference

with 1. We have corrected this.

- Do not use acronyms without previous definition (e.g. PA, although is used in the abstract authors should define when using for the first time in the main text).

We have corrected this.

- Page 5, line 3, provide reference for the statement “typically seen in an elderly cohort”). This statement has been removed as part of our re-write of the introduction.

Methods:

- Page 5, line 15, I strongly recommend using published data for reference purposes. Clarke CL, et al. Validation of the AX3 triaxial accelerometer in older functionally impaired people. Aging Clin Exp Res. 2017 Jun;29(3):451-457.

We have added this reference to indicate that this device has been used before in a comparable group and is therefore likely to be an appropriate device.

Unfortunately, Clarke et al fail to give raw ENMO data and focus on specific activities of daily living comparing them with 'counts' which are not generalisable. For the reasons described above, it is therefore not possible to compare this with our data.

- Page 9, line 11: data processing should be move to "accelerometer and data collection" section. Keep the statistical analysis section only with the methods for analysing data (not for management of that).

Moved accordingly. "Statistical analysis" is now a separate section.

Results:

- Table 1. Since high-risk surgical population is characterised by multiple comorbidities, authors should add a measure of comorbidities (some index) or state the number of comorbidities that the patients presented.

We do not have access to detailed comorbidities in our study group as we felt that this was outside of the scope of our study. To fully characterise this would require a much larger study group due to the heterogeneity of these patients which is why we did not set out to do this. As a summary measure, however, we presented ASA in this table as an indication of the impact of comorbidities upon the patient's life. Although an 'aggregate' measure, we felt that this is the most appropriate one since this has been widely used in the anaesthetic literature for preoperative risk stratification. We have added the text to the results:

"Our study was not powered to fully define the spectrum of comorbidities in this group. Instead, we summarised physical status in terms of the American Society of Anaesthesiologists physical status classification score (ASA score) which is widely used for perioperative risk adjustment."

Discussion:

- Page 14, line 28. Although is very logical to think that the preoperative period is a unique period to implement an effective behavioural intervention, authors should avoid interpreting the results in that way because the desing of the study (and the small sample size) do not support that conclusion.

Our intention here was to propose possible reasons to support our finding of an increased PA following the intervention. We do not know whether the increase in PA was of any clinical significance in this increase in PA, as discussed in the discussion. The fact that a measurable increase in PA is detected after an unoptimised intervention (forming part of standard care) is encouraging in that a properly designed and implemented intervention may have a bigger impact on PA. Of course, again we do not know if this will be clinically significant and this would be the purpose of future studies. We have changed the wording...

" Our findings provide some evidence to suggest that the preoperative setting may indeed represent a unique period during which behavioural interventions are more likely to [removed

“be successful”] result in improvements in PA, perhaps due to the well-defined end-point (surgical procedure) and the motivation that physical activity may impact perioperative outcome”

VERSION 2 – REVIEW

REVIEWER	Cynthia Olotu, MD Department of Anaesthesiology Geriatric Anaesthesia Research Group University Medical Centre Hamburg Hamburg, Germany
REVIEW RETURNED	04-Oct-2019
GENERAL COMMENTS	Only two little comments remaining: p4, l5/6: "Many" or "Often, " should be added to this sentence, as there are some very active elderly, too. p14, l5/6: typo: "be" should be removed