Author's response to reviews

Title: Self-reported knee joint instability is related to passive mechanical stiffness in medial knee osteoarthritis

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Version: 2 Date: 10 October 2013

Author's response to reviews: see over
Reviewer's report

Reviewer: JONATHAN JEFFERS

All comments are Minor Essential Revisions

This paper presents a varus valgus laxity and stiffness measurement of the knee using a dynamometer. Stiffness is measured as the measured varus valgus torque divided by the angular displacement. A significant relationship is found between stiffness at small varus/valgus angles/moments and instability, but not at large angles of varus/valgus angles or moments. Neither is significance found between laxity (angular displacement at maximum torque applied) and instability. This finding is of interest as prior work has mainly focussed on laxity only. Overall this is a well written paper that presents interesting findings that will be of interest to the field as the topic of instability is current. I have some queries and clarifications as outlined below, perhaps the authors could be asked to comment on these relatively minor points?

ABSTRACT:

Comment: Line 2: I would say all knee instability compromises function, not just that which is self reported, suggest deleting first two words of this sentence. Otherwise fine.
Response: We agree entirely with the reviewer that all forms of knee joint instability have the potential to compromise function in any individual. In the sentence the reviewer is referring to however, we chose to specifically refer to “self-reported” knee instability in order to focus the readers attention upon the specific question posed in our study, i.e. the relationship between self-reported instability and passive mechanical stiffness.
Change: No change. If the reviewer strongly feels the current wording is to the detriment of the manuscript we would be willing to consider modifying the manuscript.

INTRODUCTION:

Comment: p3 line 2. Same comment as above.
Response: Please refer to the previous response.
Change: No change.

Comment: P4 line 14: Why only the laxity in varus/valgus? Some justification could be added here why the study omits AP and rotational instability, also commonly reported e.g. if ACL is deficient in OA knee. Patient reported instability is a sum of all possible modes of instability unlikely to be fully characterised by analysing only one potential mode. Only a sentence or two to justify is needed. Otherwise good introduction to study.
Response: We agree with the reviewer that the stiffness and/or laxity in all planes of motion may relate to the symptomatic stability of the joint. Indeed, in the original submission (and retained in the revised manuscript), we
highlight that our focus upon only frontal plane laxity as a limitation of the study (and we also explain why frontal plane mechanics in particular were our focus): “Second, our findings are limited to the varus-valgus stiffness of the knee. Conceivably, sagittal and transverse plane stiffness of the knee may also be related to perceived joint instability and this is worthy of investigation in future research. In the current study however, we focussed upon varus-valgus stiffness, given the high frontal plane loads and reported involvement of passive varus-valgus stiffness in medial knee OA [7, 9-11].”

Change: In order to clarify up-front the influence that mechanical stiffness in all three planes will influence the overall stability of the knee, we have included an additional sentence in the Introduction (page 3, lines 12-14).

METHODS:

Comment: p6 line 14: A photograph of the dynamometer identifying the position of the load cell and lever arm would be useful to readers who are not familiar with the device.
Response: Thank-you for this suggestion.
Change: We have included a figure of the experimental setup in the revised submission (new Figure 1).

Comment: P6 line 17. Why was only 20deg flexion considered? Needs to be justified else could be missing mid flexion instability at other flexion angles.
Response: We designed the instrumented knee varus-valgus laxity test to mimic the way in which the test is performed clinically to assess ligamentous laxity, i.e. in slight flexion, such that the posterior capsule is relaxed and the major resistance to motion comes from medial and lateral soft tissues. Further, it is at this angle of flexion that previous work has demonstrated differences in varus-valgus laxity behaviour between individuals with and without knee osteoarthritis (Sharma et al., 1999; Creaby et al., 2010). The choice of measurement angle is thus not directly related to the question of instability addressed in this study. Whether or not there is a typical flexion angle range in which knees give way in this population has not been investigated as far as we are aware.
Change: We have now included reference to previous work in this area that has employed the 20deg flexion angle to examine knee laxity in OA populations (page 7, line 8).

