PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Cognitive screening improves the predictive value of stroke severity scores for functional outcome 3–6 months after mild stroke and transient ischemic attack: an observational study
AUTHORS	Dong, Yanhong; Slavin, Melissa; Chan, Bernard; Venketasubramanian, Narayanaswamy; Sharma, Vijay; Crawford, John; Collinson, Simon; Sachdev, Perminder; chen, christopher

VERSION 1 – REVIEW

REVIEWER	Hilde Bergersen, psychologist, specialist in clinical neuropsychology, Dept. of brain injury, stroke section, Sunnaas rehab. hospital, Norway. I have no competing interest.
REVIEW RETURNED	03-Jun-2013

THE STUDY	The abstract and the introduction describes the aim of the study to "investigate the prognostic value of the neurocognitive status (...) obtained at (...) ≤ 2 weeks (...) for functional outcome 3–6 months later. The outcome measure is mRS. When the discussion (page 10) informs that: "this study was designed to investigate cognitive outcomes after stroke" it seems problematic. This sentence needs to be removed or reformulated. If the study intended to investigate cognitive outcomes the design would be different and the cognitive assessment more thorough. Table 1 I miss information about how the univariate analyses were done. Which tests? Was dummy variables used? What were done in the cases with n=1 ("others" and "OC")? It seems strange with p<0.001 when the characteristic is normal (premorbid mRS=0). The table is confusing. It would be easier to read if the heading contained more details. It should make explicit that the dichotomized mRS 0-2 and mRS > 2 in the table is mRS at follow up. It should make explicit how the univariate analysis have been found and if the outcome measure used in the univariate analysis is the continous or the dichotomized mRS at follow-up. I suggest "days" be specified in the table ("Mean interval (days) between.."). I miss an explanation of why median and not mean NIHSS and mRS (premorbid and baseline) were chosen. I miss an explanation of why binary outcome of mRS were chosen in some of the univiariate analyses. Table 2 and 3 The analysises and tables seem unnecessary complicated. I would

	suggest all three assessments (NIHSS, MMSE and MoCA) be included in block 2. The statistical methods may be appropriate, but I do not have the statistical expertise to judge. I assume or recommend the editors have their own statistician as reviewer. From page 6 I see some details in order of punctuation that do not seem correct. "3–6 months later,[4] but" Change to: "3-6 months later (4), but" "cognitive function.[5]" Change to: "cognitive function (5)." And so on. Another detail (same page): "predictive o r have". Should it be: "predictive or have"?
RESULTS & CONCLUSIONS	I think the univariate analyses are not presented in sufficient detail (comments above). To me it is surprising that it is concluded that MMSE and MoCA have incremental explanatory value. Even if their incremental values are statistically significant, I think a more reasonable conclusion here would be that almost 4,5 % of the functional outcome after 3-6 months can be predicted early after admission by NIHSS, with its many functional and only few cognitive items. Premorbid and baseline factors alone however, explain almost half of the variance. These findings are interesting. Only in the poorest functioning patients will an assessment with MMSE or MoCA be of probable use in predicting functional outcome, but even in these patients the incremental values are small. Maybe both the cognitive and the functional measurement instruments need to be more fine grained. "Unexpectedly, in patients with more severe stroke defined by baseline NIHSS score >2, both baseline MMSE and MoCA improve the predictive value of stroke severity scores for functional outcome 3–6 months later." Is this really unexpected? It is well known that MMSE is not sensitive to mild cognitive disturbances. That may be the case also for MoCA. Hence it can be expected that these instruments are more useful in the more severely injured patients. NIHSS contains only few items measuring cognition. As it is well known that cognitive factors like anosognosia and neglect predicts poor functional outcome, it is not surprising that measuring cognition improves the explanatory value of the model. It could be somewhat disappointing that the incremental values were so small. On the other hand this finding could support the continued use of NIHSS. I do not get the logic in this sentence: "so better prognostic tools are required". In what way would prognostic tools be of help?
GENERAL COMMENTS	The article is nice and short and relatively easy to read. Even if many researchers have looked at the associations between different explanatory variables and functional outcomes in different time windows after stroke, the objective is still interesting and relevant. This article presents a new way of doing it, and the results are interesting. The study explores and compares the predictive value of some brief and well known instruments that can easily be administered. The results have clinical relevance.

