PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Early prediction of physical activity level one year after stroke, a longitudinal cohort study.
AUTHORS	Olsson, Ola; Persson, Hanna; Alt Murphy, Margit; Sunnerhagen, Katharina

VERSION 1 - REVIEW

REVIEWER	Torunn Askim Norwegian University of Science and Technology
REVIEW RETURNED	27-Feb-2017

GENERAL COMMENTS	Comments to the Authors Overall, this is a well-designed study addressing an important research question. As stroke survivors generally have poor longer-term outcomes, it is of great importance to identify predictors for inactivity and low activity levels. The results showed that mRS score at discharge from hospital, age and pre-stroke physical activity levels were strong predictors for being inactive one year later, while mRS score at discharge and age were strong predictors for a low activity level. It was a bit surprising that stroke severity not turned out as a significant predictor. How was the association between stroke severity as measured by NIHSS and mRS? Regarding Table 1: Patients unable to walk independently (grade 4-6). Because mRS=6 means dead, it would be more correct to replace 6 with 5 in this table. On bottom of page 11 and top of page 12 the authors claim that the odds for being inactive increased by 6 times for patients who not were able to walk independently at discharge and 6.5 times for being mostly inactive prior to the stroke, while the respective OR in Table 2 are 7.01 and 7.46. According to my knowledge, this means that the odd for being inactive increased by 7 times and 7.5 times respectively. Please revise the text accordingly. Over all the authors discuss their results thoroughly in relation to relevant literature. The strengths and weaknesses are also carefully discussed. However, the inclusion of patients into the original study, the SALGOT-study, required arm impairment. How do the authors think that this inclusion criterion has influenced the results? Please add some considerations regarding this issue to the discussion. I hope these minor comments will help to further improve the paper

	before publication.

REVIEWER	Dr Kate Scrivener Macquarie University, Australia
REVIEW RETURNED	03-Mar-2017

GENERAL COMMENTS	The authors should be congratulated on a well written paper. Major concerns: * For the results of this paper to be clinically useful the prediction model needs to be validated in an independent group of stroke survivors. The authors should describe this and take more caution throughout the paper when describing the clinical implications of this study. Minor concerns Abstract * Objective needs to be rewritten as sentence doesn't make sense. * Please define why UL deficits and living local were inclusion criteria. * Please name the scale used as the primary outcome measure. Introduction * This is an excellent summary of the literature. * Please list the specific research questions at the end of the introduction. Methods * Please clarify which assessments occurred in the home? Was the self-report of PA completed in the home at 12 months? This is unclear. * Please provide statistical justification of analysing 13 predictor variables. This is a large number of variables for the study size (especially considering loss to follow-up) Results * You find arm function to be predictive, however I cannot see how this would have a direct effect on PA. Probably likely to be a confounding variable e.g. indicative of stroke severity. Also, didn't all participants have UL deficit, would the same results occur in those that do not. Please discuss. Throughout * Please refrain from the use of 'patients'. Individuals after stroke (especially when in the community!) do not wish to be referred to as patients.

REVIEWER	E.vanWegen VU University Medical Center, Netherlands
REVIEW RETURNED	09-Mar-2017

GENERAL COMMENTS	This manuscript deals with prediction of post-stroke Physical Activity. The data is from a cohort study that does not seem to be explicitly designed for prognostic research on PA but for studying upper limb recovery, however it provides some relevant insight into pre-stroke PA, age and functional dependence at discharge as