Comment: P6 line 25: Can authors briefly justify 25Nm? It seems low to stress the full laxity of the joint, assuming lever arm of 0.5m to ankle is a load of 50N (0.5kg). But understand may be ethical concern about hurting patients at higher load. Similarly at 1deg for mid range stiffness moment is 1.5Nm making load of 15N (0.15kg) at the ankle is very low, roughly the weight of an apple, can authors comment on this very small load being resisted by the passive structures in the knee and not very small involuntary muscle contraction, the clothes/socks the patient may
be wearing (even a stiff pair of jeans might partially resist this small moment) and the ability of the dynamometer to apply and record (through the load cell) this small load/moment? What kind of hysteresis exists in the knee/dynamometer system, the small load/moment may reside in the hysteresis of system (looking briefly at Figure 1 in reference 7 it looks like this is the case). In short, some data on the methodology being capable of this resolution of measurement would address this issue, maybe has been addressed in previous work? All could be answered with a sentence or two in this section.

Response: The passive torque applied in this study is up to 12 Nm (not 25 Nm). 12 Nm appears to be the most common load that has been used for this assessment, by ourselves and others (e.g. Sharma et al., 1999, Arthritis Rheum; Bragge et al., 1994, Clin Orthop Rel Res). A few studies have used a lower load (e.g. Knoop et al., 2012, Arthritis Care Res), and one group has used a higher loads, albeit in young healthy individuals (Cammarata & Dhaher, 2008, Clin Biomech).

As the reviewer suggests, our concern was that the use of higher loads may have elicited pain in these individuals. Based on the following evidence, we believe that implementing the test at higher peak torques would be unlikely to glean additional relevant information regarding the relationship between laxity and instability:

(1) Previous findings with respect to knee laxity in individuals with knee OA (e.g. Sharma et al., 1999; Creaby et al., 2010), and knee OA and symptomatic instability (Knoop et al., 2012) have been identified at torques of 12 Nm or below.

(2) At the 12 Nm used in this study we are able to move the knee through a range of motion that is typically greater than the frontal plane motion normally experienced during typical daily activities; in this study our focus was on examining the relationship between indices of laxity/stiffness and symptomatic instability during daily activities.

The patients’ legs are bare (wore only shorts and t-shirt during testing) so there is no other resistance to rotation about the single rotational degree of freedom allowed (and constrained to occur about the knee joint) other than that from the soft tissue structures around the knee, and possibly small joint contact forces.

The hysteresis of the knee soft tissues is consistent with that which has been consistently shown in the literature over several decades, both in vivo (e.g. Markolf et al., 1978, JBJS-A), and ex vivo (e.g. Markolf et al., 1981, JBJS-A).

Change: In this section of the methods clear reference has been made to previous works justifying the 12 Nm upper torque limit, and we have also clarified that only shorts were worn to remove any possible resistance that clothing may provide (page 7, lines 9-20).

We also now include addition comment in the Discussion regarding the low absolute magnitude of varus-valgus torques acting in the mid-range (page 12, lines 12-15).

Comment: P7 line 8: is there a reference for defining the mid range stiffness as +/- 1deg from neutral? I.e. if mid range stiffness was defined as +/-
2 degrees would significant relationship with instability still be found?

How many repeat measures were taken per knee?

Response: The choice of the 2 degree window allows for a measurement of the slope of the curve over a region in which it is relatively stable, as the knee passes through the zero load point. Any larger window and it would be likely to include the increasing slope that occurs as the joint starts to resist the movement more. At the stated sample rate and velocity, the slope measurement is made from 40 data points. The 2 degree range employed in this study was based on our previous work where we identified differences in mid-range stiffness between different severities of knee OA; others have also employed the same definition of neutral stiffness e.g. Cammarata & Dhaher, 2012. The torque-angle curve from which the slope is taken is the ensemble average of passing through this angular window 10 times.

Change: A reference to previous work employing the 2 degree window is now provided at the end of the relevant sentence: “Mid-range stiffness was calculated from the averaged varus and valgus movement over a 2° window, 1° either side of mechanical neutral [8, 9]” (page 8, line 6). Our 3 other works on this subject were also cited at the start of the “Knee joint laxity and stiffness” section of the Methods for further methodological detail for the interested reader (page 7, lines 6-7). We have modified the end of the first paragraph in the Methods on “Knee joint laxity and stiffness” to include reference to the number of repeat trials: “…thus ensuring a gravity-neutral position. Following a period of familiarisation to ensure the participant was comfortable with the test procedure, was not experiencing pain, or contracting the muscles crossing the knee joint [25], varus and valgus angles were determined by passive rotation to the point where 12N.m of passive resistance was reached [8]. The leg was then passively rotated by the dynamometer from varus to valgus and valgus to varus at 5 degrees per second [8]. This movement was repeated 10 times, with the extracted data averaged across the 10 rotations.” (page 7, lines 13-20).