REVIEWER	Dr John Reid

	Consultant Neurologist Aberdeen Royal Infirmary Aberdeen UK AB252ZN
REVIEW RETURNED	11-Jun-2013

THE STUDY	The authors have taken a population of stroke patients which is very non-representative. The NIHSS score has a maximum of 42. A median NIHSS of 2 suggests a very mild group of stroke patients, indeed they included TIA patients. The reason cognitive scales have additional predictive power to the NIHSS is likely because the strokes were too mild. Also I am unclear if pre-stroke cognitive or disability status would be equally valuable in predicting post-stroke outcomes. It also seems counter intuitive to look at a functional disability score (modified rankin) as an outcome when using cognitive scores to predict outcome, since much of the modified rankin score is about independence for mobility and self-care. In terms of methods I am not sure if the authors included the strong predictors of age and pre-stroke functional status in their predictive models, and if so is it possible the cognitive scores offer no further predictive benefit. Most predictive scores of functional status at 3-6 months (i.e. modified Rankin score) include age and a measure of comorbidity (either functional status or medical conditions). The authors make no mention of other predictive scores i.e. PLAN score, I score, Six simple variable and five simple variable scores to name a few. The NIHSS score itself has limitations being a very large scale with some redundancy and also requiring special training. I also suspect that many stroke patients with more severe stroke and dysphasia would struggle to complete either the MMSE or MOCA and as such these data are surely only applicable to a small subset of mild stroke patients. Also in terms or practicality and generalizability it is recognised in the Get with the Guidelines data collection from the USA that in routine practice relatively complex stroke scales such as NIHSS are often not completed in as much as 50% of cases.
RESULTS & CONCLUSIONS	As detailed above I am unclear that NIHSS alone is a good enough comparator in this patient group with very minor stroke and TIA. As detailed above, little discussion of other predictive models or scores is made

VERSION 1 – AUTHOR RESPONSE

Dear Dr Trish Groves, Mr. Richard Sands and reviewers

Thank you for your comments and suggestions. We are grateful for the opportunity to revise and resubmit our manuscript. Please find attached an amended paper together with our point-by-point responses.

Reviewer(s)' Comments to Author:

Reviewer 1: Hilde Bergersen, psychologist, specialist in clinical neuropsychology, Dept. of brain injury, stroke section, Sunnaas rehab. hospital, Norway.

I have no competing interest.

1.1 The abstract and the introduction describes the aim of the study to "investigate the prognostic value of the neurocognitive status (...) obtained at (...) ≤ 2 weeks (...) for functional outcome 3–6 months later. The outcome measure is mRS. When the discussion (page 10) informs that: "this study was designed to investigate cognitive outcomes after stroke" it seems problematic. This sentence needs to be removed or reformulated. If the study intended to investigate cognitive outcomes the design would be different and the cognitive assessment more thorough.
We thank the review for this comment. We have revised the discussion (page 10) as the following:
“We did not examine rehabilitation services systematically as this information was not collected.”
We assure the reviewer that a more thorough cognitive assessment was conducted but at 3-6 months and not in the acute post-stroke phase.