	determinants for post stroke PA. An important issue is that the data collected at moment of discharge is probably highly variable due to large variation in moment after stroke onset while post stroke PA was assessed at a fixed time point, i.e. 1 year, which makes it hard to compare determinants and combine them into one model. Potentially patients with longer length of stay also got higher doses of rehab. therapy, which is not reported on. Also pre-stroke PA level is highly susceptible to recall bias and could be influences by stroke severity which is only marginally discussed. Specific comments: Abstract objective; grammar incorrect Page 2 line 38: how do the data help target interventions for improving physical activity? Intro page 4 line: 27-29: grammar: why question mark? Page 4 line 34 have = has.. Page 4 line 39 correlates with an S and correlates WITH Page 4 line 47-50: you state earlier: Higher PA level pre-stroke may predict a less severe stroke, decrease the overall risk for death from first time stroke and is associated with a better functional status post stroke: is better functional status not relate d to PA level after stroke: so what will you be adding? Page 5 line 13-29: this is one sentence. Please cut up Page 5 line 45, this is mRS 6? Were these excluded regardless? Page 6 line 5 to 10: what was the basis/rationale for the theorized predictors? What literature? Expert opinion? I can think of several more… Page 7 line 5: I see in the protocol paper that you also measured fugl mEyer scores?, why are these not reported? They may be the closest measure for true neurological recovery, cf ARAT. Was FM lowere extremity also assessed? What level of education? Could this have a role in PA levels post stroke (i.e., in adopting healthy behaviors?) Page 7 line 32: What was the length of stay ? this could highly confound the analysis if there is large variability in the time post stroke that mRS is assessed. Page 7 line 36. MRs 4-6? This implies that grade 6 was included? How? Page 8 line 13: the mRS, what is the validity of this dichotomization: literature/references? And scores 5 and 6 were excluded? Unclear Page 9 line 19: PA scale: what is the methodological quality of this scale? What is the influence of cognitive problems , aphasia/apraxia on scoring? What is the potential for recall bias?

	Could there be a correlation between stroke severity and recall>? Page 9 line 10: I do not understand this step, observations equals patients? does this mean that potentially relevant predictors were eliminated just due to less data than others? How did this happen? Incomplete medical records, no assessment? Please explain. I see in table that variables were not completely eliminated, so explain here svp. Page 9 line 16: what was a priori planned for collinearity diagnostics?? Page 9 line 53 I like the fact that you provide data in de dropouts, informative Page 10 Section selction of predictor variables: please provide the numbers/correlations of LRT not just the p-values Page 10 line 36 was significant must be were significant (plural) Page 12 line 46 please start discussion with the initial aim of the study to help the reader Page 13 line 34 age a greater impact: greater than what? Page 13 line 41. OK in univariable arat is significant but drops out in in multivariable analysis, so in the absence of PA information it would be part of the model? What does this day about the robustness of the model? Page 13 line 50: indicates Page 13 line 54: so which model can we consider the most usefull in this context?? page 14 line 36 with impairment do you mean motor impairment? Please be accurate page 14 line 46-52: do you have any idea how your cohort relates to age matched controls or other stroke studies in terms of the PS levels? i.e how representative is your cohort? Page 15 Line 43: I agree that this study corroborates a lot of previous work, however, what is the really innovative/ new insight presented here, please explicate Page 16 line 5-9 please see earlier comment, is there is an interaction between recall and disease severity this may be especially problematic…please discuss Page 16 line 38 a-49 I agree that such prediction is important,. However, what is need to make this prediction more accurate? Can you go a bit firther than concluding “other predictors need to be further explored.” The reviewer also provided a marked copy with additional comments. Please contact the publisher for full details.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1.
Thank you for your important comments. We have respond to the comments in point to point, please see below.
Comment Response
It was a bit surprising that stroke severity not turned out as a significant predictor. How was the association between stroke severity as measured by NIHSS and mRS?
Thank you for this comment. We have added information of the time of discharge in Table 1. The NIHSS was obtained at admission to the stroke unit and mRS at discharge from stroke unit. However when we checked for collinearity between predictor variables we could see that the correlation between NIHSS and mRS was 0.371.
Regarding Table 1: Patients unable to walk independently (grade 4-6). Because mRS=6 means dead, it would be more correct to replace 6 with 5 in this table.
Thank you. The number of 6 has been replaced with 5 since dead patients were obviously lost to follow up.
On bottom of page 11 and top of page 12 the authors claim that the odds for being inactive increased by 6 times for patients who not were able to walk independently at discharge and 6.5 times for being mostly inactive prior to the stroke, while the respective OR in Table 2 are 7.01 and 7.46. According to my knowledge, this means that the odd for being inactive increased by 7 times and 7.5 times respectively. Please revise the text accordingly.
Thank you. Although to our knowledge, the OR indicates the change from the original Odds. Since the OR of 1.0 means that there is no change, an OR of 2.0 indicates an increase of 100% or 1 time. We still argue that the correct increase is reported, however the increase could be reported in percent instead.
Over all the authors discuss their results thoroughly in relation to relevant literature. The strengths and weaknesses are also carefully discussed. However, the inclusion of patients into the original study, the SALGOT-study, required arm impairment. How do the authors think that this inclusion criterion has influenced the results? Please add some considerations regarding this issue to the discussion.
Thank you. This topic has been highlighted as limitation in the discussion and whether the results from our study can also yield to those with no upper limb impairments needs to be investigated more. Reasons for not having any upper limb impairment early after stroke may be diverse (minor strokes in other areas than incorporating the motor system) and more studies are needed to be able to give some closer approximation based on our results.