Comment: P7 line 16: include the name of the test used to check for normal dist and the result of this test.

Response: We apologise for this oversight in the original submission of the manuscript. To clarify, the primary purpose of the paper is to establish the predictive relationship between laxity/stiffness indices and symptomatic knee instability. Given that regression analyses were used for this purpose, it is important that the residuals, not the outcome variables, are normally distributed (Peat, J., & Barton, B. 2008. Medical Statistics: A Guide to Data Analysis and Critical Appraisal. Chichester, GBR: Wiley. Page 165). This was checked statistically with a Kolmogorov-Smirnov test with Lilliefors significance correction and confirmed as normally distributed.

Change: The specific test used to check the distribution of the data is now included in the Statistical analysis section of the Methods (page 8, lines 24-25). The result of this test is now described in the Results section (page 10, lines 4-5).
Comment: P7 line 22: I've recommended to editor the stats are reviewed by statistician due to relating parametric to non parametric data.

Response: From the conception stage of this study we have been cognisant that careful consideration of our statistical methods is paramount, particularly as our aim was to evaluate the relationship between continuous variables (laxity and stiffness) and an ordinal variable (symptoms of instability). Following consultation with a biostatistician, we were directed to a contemporary textbook describing, in detail, the assumptions that our data must first meet in order to provide a valid result (Peat, J., & Barton, B. 2008. Medical Statistics: A Guide to Data Analysis and Critical Appraisal. Chichester, GBR: Wiley. Pages 162-166). As outlined in the Statistical analysis section of our methods, the various assumptions were checked prior to statistical test in regression modelling.

Change: No change.

RESULTS:

Comment: P9, line 3-13: this paragraph may be better in the methods as more a justification of methodology rather than results.

Response: As outlined in the response above, the nature of the research question required a statistical approach that is not typically used (i.e. an ordinal dependent variable in linear regression). Given this fact we wanted to ensure complete transparency in our statistical approach. Thus, in our Methods we outlined the data checking that was performed to ensure that our data met the assumptions for linear regression analysis e.g. “the data were checked to ensure that…residuals are normally distributed”, and in the Results section we report if the assumptions were met e.g. “the data met the standard assumptions required for valid linear regression modelling, including the normal distribution of residuals ($P=0.20$)”.

Change: In the revised version of the manuscript we have left this information in both the Methods and Results sections for the reasons outlined above. However, if the Reviewer and/or Editor strongly feels that this information is excess to requirements we would be happy modify the manuscript appropriately.

DISCUSSION:

Comment: Good and interesting discussion, nice comparison to literature. Would also be nice to see study on knee post treatment, e.g. pre/post ACL repair or pre/post UKR surgery. P 10 line 1: The stress radiography methodology differs from the presented methods as the x-ray ensures the measure of laxity under fixed torque is measured at the joint, thus eliminating any contribution that may be made by patient's clothing, muscle contraction, machine hysteresis etc, the authors could comment on the advantages and disadvantages of the different methods (radiation dose etc).

Response: There a number of different ways that joint 'laxity' has been measured. Comparison of their pros and cons is a complex subject unfortunately
beyond the scope of this paper, although we do mention some issues briefly, including the uncertain meaning of the stress radiography measures, and the typical lack of any normalization for body size differences in published results (i.e. the same load is applied to all knees, big or small, and the data is typically not adjusted for the likely effect).

As the load is applied to the knee externally in the x-ray technique, any other force (e.g. muscle contraction) that resists the application of that load would in fact limit measured joint opening in exactly the same way that it might limit measured joint angular movement in our technique; joint opening is a reflection of angular movement, not somehow independent of it.

**Change:** As the original version of the manuscript highlighted the primary difference between the angular laxity and stress radiography methods (page 11, lines 1-5), and no differences exist with respect to the influence of muscle contraction, patient clothing etc., upon the measurement, between the two techniques, we have not modified the manuscript in response to this comment.
Reviewer's report

Reviewer: Martha Cammarata

This paper provides interesting and useful data on the relationship between knee instability and passive frontal plane joint stiffness in patients with knee OA. It was well conducted and well written. My major comments concern presentation of appropriate, detailed results and the interpretation of finding.