1.2 Table 1
1.2.1 I missed information about how the univariate analyses were done. Which tests? Was dummy variables used? What were done in the cases with n=1 ("others" and "OC")? It seems strange with p<0.001 when the characteristic is normal (premorbid mRS=0).
We apologise for the omission of the description of the univariate analysis conducted for Table 1. We have included the description of the univariate analysis and amended the Statistical analyses section as the following:
“Between-group differences were examined using independent-sample t test for quantitative variables and Pearson’s $\chi 2$ test for categorical variables.”
We have collapsed two groups with small sample size as one group, such as Indians and others for ethnicity, as well as UND and OC for stroke classification. Table 1 has been amended accordingly.
We agree with your comment and have replaced the median scores of premorbid mRS to mean scores with SD.
1.3 The table is confusing. It would be easier to read if the heading contained more details. It should make explicit that the dichotomized mRS 0-2 and mRS> 2 in the table is mRS at follow up. It should make explicit how the univariate analysis has been found and if the outcome measure used in the univariate analysis is the continuous or the dichotomized mRS at follow-up. I suggest "days" be specified in the table ("Mean interval (days) between..").
We apologize for the confusion. We have amended the Table title as the following:
“Table 1. Population characteristics according to the functional outcome defined by mRS scores at 3-6 months after stroke”
We also amended the results to include the findings of the univariate analysis and that the outcome measure used in the univariate analysis is the dichotomized mRS scores at 3-6 month follow-up. The following is the amended manuscripts.
“We defined favorable functional outcome as mRS score ≤1 and poor functional outcome as mRS score ≥2. This dichotomized mRS scores for favorable and poor functional outcome is commonly used and is in keeping with the recommendation from previous analyses [Weisscher, N, Vermeulen M, Ross YB, et al. What should be defined as good outcome in stroke trials; a modified Rankin score of 0-1 or 0-2? J Neurol2008;255:867-874.]. The majority of the patients (n=252, 64.9%) had good functional outcomes (mRSscore ≤1) while approximately one third of the patients (n=136, 35.1%) had poor functional outcomes (mRS score ≥2). Patients with poor functional outcome were significantly older, women, of Malay ethnicity, less educated, more neurologically impaired with poorer premorbid and baseline functioning, and assessed later following cerebrovascular event. They also had more stroke classification of large artery occlusion and cardioembolic stroke, as well as higher number of cardiovascular risk factors. In addition, patients with poorer functional outcome had significantly lower scores of the MMSE and the MoCA. The population characteristics of patients with favorable and poor functional outcomes can be found in Table 1.”
We thank the reviewer for the suggestion of including “days” for “Mean interval between stroke/TIA and assessment” in the table. We have amended this in the table as “Mean interval (days) between

stroke/TIA and assessment".
1.4 I miss an explanation of why median and not mean NIHSS and mRS (premorbid and baseline) were chosen. I miss an explanation of why binary outcome of mRS were chosen in some of the univiariate analyses.

We thank the reviewer for pointing this out. We have amended the Table using mean and SD for NIHSS and mRS (premorbid and baseline) for the purpose of consistency.
Our research aims are primarily addressed by hierarchical regression analyses of the continuous mRS scores. We therefore removed the logistic regression analysis of the dichotomised mRS scores in Table 1 to prevent confusion.

1.5 Table 2 and 3
The analyses and tables seem unnecessary complicated. I would suggest all three assessments (NIHSS, MMSE and MoCA) be included in block 2. The statistical methods may be appropriate, but I do not have the statistical expertise to judge. I assume or recommend the editors have their own statistician as reviewer.
The inclusion of all three assessments (NIHSS, MMSE and MoCA) will not allow us to address our study aim, i.e., examine the predictive ability of MMSE and MoCA individually and in combination with the NIHSS at the subacute stroke phase for functional outcome 3–6 months later.Therefore, hierarchical regression analyses were conducted in 3 blocks to examine the incremental contribution of baseline MMSE and MoCA compared with the baseline NIHSS in predicting functional outcomes defined by mRS scores at 3–6 months after stroke.

1.6 From page 6 I see some details in order of punctuation that do not seem correct.
"3–6 months later,[4] but"
Change to: "3-6 months later (4), but"
"cognitive function.[5]"
Change to: "cognitive function (5)."
And so on.
Another detail (same page): "predictive o r have". Should it be: "predictive or have"?

We thank the reviewers for pointing out these typological errors. We have amended the manuscripts as suggested.
1.7 To me it is surprising that it is concluded that MMSE and MoCA have incremental explanatory value. Even if their incremental values are statistically significant, I think a more reasonable conclusion here would be that almost 4,5 % of the functional outcome after 3-6 months can be predicted early after admission by NIHSS, with its many functional and only few cognitive items. Premorbid and baseline factors alone however, explain almost half of the variance. These findings are interesting.
We thank the reviewer for this suggestion and the acknowledgement of the interesting findings of our study. We have amended the manuscripts as the following:
"In conclusion, 4.3% of the functional outcome after 3-6 months can be predicted early after admission by NIHSS, with its many functional and only few cognitive items. Premorbid and baseline factors alone however, explain almost half of the variance. In addition, neurocognitive status at the subacute stroke phase is independently predictive of functioning at early convalescent stroke phase.Baseline MMSE scores can add incremental prediction to baseline stroke severity score for functional outcome 3-6 months later. …"

1.8 Only in the poorest functioning patients will an assessment with MMSE or MoCA be of probable use in predicting functional outcome, but even in these patients the incremental values are small. Maybe both the cognitive and the functional measurement instruments need to be morefine grained.