Reviewer 2
Thank you for your important comments. We have respond to the comments in point to point, please see below.
Comment Response
Major concerns:
* For the results of this paper to be clinically useful the prediction model needs to be validated in an independent group of stroke survivors. The authors should describe this and take more caution throughout the paper when describing the clinical implications of this study.
Thank you for this comment. We have rewritten the conclusions with regards to this and tried to describe this further in the discussion part.
Minor concerns
Abstract
* Objective needs to be rewritten as sentence doesn't make sense.
* Please define why UL deficits and living local were inclusion criteria.
* Please name the scale used as the primary outcome measure.
• Objective has been rewritten with a more correct grammar.

• Both UL impairment and local residency are the inclusion criteria for the SALGOT cohort, from where the sample of this study is based on.
• The name of the scale 6-level Saltin-Grimby scale has been added to the abstract.
Introduction
* This is an excellent summary of the literature.
* Please list the specific research questions at the end of the introduction.
Thank you, we are very pleased that you appreciated this part. This is an exploratory study, and many predictors were considered for the model building. The potential predictor variables are described in the methods section.

Methods
* Please clarify which assessments occurred in the home? Was the self-report of PA completed in the home at 12 months? This is unclear.
* Please provide statistical justification of analysing 13 predictor variables. This is a large number of variables for the study size (especially considering loss to follow-up)
• Thank you for pointing that out. We have added: Most assessments were performed at the hospital and only at persons' home or nursing home when the participant was unable to travel.
• Yes, we agree that the number of potential predictor variables is large. However, as not all predictor variables were included in the final analysis (ruled out in an earlier stage), we argue that we have followed the statistical advices, (10 participants/included predictor variable).

Results
* You find arm function to be predictive, however I cannot see how this would have a direct effect on PA. Probably likely to be a confounding variable e.g. indicative of stroke severity. Also, didn't all participants have UL deficit, would the same results occur in those that do not. Please discuss.
Thank you. We have added an extra part in the discussion area for this, considering both the possibility for being confounders as well as if these findings may be seen in other stroke-populations.
Throughout
* Please refrain from the use of 'patients'. Individuals after stroke (especially when in the community!) do not wish to be referred to as patients.

Thank you for this comment. With respect to people that has suffered from stroke we have changed this term throughout the manuscript.

Reviewer 3
Thank you for your important comments. We have respond to the comments in point to point, please see below.

Comment Response
An important issue is that the data collected at moment of discharge is probably highly variable due to large variation in moment after stroke onset while post stroke PA was assessed at a fixed time point, i.e. 1 year, which makes it hard to compare determinants and combine them into one model. Potentially patients with longer length of stay also got higher doses of rehab. therapy, which is not reported on.

Also pre-stroke PA level is highly susceptible to recall bias and could be influences by stroke severity which is only marginally discussed.

Thank you for these comments. Yes we agree that data from variables collected at discharge, is more

complicated than handle data from fixed time points. In the present study, the mRS was collected at discharge from acute hospital stay. To clarify the time window for discharge from the acute hospital care, the mean length of stay in acute hospital (SD) is added in table 1. We have also added information about were persons were referred to after the acute hospital stay.