Major compulsory comments:

ABSTRACT:

Comment: In the conclusion of the abstract the authors mention interventions that could overcome a lack of passive stiffness in OA patients. However, there are no mentions of such interventions in the discussion section. The authors should either remove this statement from the abstract or briefly elaborate upon this idea in the discussion section.

Response: Thank-you for highlighting this discrepancy.
Change: The conclusion of the Abstract has been modified to reflect the content of the Discussion and Conclusions.

INTRODUCTION:

Comment: final paragraph: please include a statement of the clinical and scientific impact this study will have on the understanding and treatment of knee OA. It would also help to summarize this again in the discussion/conclusion section.

Response: Thank-you for this suggestion.
Change: We have included an additional sentence in the Introduction to outline the potential clinical and scientific impact (Page 3, line 24 – Page 4, line 2).

METHODS:

Comment: statistical analysis: why is it necessary to have a linear relationship between the two variables? What if there was an exponential relationship between stiffness and joint instability?

Response: In the Statistical analysis section of the Methods, we outline the several criteria that the data must meet in order to be considered for regression modelling. All of these criteria, including the requirement for an approximately linear relationship between the explanatory variables and outcome variable, reflect the standard assumptions required for valid regression modelling (Peat, J., & Barton, B. 2008. Medical Statistics: A Guide to Data Analysis and Critical Appraisal. Chichester, GBR: Wiley. Page 165).

Change: We have extended the sentence in question to clarify that these criteria were instituted to ensure the standard assumptions for valid linear regression modelling were met (Page 8, lines 21-23).
**Comment:** statistical analysis: Please explain the rationale for requiring significant correlation using both Pearson and Spearman correlation coefficients. Why were both parametric and non-parametric coefficients used?

**Response:** As the outcome variable used in this study (presence and severity of self-reported instability) was ordinal, parametric and non-parametric correlations were performed to ensure that our data met the assumptions of parametric statistics and thus would be valid.

**Change:** In the original submission we outlined the justification for thorough checking of the data given the use of an ordinal outcome variable, but realise that this may have not linked clearly to the following sentence about running both Pearson (parametric) and Spearman (non-parametric) correlations. We have therefore reworded the start of the second sentence to make the link between the two more explicit: “Given that the outcome variable in these analyses (presence and severity of self-reported knee instability) is ordinal, thorough checking of the data were performed to ensure that the assumptions of parametric statistics were met. This involved the calculation of both Pearson (parametric) and Spearman (non-parametric) correlation coefficients to determine the degree of correlation between the presence and severity of self-reported knee instability and indices of knee angular laxity and stiffness.” (page 8, line 13-19).

**RESULTS:**

**Comment:** Paragraph 1: Average varus/valgus laxity and stiffness are reported for the entire cohort. Because the purpose of the study is to assess correlation between these measures and instability, please provide a break-down of these measures according to self-reported knee instability, either in tabular or figure format.

**Response:** Thank-you for this suggestion. We agree that the inclusion of such data would be helpful.

**Change:** We have now included a new table (new Table 3) to provide these data and have made reference to this table ion the first paragraph of the Results section.

**DISCUSSION:**

**Comment:** paragraph 1: Results indicated one statistically significant correlation between mid-range stiffness and instability. However, the r-value of this correlation is relatively low, at 0.27, and only explains 7% of the variance in joint instability. The authors should examine the meaning of this relatively low correlation and provide a context of their results for readers.

**Response:** We agree that with an $r^2$ of 0.07, the variance in self-reported knee instability explained by mid-range stiffness is modest. In the original submission we have attempted to reconcile the explained variance with the various mechanical factors that are likely to contribute towards self-reported instability e.g. active and passive contributions to joint stability (page 11, line 24 – page 12, line 8 of the current manuscript), the
interaction between active and passive systems (page 12, lines 9-12 of the current manuscript), and the possible role of sagittal and transverse plane stiffness (page 13, lines 15 – 20 of the current manuscript).

Change: We have included an additional sentence in the paragraph discussing the probable role of the active neuromuscular system upon symptomatic instability to spell out the fact that it’s role may explain a greater proportion of the variance in symptomatic instability, than passive stiffness does (page 12, lines 12-17). Similarly, we have modified a sentence in the section outlining the role that sagittal and transverse plane loading may have to explain that these factors may explain some additional variance in symptomatic instability (page 13, line 17).

Comment: Figure 1: The color scheme makes interpretation difficult, especially for identifying the mid-range stiffness region for the patient with no symptoms of instability. Please revise.
Response: We agree.
Change: The colour scheme has been updated to more clearly delineate between the two curves included in the figure.