"Unexpectedly, in patients with more severe stroke defined by baseline NIHSS score >2, both baseline MMSE and MoCA improve the predictive value of stroke severity scores for functional outcome 3–6 months later." Is this really unexpected? It is well known that MMSE is not sensitive to mild cognitive disturbances. That may be the case also for MoCA. Hence it can be expected that these instruments are more useful in the more severely injured patients. NIHSS contains only few items measuring cognition. As it is well known that cognitive factors like anosognosia and neglect predicts poor functional outcome, it is not surprising that measuring cognition improves the explanatory value of the model. It could be somewhat disappointing that the incremental values were so small. On the other hand this finding could support the continued use of NIHSS.
We thank the reviewer for the above comments. We have amended our manuscripts as the following:
“Additionally,in patients with more severe stroke defined by baseline NIHSS score ≥2, both baseline MMSE and MoCA improve the predictive value of stroke severity scores significantly for functional outcome 3–6 months later. However, the incremental predictive value of the MMSE and MoCA is relatively smaller than the NIHSS.”

1.9 I do not get the logic in this sentence: "so better prognostic tools are required". In what way would prognostic tools be of help?
There were approximately one third of these mild stroke and TIA patients had poor functional outcome (mRS≥2). The current instruments (NIHSS in combination with MMSE or MoCA) could only predict for 51% of the functional outcome. Therefore, it would be helpful if a better prognostic tool can improve the prediction for functional outcome to 70%-80%. We amended the conclusion as the following:
“However, the current instruments (NIHSS in combination with MMSE or MoCA) could only predict for 51% of the functional outcome. Therefore, it would be helpful if a better prognostic tool can improve the prediction for functional outcome to 70%-80%.
Future studies may establish a modified scale combining the NIHSS and items from the MMSE and MoCA to improve the predictive ability for functional outcome.”

1.10 The article is nice and short and relatively easy to read. Even if many researchers have looked at the associations between different explanatory variables and functional outcomes in different time windows after stroke, the objective is still interesting and relevant. This article presents a new way of doing it, and the results are interesting. The study explores and compares the predictive value of some brief and well known instruments that can easily be administered. The results have clinical relevance.
We thank the reviewer for the above compliments.

Reviewer 2: Dr John Reid
Consultant Neurologist
Aberdeen Royal Infirmary
Aberdeen
UK
AB252ZN

2.1 The authors have taken a population of stroke patients which is very non-representative. The NIHSS score has a maximum of 42. A median NIHSS of 2 suggests a very mild group of stroke patients, indeed they included TIA patients. The reason cognitive scales have additional predictive power to the NIHSS is likely because the strokes were too mild. Also I am unclear if pre-stroke cognitive or disability status would be equally valuable in predicting post-stroke outcomes. It also seems counter intuitive to look at a functional disability score (modified rankin) as an outcome when using cognitive scores to predict outcome, since much of the modified rankin score is about independence for mobility and self-care.
The pre-stroke cognitive status (IQCODE) and pre-stroke disability scores (premorbid mRS) have