The recall bias is always a factor when scoring the PA back to time. We have not investigated possible correlations between the stroke severity and recall, and we do not have data to control whether the reported PA is correct.
Abstract objective; grammar incorrect

Objective has been rewritten with a more correct grammar
Page 2 line 38: how do the data help target interventions for improving physical activity?
Thank you for this comment.
We have now revised the text in the abstract.
Intro page 4 line: 27-29: grammar: why question mark?
Thank you for this comment.
We have changed this sentence to end by a dot.
Page 4 line 34 have = has..
Thank you, we have changed into has

Page 4 line 39 correlates with an S and correlates WITH
Thank you, we have changed into correlates with

Page 4 line 47-50: you state earlier: Higher PA level pre-stroke may predict a less severe stroke, decrease the overall risk for death from first time stroke and is associated with a better functional status post stroke: is better functional status not relate d to PA level after stroke: so what will you be adding?
Thank you for this comment. A lot of previous research has been focusing on the effect of PA regarding different aspects of stroke. The main purpose for our study has, however, been to investigate which variables that have impact in the PA level after stroke and is not focusing on other effects of previous PA. We also don't think that functional status automatically can be assumed to be related to PA level after stroke, since motor disability has not been found to correlate with PA level after stroke.
Page 5 line 13-29: this is one sentence. Please cut up
The sentence has been cut up. The inclusions criteria are still separated by semicolons.
Page 5 line 45, this is mRS 6? Were these excluded regardless?
Thank you for pointing this out. The patients that died were excluded for analysis, we have changed the numbers for the mRS throughout the article into 0-5.
Page 6 line 5 to 10: what was the basis/rationale for the theorized predictors? What literature? Expert opinion? I can think of several more…
Potential predictors prior and close to the stroke onset were chosen to be considered for model building. The potential predictors were chosen from our clinical experience and from the literature used in the introduction.
Page 7 line 5: I see in the protocol paper that you also measured fugl mEyer scores?, why are these not reported? They may be the closest measure for true neurological recovery, cf ARAT. Was FM lowere extremity also assessed?
What level of education? Could this have a role in PA levels post stroke (i.e., in adopting healthy behaviors?)
In the present study NIHSS was used for stroke severity instead of FMA-UE.

FMA for lower extremity function and education level were not included in the SALGOT assessments.

Page 7 line 32:
What was the length of stay ? this could highly confound the analysis if there is large variability in the time post stroke that mRS is assessed.

Thank you for pointing this out. The length of hospital stay has now been included in table 1.
Page 7 line 36. MRs 4-6? This implies that grade 6 was included? How?
Thank you for pointing this out. We have changed into mRS 4-5. Grade 6 was not included.
Page 8 line 13: the mRS, what is the validity of this dichotomization: literature/references? And scores 5 and 6 were excluded? Unclear
Thank you for your comment. We have not included mRS grade 6 since these patients died. We have changed this accordantly in the manuscript.
Page 9 line 19: PA scale: what is the methodological quality of this scale?
The concurrent validity of the original Saltin-Grimby scale (4 grades), with respect to aerobic capacity and movement analysis using objective measurements has been shown to be good, as has the predictive validity with respect to various risk factors for health conditions and for morbidity and mortality. The 4-grade scale is extensively used in different populations. An review of the use of the scale has been published in 2015; Grimby et al Scand J Med Sci Sports.
However, the 6 grade scale was developed from the 4-grade scale, (with adding activities during leisure-time, occupational and household activities) and the 6 grade scale is also extensively used both in research and in the clinic and has been validated (Frändin K and Grimby G: Scan J Med Sci Sports 1994 and Frädnin K et al Gerontology 1994)