Discretionary Comments:

METHODS:

Comment: Under Knee joint laxity and stiffness (1st paragraph): Subjects were asked to not contract the muscles crossing the knee during testing. How was this assessed to ensure no muscle contraction? EMG?
Response: In the current study several approaches were used to minimise the possibility of muscle contraction during the test. First, prior to the commencement of data collection the knee was passively rotated by the tester at very low velocity (~1deg./sec.) to ensure the participant was familiar with the test, did not experience pain, and had the opportunity to practice and ensure muscle relaxation for the test. During testing the tester visually observed the torque-angle curves for any inflections that might indicate inadvertent muscle contraction.
Change: In the modified and extended description of the laxity and stiffness test we have now included reference to our previous work where our approach to minimising the risk of muscle activation is described (page 7, lines 9-20).

RESULTS:

Comment: Paragraph 2: Can the authors provide a figure demonstrating the relationship between stiffness and instability to complement the tabular results of correlation coefficients? I personally prefer figures to tables when results are presented and I’m sure many other readers do as well.
Response: In this study regression analysis was used to interrogate the relationship between indices of knee joint laxity/stiffness and symptomatic instability. As described in the Statistical analysis section
of the Methods, the bivariate correlations reported in Table 4 (Table 3 in the original submission), were used purely as a check to ensure that the assumptions of regression analysis were met. Further, this would require the inclusion of six scatter plots (provided all laxity/stiffness indices were plotted), and would duplicate the data presented in Table 4. We felt that for the above reasons inclusion of these scatter plots would have the potential to detract from the main finding and analysis in this study: that in regression analysis, when co-varying for the appropriate confounders, a moderate amount of variance in symptomatic instability was explained by mid-range stiffness, but no other laxity/stiffness index.

Change: For the reasons outlined above, no change was made in the revised version of the manuscript in response to this comment. If the reviewer strongly feels that the inclusion of these additional figures are necessary, we would be willing to consider a further revision (for example, by removing the tabular data in order to avoid duplicating the presentation of data).

Comment: paragraph 2:Here the authors refer criteria of “...significantly and consistently correlated...” Previously (Methods: statistical analysis) the authors use the phrasing “significant and similar correlations.” Consistent phrasing will make the manuscript read better.

Response: Thank-you for picking this up. We agree that consistent wording throughout would be helpful.

Change: The sentence in the Results section (page 10, line 2) has been modified to reflect the wording used in the Methods section of the manuscript.

DISCUSSION:

Comment: Paragraph 6: The overall theme of this paragraph is unclear. The beginning of the paragraph seems as if the authors intend to discuss the potential functional implications of lower passive stiffness joints in knee OA. However, the end of the paragraph implies that potential variations in neuromuscular control across subjects affected the results of the current study. Stylistically, the manuscript may flow better if the authors revise this paragraph to focus on factors which may have influenced their results.

Response: Consistent with the reviewer’s suggestion, our intention with this paragraph was to focus on factors which may have influenced our results, specifically the interaction between active and passive stiffness (each sentence within the paragraph refers by name to the passive and/or active systems).

Change: We have modified the final sentence of the paragraph in order to clarify the focus of the paragraph (page 13, line 7).

Comment: paragraph 6: The article by Lewek et al (2005) also provides data on muscular control strategies in knee OA patients with high instability vs. low instability and should be cited in this paragraph.
Response: We are aware of the Lewek et al (2005) study (cited in our original submission in the Introduction). Unlike the Schmitt et al. (2008) study however, Lewek and colleagues examined muscle activation in response to a perturbation from a standing posture; Schmitt and colleagues examined muscle activation in response to a perturbation during walking. It is for this reason that we omitted the Lewek et al (2005) study from the original submission.

Change: We now include reference to the Lewek et al (2005) study and its findings, and highlight the different tasks in which co-contraction was measured in the Lewek et al and Schmitt et al studies (page 13, lines 3-5).
Reviewer's report

Reviewer: Jesper Knoop

This study on the association between patient-reported knee instability, laxity and stiffness is highly relevant and important. I only have the following minor comments for further improvement.

Minor Essential Revisions

ABSTRACT:

Comment: you could add 'inverse' to the significant relationship at line 12. Otherwise, it could be confusing.
Response: Changed as suggested.
Change: The sentence beginning page 2, line 12 now reads: “Forward linear regression modelling identified a significant inverse relationship between passive mid-range knee stiffness and symptoms of knee instability (r=0.27; P<0.05): reduced stiffness was indicative of more severe instability symptoms.”