been included as the variables to be controlled for in the first block of hierarchical regression analysis. Pre-stroke disability is a significant predictor for functional outcome while IQCODE is not. We chose the functional disability measure, the mRS at 3-6 month, as an outcome measure in this study for the following reason: 1) it is a commonly used functional status measure in stroke clinical trials and research studies; 2) It is used in studies that employ cognitive measures. We acknowledged the limitation of mRS as a crude outcome measure in our manuscripts as the following:
“In addition, the mRS has been criticized for its lack of specificity,[5] however, it is a summary of functional outcomes and has been widely used in clinical trials as a primary efficacy measure.”
2.2 In terms of methods I am not sure if the authors included the strong predictors of age and pre-stroke functional status in their predictive models, and if so is it possible the cognitive scores offer no further predictive benefit. Most predictive scores of functional status at 3-6 months (i.e. modified Rankin score) include age and a measure of comorbidity (either functional status or medical conditions). The authors make no mention of other predictive scores i.e. PLAN score, I score, Six simple variable and five simple variable scores to name a few. The NIHSS score itself has limitations being a very large scale with some redundancy and also requiring special training.
Yes, we have included age and pre-stroke functional status in our hierarchical regression analysis. The significant control variables in the model include the following :age, sex, education, composite of cardiovascular risk factors, premorbid mRS and baseline mRS.These variables were stated in the footnotes of Table 2 and 3. Controlling for these significant predictors, cognitive measure such as MMSE still offers a small yet statistically significant incremental predictive value to the NIHSS for functional outcome at 3-6 months. Additionally,in patients with more severe stroke defined by baseline NIHSS score >2, both baseline MMSE and MoCA improve the predictive value of stroke severity scores significantly for functional outcome 3–6 months later. However, the incremental predictive value of the MMSE and MoCA is relatively smaller than the NIHSS.
We have revised our conclusion as suggested by the comments of Reviewer 1 (Point 1.7 and 1.8).
2.3 Most predictive scores of functional status at 3-6 months (i.e. modified Rankin score) include age and a measure of comorbidity (either functional status or medical conditions). The authors make no mention of other predictive scores i.e. PLAN score, iScore, Six simple variable and five simple variable scores to name a few.
We thank the reviewer for the suggestion that we should review the existing predictive scores such as PLAN score, iScore, Six simple variable and five simple variable scores suggested by previous studies. We have mentioned these predictive scores in our discussion as the following:
“Last, we did not consider other predictive scores (e.g., PLAN score (11), iScore (12), six simple variable (13) and five simple variable scores (14)) for our models primarily due to the following reasons: 1) None of these scores include a cognitive measure.; 2) PLAN scores are developed using more severe functional outcome measure, such as mRS scores of 5 to 6 at discharge. Similarly, iScore has been used to estimate poor functional outcome defined by mRS 3 to 5. ; 3) Six simple variable and five simple variable scores require Glasgow Coma Scale which we did not collect in this study. Therefore, we are unable to adopt these models to predict functional outcome in this study. However, in line with our aims, we included significant and clinically relevant predictors as control variables (age, sex, education, composite of cardiovascular risk factors, premorbid mRS and baseline mRS) in our models.”
11. O’DonnelL MJ, Fang J, D’Uva C, et al. The PLAN Score: A bedside prediction rule for death and severe disability following acute ischemic stroke. Arch Intern Med 2012;172:1548-1556.
12. Saposnik G, Raptis S, Kapral MK, et al. The iScore predicts poor functional outcomes early after hospitalization for an acute ischemic stroke. Stroke 2011;42:3421-3428.
13. Reid JM, Gubitz GJ, Dai D, et al. External validation of a six simple variable model of stroke outcome and verification in hyper-acute stoke. J Neurol Neurosurg Psychiatry 2007;78:1390-1391.
14. Ayis SA, Coker B, Rudd AG, et al. Predicting independent survival after stroke: a European study for the development and validation of a standardised stroke scales and prediction models of outcome.J Neurol Neurosurg Psychiatry 2013;84:288-296.

1.3 The NIHSS score itself has limitations being a very large scale with some redundancy and also requiring special training.I also suspect that many stroke patients with more severe stroke and dysphasia would struggle to complete either the MMSE or MOCA and as such these data are surely only applicable to a small subset of mild stroke patients. Also in terms or practicality and generalizability it is recognised in the Get with the Guidelines data collection from the USA that in routine practice relatively complex stroke scales such as NIHSS are often not completed in as much as 50% of cases.

We thank the reviewer for this comment. We have mentioned the limitation of NIHSS in the introduction section as the following:

"A widely used stroke severity scale, the National Institute of Health Stroke Scale (NIHSS), administered at the subacute stroke phase is predictive of patients' functional outcomes 3–6 months later (4), but has limited representation of cognitive function (5)."

In addition, we included the following sentences and a reference for conclusion to highlight the feasibility and applicability of the MoCA in acute stroke patients.

"We have previously shown that these screening tests administered at the subacute stroke phase could also predict cognitive outcomes 3–6 months later (6). In addition, MoCA administration has been reported to be applicable to the majority of acute stroke patients(ischemic or hemorrhagic)(82.5%),and therefore feasible to be used in acute stroke phase (Pasi M, Salvadori E, Poggesi A, et al. Factors predicting the Montreal cognitive assessment (MoCA) applicability and performances in a stroke unit. J Neurol 2013;260:1518-1526.). Therefore, the predictive value and brevity of the MMSE and MoCA warrants their routine use in the subacute stroke phase in clinical service and early acute stroke trials."