What is the influence of cognitive problems , aphasia/apraxia on scoring? What is the potential for recall bias?
Could there be a correlation between stroke severity and recall>?
Cognition was screened within the SALGOT protocol using BNIS screening. In case of uncertainty or significant cognitive limitations so that an answer could not be collected from the participants, the assessors had possibility also to ask next to kin. If the PA was not possible to assess then this variable was missing, and in this case the patient was not included in this study. The participants included in the current study all had a valid value on PA. The PA was scored based on an interview which allowed follow-up questions if needed. The recall bias is always a factor when scoring the PA back to time. We have not investigated possible correlations between the stroke severity and recall, and we do not have data to control whether the reported PA is correct.
Page 9 line 10: I do not understand this step, observations equals patients? does this mean that potentially relevant predictors were eliminated just due to less data than others? How did this happen? Incomplete medical records, no assessment? Please explain.
I see in table that variables were not completely eliminated, so explain here svp.
Some of the predictor variables were only observed in few participants when the group was dichotomized into separate PA levels. These variables are listed in the results (selection of predictor variables). It was not due to missing data.
Page 9 line 16: what was a priori planned for collinearity diagnostics??
The correlations larger than 0.7, as stated in the statistics section.

Page 9 line 53 I like the fact that you provide data in de dropouts, informative
Thank you.
Page 10 Section selection of predictor variables: please provide the numbers/correlations of LRT not just the p-values
Thank you, we have in the results added the numbers/correlations of the LRT next to p-values.
Page 10 line 36 was significant must be were significant (plural)
Yes, thank you. This have been changed accordantly.
Page 12 line 46 please start discussion with the initial aim of the study to help the reader
Thank you for this comment. We prefer not to repeated the aim word for word, but rather provide the

results of our study. We hope that this help the reader understand the study and the discussion.
Page 13 line 34 age a greater impact: greater than what?
Yes we agree, this sentence was unclear, and we have now changed it.
Page 13 line 41. OK in univariable arat is significant but drops out in multivariable analysis, so in the absence of PA information it would be part of the model? What does this say about the robustness of the model?
The ARAT score and mRS showed collinearity and therefore these were added separately to the model, but their effect on PA was similar.
Page 13 line 50: indicates
Yes, thank you. This have been changed.
Page 13 line 54: so which model can we consider the most usefull in this context??
We assume that for most instances the level PA reflecting 30 min activity per day is the most useful in order to reflect healthy behavior.
page 14 line 36 with impairment do you mean motor impairment? Please be accurate
Thank you. We have now changed the sentence.
page 14 line 46-52: do you have any idea how your cohort relates to age matched controls or other stroke studies in terms of the PS levels? i.e how representative is your cohort?
We do not have matched control regarding level of PA. However, the cohort is representative of the persons admitted to the stroke unit at the hospital during the time period who had UE impairment (Persson et al, BMC Neurology, 2012)

Page 15 Line 43: I agree that this study corroborates a lot of previous work, however, what is the really innovative/ new insight presented here, please explicate

The study provides pre-stroke and early predictors variables that have impact on the level of physical activity one year post a stroke.

Strengths with the present study is the use of important parameters prior to the stroke, the follow-up over 1 year.
The study also provide clinically relevant dichotomizations of the physical activity scale.

The conclusion has been re-written in order to highlight the benefits from the study.
Page 16 line 5-9 please see earlier comment, is there is an interaction between recall and disease severity this may be especially problematic…please discuss
We agree that in a population where cognition may be affected, that recall bias is problematic. We tried to confirm the level of reported activity with other questions and sometimes with the next-of- kin. However, the questionnaire is simple, which probably reduces possible bias. However, this has not been investigated as far as we know.
Page 16 line 38 a-49 I agree that such prediction is important,. However, what is need to make this prediction more accurate? Can you go a bit firther than concluding “other predictors need to be further explored.”
The conclusion is re-written. Co-morbidities may of course influence PS, however, in this population those recorded did fall out. An index, such as Charlston co-morbidity index could be useful.

VERSION 2 – REVIEW

REVIEWER	Kate Scrivener Macquarie University Australia
REVIEW RETURNED	28-Apr-2017

GENERAL COMMENTS	I have reviewed your revised manuscript and your response to my initial comments.