INTRODUCTION:

Comment: p3, line 20 and further on: please explain what you exactly mean by symptomatic knee instability
Response: We thank the reviewer for picking this up. In the original submission we describe some of the symptoms of knee joint instability in the first sentence of paragraph 2 on page 3, but realise that a definition was lacking.
Change: Given the importance of clearly defining knee joint instability, we have incorporated this into the first paragraph of the Introduction (page 3, lines 3-4).

Comment: p3, line 23: please remove medial as not all studies did only apply to medial OA.
Response: Apologies for this mistake.
Change: The sentence has been changed to remove the word “medial”: “Measurements related to frontal plane knee laxity (knee varus-valgus range-of-motion or medial joint opening on valgus stress x-ray) indicate that such laxity does not differ between self-reported stable and unstable OA knees [2, 3, 13].”

Comment: p.4 line 1-13: this part raised the following question: why did you aim to study the laxity-instability association, as several studies already did that. Is this because you think those earlier studies did something wrong? or because you want to replicate this negative finding? If so, please mention this hypothesis. If not, than the part were you explain that laxity may not be a good test (as it does not necessarily indicate stiffness) should be rephrased. Otherwise, why do you still hypothesize
a relationship between laxity and instability if your theory is that laxity is not a good measure?

Response: Thank-you for highlighting this. We now realise that in the original submission we did not suitably justify the inclusion of our angular laxity measures. We have included separate measures for varus angular laxity and for valgus angular laxity because they have not previously been reported in relation to symptoms of knee instability. We were able to separate angular laxity into its varus and valgus components by establishing a “mechanical neutral” at the point of zero varus-valgus torque. Earlier work that has examined the relationship between symptoms of knee instability and laxity however, have measured either the angular range-of-motion (e.g. Knoop et al., 2012) or change in joint space width (Schmitt et al., 2008) between extreme varus and extreme valgus; these measures are akin to our total angular laxity measure, but not varus or valgus angular laxity measures.

Change: We have included additional sentences in the relevant paragraph (p4, lines 8-12), to highlight that previous work examining the relationship between symptomatic instability and angular laxity has been limited to measures of total varus-valgus joint laxity and that separate examination of varus laxity and valgus laxity is merited.

Comment: p4, line 4: dependent instead of dependant

Response: Apologies for this mistake.

Change: Changed to “dependent”.

METHODS:

Comment: p.5 line 1: why only medial TF OA?

Response: On page 3, in paragraph 2, (lines 13-20) we explain that the medial TFJOA knee is reportedly exposed to high frontal plane moments during locomotion; this is not known to be the case in those with lateral compartment TFJOA or PFJOA. Given that these higher local mechanical loads on the medial OA joint may influence the mechanical stability of the joint, we considered it prudent to first examine the relationship between laxity/stiffness and symptomatic instability in this somewhat more homogenous group. This is not to say that individuals with lateral compartment TFJOA, or PFJOA, do not experience symptomatic instability, but that the relationship between laxity/stiffness and instability may differ as a result of known differences in the local mechanical environment of a knee affected by lateral TFJOA or PFJOA. This argument is put forward within the second paragraph of the Introduction (page 3, line 7 – page 4, line 2).

Change: We have included an additional sentence in the Introduction to highlight the importance and particular relevance of frontal plane mechanics – such as varus-valgus laxity/stiffness – to those with medial TFJOA (page 3, lines 12–14).

Comment: p.5 line 9: why is a lower limb strengthening program an exclusion criterion
Response: As outlined at the beginning of the Methods these data were obtained as part of the baseline testing session for a randomised controlled trial. Thus the exclusion criteria for this study reflect the exclusion criteria for that trial, one of which was participation in a lower limb strengthening program.

Change: The exclusion criteria sentence has been modified to clarify that these exclusion criteria relate to those required for the purposes of the RCT (page 5, lines 19-20).

Comment: p.6, line 8: please add all categories as not everyone is familiar with this questionnaire.

Response: Each category on the 6-point scale referred to is written in full in Table 1 of the paper. A reference is made to Table 1 in this sentence: “…using a 6-point likert scale (see Table 1)...”. We have not written the categories in full in the text as we felt this would be duplicating information. If it was strongly felt that including the written categories in the text of the manuscript (in addition to the table) would be helpful, we would be happy to consider this.