VERSION 2 – REVIEW

REVIEWER	Dr John Reid Consultant Neurologist Aberdeen Royal Infirmary
REVIEW RETURNED	29-Jul-2013

THE STUDY	The patients described are typically very mild stroke patients or even TIA patients. The authors should not refer to them simply as stroke patients but should describe their study predominnanlty as one of minor stroke and TIA patinets as the affirmation that these are typical stroke patients is misleading. It almost approximates to an out-patient TIA/minor stroke clinic population. 20% of patients were TIA.
RESULTS & CONCLUSIONS	As above it would be important to highlight how mild some of the strokes are and inlcude TIA, and as such these cognitive scales (MMSE and MOCA) migh have more predictive value (in addition to NIHSS) compared to models for a more severe stroke population. Also most other models include prior functional status (Oxford handicap score or modified Rankin score pre-stroke). It is possible pre-functioncal status (as in PLAN and FSV scores) encompasses elements of pre-stroke cognition and functioning that would provide similar predictive power to the additional cognitive scores. Also mention of how such models should be used practically should be made, and the limitation that they have not been externally validated and so may not generalisable.

VERSION 2 – AUTHOR RESPONSE

Dear Dr John Reid,

Thank you for your comments and suggestions. We are grateful for the opportunity to revise and resubmit our manuscript. Please find attached an amended paper together with our point-by-point responses.

Reviewer(s)' Comments to Author:

Reviewer: Dr John Reid
Consultant Neurologist
Aberdeen Royal Infirmary

1.1 The patients described are typically very mild stroke patients or even TIA patients. The authors should not refer to them simply as stroke patients but should describe their study predominantly as one of minor stroke and TIA patients as the affirmation that these are typical stroke patients is misleading. It almost approximates to an out-patient TIA/minor stroke clinic population. 20% of patients were TIA.

We thank the reviewer for this comment. We have included “mild stroke and transient ischemic attack” in the title and Article focus as the following:

“Cognitive screening improves the predictive value of stroke severity scores for functional outcome 3–6 months after mild stroke and transient ischemic attack: an observational study.”

• “We examined the predictive ability of MMSE and MoCA individually and in combination with the NIHSS for functional outcome 3–6 months after mild stroke and transient ischemic attack.”

1.2 As above it would be important to highlight how mild some of the strokes are and include TIA, and as such these cognitive scales (MMSE and MoCA) might have more predictive value (in addition to NIHSS) compared to models for a more severe stroke population.

We stated that the study population including patients with a recent ischemic stroke or transient ischemic attack in the Method section:

“Briefly, we recruited 400 consecutive patients (≥21 years old) with a recent ischemic stroke or transient ischemic attack (TIA) (≤14 days) during their inpatient admission (subacute stroke phase or baseline) at the National University Health System in Singapore.”

In addition, we described the scores of NIHSS and mRS to indicate stroke severity in Subject characteristics. Moreover, we include a sentence to highlight the proportion of TIA patients in the study sample as the following:

“Most patients (79.8%) had a mild ischemic stroke and less disability (median NIHSS =2, median mRS =2, median premorbid mRS =0), while a minority of patients had TIA (20.3%).”

The above paragraph was also inserted in the abstract.

1.3 Also most other models include prior functional status (Oxford handicap score or modified Rankin score pre-stroke). It is possible pre-functional status (as in PLAN and FSV scores) encompasses elements of pre-stroke cognition and functioning that would provide similar predictive power to the additional cognitive scores.

We agree that pre-stroke cognition and functioning could predict functional outcome. This was shown in the control variables in our models (Table 2 and Table 3), that included age, sex, education, composite of cardiovascular risk factors, premorbid mRS and baseline mRS.

We included pre-stroke functional status such as premorbid mRS scores in the prediction model as stated in study limitations as the following:
“However, in line with our aims, we included significant and clinically relevant predictors as control variables (age, sex, education, composite of cardiovascular risk factors, premorbid mRS and baseline mRS) in our models.”

1.4 Also mention of how such models should be used practically should be made, and the limitation that they have not been externally validated and so may not generalisable.

We thank the reviewer for this suggestion. We have inserted the following paragraph in the study limitation.

“Our prediction model can be applied to patients with mild ischemic stroke and TIA, especially in those with NIHSS score >2. The routine cognitive screening at subacute stroke phase with either MoCA or MMSE could add incremental predictive value to the NIHSS of patients with NIHSS score >2 for functional outcomes at 3-6 months. However, this model has yet to be validated externally, therefore it may not be generalizable to other stroke population.”