	I believe you have made some improvements to the manuscript, particularly regarding describing the study limitations. However, I find your response to my reviewer comments inadequate and feel that there are still issues to address. There are some major study limitations that limit the clinical relevance of this study to readers. Firstly, the fact that this study only included people after stroke with upper limb deficits and secondly the exploratory nature of the study, namely the number of predictor variables included. The major points in my initial review that you have not addressed adequately are: 1. You have not specifically defined your research question. You need to list your research question/s at the end of the introduction. 2. You have not described your methods adequately. In particular you state that measures were taken in the hospital, is that true for self-report of PA at 12-months? Did participants really come in just for that? Were they back into hospital for the other study at that point so you did your measure then as well? Please provide more details. 3. Throughout the manuscript you describe the inclusion criteria for your study, as this is really the inclusion criteria for the larger RCT I feel you need to specify this. For example it is still unclear to a reader initially reading the abstract, as to why UL etc is an inclusion criteria. By simply rewording to "inclusion criteria for the larger study were....." may solve the problem. 4. I believe a statistical review is warranted. The number of predictor variables continues to concern me.

REVIEWER	Charles B Hall Albert Einstein College of Medicine Bronx, New York, USA
REVIEW RETURNED	18-May-2017

GENERAL COMMENTS	This manuscript finds that physical activity prior to stroke, functional dependency at discharge, and age all predict activity one year after stroke. Statistical methods are largely standard and a standard goodness of fit test (Hosmer-Lemeshow) is used to check the model fit. Surprisingly, stroke severity did not predict activity; the authors allude to the fact that severity may be captured in the dependency measure and it would be interesting to present an analysis showing the association of the NIHSS with functional dependency at discharge; weak association might be associated with heterogeneity of recovery. There are some methodological concerns that should be addressed by the authors. First, the authors present "complete case" analyses in which any missing data in any variable in any individual results in that individual being excluded from that analysis. It appears that there may not have been many such exclusions, but that manuscript should indicate this and if the number of exclusions is large then some method appropriate for addressing missing covariate

	information should be applied. There was significant loss to follow up; the authors have done a good job at identifying the reasons but the discussion should make clear that the analyses are to be interpreted to be conditional on survival. The manuscript would be strengthened by modeling whether the same predictors that predict inactivity one year after follow-up also predict loss to follow up, or mortality, in this cohort; if they do it would help to eliminate concerns that loss to follow up may have unduly influenced the results. Alternately, sensitivity analyses could be used to assess the robustness of the findings to informative missingness. A final concern is that the first figure seems to indicate that there were no mostly inactive non-walkers below age 70; the manuscript should point out that the models assume that the same logit linear relationships hold below age 70 but that strictly speaking the sample does not have data to confirm that. In a minor point, all tables should include units. For example, age should be indicated as being in years.

VERSION 2 – AUTHOR RESPONSE

The major points in my initial review that you have not addressed adequately are:

1. You have not specifically defined your research question. You need to list your research question/s at the end of the introduction.

Response: We have rephrased the aim slightly. The study had an explorative research approach and aimed to add all possible predictor variables available for this large longitudinal cohort.

2. You have not described your methods adequately. In particular you state that measures were taken in the hospital, is that true for self-report of PA at 12-months? Did participants really come in just for that? Were they back into hospital for the other study at that point so you did your measure then as well? Please provide more details.

Response: To meet these concerns we have added information on the assessments made within the larger SALGOT study. Now it reads: In SALGOT, the patients were assessed at admission and discharge as well as at 3 and 10 days, at 3, 4, and 6 weeks; and at 3, 6 and 12 months post stroke. In the current study, data from admission, discharge, 3 days and 12 months were used.

3. Throughout the manuscript you describe the inclusion criteria for your study, as this is really the inclusion criteria for the larger RCT I feel you need to specify this. For example it is still unclear to a reader initially reading the abstract, as to why UL etc is an inclusion criteria. By simply rewording to "inclusion criteria for the larger study were....." may solve the problem.