Change: No change.

Comment: p.7 line 21: how did you check for the assumptions. According to Table 1, the data does not seem normally distributed (because of the large group with score 5)

Response: To clarify, the primary purpose of the paper is to establish the predictive relationship between laxity/stiffness indices and symptomatic knee instability through regression modelling. In regression modelling it is the residuals, not the outcome variable that must be normally distributed (Peat, J., & Barton, B. 2008. Medical Statistics: A Guide to Data Analysis and Critical Appraisal. Chichester, GBR: Wiley. Page 165). This was checked statistically with a Kolmogorov-Smirnov test with Lilliefors significance correction and confirmed as normally distributed. We apologise for not stating this clearly in the original submission.

Change: We have reworded the Statistical analysis section of the Methods to clarify that the tests for normal distribution relate to the residuals within the regression analysis (page 8, line 24-25). The result of this test is now described in the Results section (page 10, lines 4-5).

RESULTS:

Comment: p.8, line 13: please add the total number of persons with knee instability (also those not affecting daily functioning).

Response: Included as requested.

Change: An additional sentence has been added to describe this: “Eleven percent of participants reported symptoms of instability, but that these symptoms did not affect their daily activity.”

Comment: p.8 line 22: you state that the only laxity index that was related was a stiffness-measure. This seems incorrect.
Response: As illustrated in Table 3, only mid-range stiffness was correlated with instability symptoms in both Pearson and Spearman correlations i.e. consistently correlated. We also highlight in this paragraph the correlation that was present for valgus angular laxity, but highlight that this was only significant in Spearman correlations, and not Pearson.

Comment: p.8, line 23: did it also mean that persons without instability had more stiffness than those with instability but without problems in daily life?

Response: Yes, this is correct. Based on the recommendation of Reviewer 2, we have now included an additional table (Table 3), and this is illustrated in the data displayed in this table.

DISCUSSION:

Comment: p.9, line 18: the van der Esch study seems to be more relevant is this study included multiple measures for activity limitations with the largest study sample.

Response: Thank-you for pointing out this omission.

Change: This sentence has now been reworded to incorporate the reference highlighted by the Reviewer, and also to clarify that two of these papers refer specifically to the medial OA knee: “Our findings are consistent with those of earlier studies that demonstrate self-reported knee instability is common and influences daily activities in a large proportion of individuals with knee OA [1, 29], and medial tibiofemoral OA specifically [2, 5].” (page 10, lines 17-18).

Comment: p.10, first paragraph: your study is in line with the others as no laxity-instability relationship was found. Why do you think this is? Please add 1-2 sentences to this paragraph.

Response: We have extended the relevant paragraph to discuss the possible reasons for the absence of a relationship between measures of angular laxity and instability.

Change: We have included additional discussion at the end of this paragraph to expand upon why it may be that no relationship was found between angular laxity and instability (page 11, lines 8-13).

Comment: p.11, line 3-5: this suggests that laxity is just the inverse of stiffness. Therefore, it would be relevant to add the stiffness-laxity relationship in your study. Furthermore, this paragraph may be improved by better explaining the difference between stiffness and laxity as line 3-5 confused me.

Response: Angular laxity and angular stiffness are different constructs, but they may be related. Angular laxity can be defined as the range-of-motion under a given fixed torque (e.g. 12N.m), whereas, angular stiffness is described by the moment-angle relationship and in this study is reported within different angular ranges (e.g. mid-range stiffness, a 2° window, 1° either side of mechanical neutral). We have been cognisant of the need to provide a clear definition of the constructs involved in the
Introduction section of the manuscript so that the reader has a clear appreciation of the measures involved in this study as early as possible.

**Change:** We have included an additional sentence on page 4, lines 17-18, to reinforce the difference between angular range of motion and angular stiffness: “Thus, stiffness within a given range of the moment-angle curve is not synonymous with range-of-motion across the entire moment-angle curve”.

**Comment:** p.11, second paragraph: here you mention muscle strength. In my opinion, the lack of a muscle strength measure (as a confounder) should be mentioned as a limitation of the study.

**Response:** We agree entirely with the reviewer that local muscle properties – not just strength – may play a confounding role in the relationship between stiffness and instability.

**Change:** We have now included the absence of measures of local muscle characteristics, including strength, as a limitation of the current study (page 13, line 20-25).