Response: As the reviewer points out, this study is part of a larger observational study (not RCT as it was interpreted by the reviewer). This is clearly stated in the Abstract where it reads: 117 individuals part of the Stroke Arm Longitudinal study (SALGOT) admitted to the stroke unit during a period of 18 months (2009-2010) were consecutively recruited. The inclusion criteria were: first-time stroke, impaired upper-extremity function, admitted to the stroke unit within 3 days since onset, local residency, ≥18 years old. The same inclusion criteria are stated in the Methods section. The inclusion criteria for this study were overlapping the inclusion criteria for SALGOT. We have made a

clarification in the abstract so it can be understood that 77 participants followed up at one year were included in the analysis. Now it reads: 77 participants followed-up at one year post stroke were included in the analysis.

4. I believe a statistical review is warranted. The number of predictor variables continues to concern me.

Response: We appreciate the reviewers comment and have added additional clarification regarding the number of predictor variables that were considered for multivariate analysis. We anticipated these concerns and selected the predictor variables considered for multivariate analysis and with care. All steps for these procedures are described under the Methods section, under Statistics. In the first step, predictor variables with too few observations were excluded from the further analysis. This is stated in the results section under the subheading: Selection of predictor variables, and reads: The type of stroke along with smoking, TIA, diabetes and atrial fibrillation prior to stroke contained too few individuals in subgroups and were therefore not included into further analysis. We have also marked these initially considered predictor variables in the Table 1. We have also added, in the same paragraph: Thus, seven possible predictor variables were considered to be entered in the multivariate models in this second step. We hope that these changes make it more clear how many predictor variables were considered for multivariate analysis. Seven predictor variables as used in this study, is reasonable for the sample size of 77. Table 2 specifies also CI for OR, which can help the reader to interpret the results.

Reviewer: 4
Charles B Hall
Albert Einstein College of Medicine
Bronx, New York, USA
Please state any competing interests or state ‘None declared’: None declared.

This manuscript finds that physical activity prior to stroke, functional dependency at discharge, and age all predict activity one year after stroke. Statistical methods are largely standard and a standard goodness of fit test (Hosmer-Lemeshow) is used to check the model fit. Surprisingly, stroke severity did not predict activity; the authors allude to the fact that severity may be captured in the dependency measure and it would be interesting to present an analysis showing the association of the NIHSS with functional dependency at discharge; weak association might be associated with heterogeneity of recovery.
Response: In the present study, NIHSS at admittance had a correlation of 0371 with mRS 3-4 at discharge.

1. There are some methodological concerns that should be addressed by the authors. First, the authors present "complete case" analyses in which any missing data in any variable in any individual results in that individual being excluded from that analysis. It appears that there may not have been many such exclusions, but that manuscript should indicate this and if the number of exclusions is large then some method appropriate for addressing missing covariate information should be applied.

Response: The exact number of observations per predictor variable is shown in Table 1, with number of cases after each variable not having 77 subjects. As it can be seen from Table 1, the number of cases missing was not large (ranging from 1 to 4 cases of 77). This was not considered to influence the results of this study.

2. There was significant loss to follow up; the authors have done a good job at identifying the reasons but the discussion should make clear that the analyses are to be interpreted to be conditional on

survival.

Response: We have added a clarification to address this in the Discussion section together with other limitations. Now it reads: …, and the results apply only to those who were followed-up at one year.

3. The manuscript would be strengthened by modeling whether the same predictors that predict inactivity one year after follow-up also predict loss to follow up, or mortality, in this cohort; if they do it would help to eliminate concerns that loss to follow up may have unduly influenced the results. Alternately, sensitivity analyses could be used to assess the robustness of the findings to informative missingness.

Response: These are interesting remarks worth to consider for future studies. Including other variables such as mortality and analyzing more closely reasons for lost-to- follow-up go beyond the scope of this study. The idea to further analyze the impact of PA on mortality and loss to follow up is an interesting one, but outside the scope of the present study.

4. A final concern is that the first figure seems to indicate that there were no mostly inactive non-walkers below age 70; the manuscript should point out that the models assume that the same logit linear relationships hold below age 70 but that strictly speaking the sample does not have data to confirm that.

Response: We are thankful for the reviewer to point out this fact. We have added a statement in the results section to clarify this. It reads: As seen in Figure 2, there were no observations on mostly inactive non-walkers below age 70, which means that the predicted probabilities are extrapolated below this age.

5. In a minor point, all tables should include units. For example, age should be indicated as being in years.

Response: We have made the corrections to Table 1.

VERSION 3 – REVIEW

REVIEWER	Kate Scrivener Macquarie University Australia
REVIEW RETURNED	15-Jun-2017

GENERAL COMMENTS	Thank you for the opportunity to re-review this manuscript. In my opinion you have not adequately addressed my reviewer comments. For example, you have not defined your specific research question. For a manuscript to be included in a peer review journal it is appropriate to expect a clearly defined research question. The fact that yours was an exploratory study does not mean that a research question is not warranted. I feel that your justification for not full addressing mine and reviewer 4's comments is not sufficient.

REVIEWER	Charles B. Hall Albert Einstein College of Medicine, Bronx, NY, USA
REVIEW RETURNED	16-Jun-2017

GENERAL COMMENTS	This manuscript finds that physical activity prior to stroke, functional dependency at discharge, and age all predict activity one year after stroke. Statistical methods are largely standard and a standard goodness of fit test (Hosmer-Lemeshow) is used to check the model fit. Surprisingly, stroke severity did not predict activity; the authors allude to the fact that severity may be captured in the dependency measure and it would be interesting to present an analysis showing the association of the NIHSS with functional dependency at discharge; weak association might be associated with heterogeneity of recovery. Response: In the present study, NIHSS at admittance had a correlation of 0371 with mRS 3-4 at discharge. Reviewers response: I think that there is a missing decimal point here. 1. There are some methodological concerns that should be addressed by the authors. First, the authors present "complete case" analyses in which any missing data in any variable in any individual results in that individual being excluded from that analysis. It appears that there may not have been many such exclusions, but that manuscript should indicate this and if the number of exclusions is large then some method appropriate for addressing missing covariate information should be applied. Response: The exact number of observations per predictor variable is shown in Table 1, with number of cases after each variable not having 77 subjects. As it can be seen from Table 1, the number of cases missing was not large (ranging from 1 to 4 cases of 77). This was not considered to influence the results of this study. Reviewer's response: I agree that there is little missing data and that it is unlikely to have affected the results of the study. 2. There was significant loss to follow up; the authors have done a good job at identifying the reasons but the discussion should make clear that the analyses are to be interpreted to be conditional on survival. Response: We have added a clarification to address this in the Discussion section together with other limitations. Now it reads: …, and the results apply only to those who were followed-up at one year. Reviewer's response: The authors' response is acceptable. 3. The manuscript would be strengthened by modeling whether the same predictors that predict inactivity one year after follow-up also predict loss to follow up, or mortality, in this cohort; if they do it would help to eliminate concerns that loss to follow up may have unduly influenced the results. Alternately, sensitivity analyses could be used to assess the robustness of the findings to informative missingness. Response: These are interesting remarks worth to consider for future studies. Including other variables such as mortality and analyzing more closely reasons for lost-to- follow-up go beyond the scope of this study. The idea to further analyze the impact of PA on mortality and loss to follow up is an interesting one, but outside the

	scope of the present study. Reviewer's response: With the limitation stated in the response to comment 2, above, this response is acceptable. 4. A final concern is that the first figure seems to indicate that there were no mostly inactive non-walkers below age 70; the manuscript should point out that the models assume that the same logit linear relationships hold below age 70 but that strictly speaking the sample does not have data to confirm that. Response: We are thankful for the reviewer to point out this fact. We have added a statement in the results section to clarify this. It reads: As seen in Figure 2, there were no observations on mostly inactive non-walkers below age 70, which means that the predicted probabilities are extrapolated below this age. Reviewer's response: The authors' response is acceptable. 5. In a minor point, all tables should include units. For example, age should be indicated as being in years. Response: We have made the corrections to Table 1. Reviewer's response: The author's response is acceptable.