PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Temporal trends and geographical disparities in comprehensive stroke centre capabilities in Japan from 2010 to 2018
AUTHORS	KUROGI, AI; Nishimura, Ataru; Nishimura, Kunihiro; Kada, Akiko; Onozuka, Daisuke; Hagihara, Akihito; Ogasawara, Kuniaki; Shiokawa, Yoshiaki; Kitazono, Takanari; Arimura, Koichi; Iihara, Koji

VERSION 1 – REVIEW

REVIEWER	Julia Ferrari St. John´s of God Hospital Department of Neurology Austria
REVIEW RETURNED	30-Aug-2019

GENERAL COMMENTS	In this hospital based cross sectional study the authors analysed changes in CSC capabilities in Japan between 2010 and 2018 and wether any changes were influenced by hospital characteristics. They concluded that there was a significant improvement in CSC capabilities over the years due to the increasing availability of endovascular treatment and multidisclipinary care. The paper is well written, however there are some major concerns on this work. Just wondering, why no neurologist is in the authors list..stroke units are usually located in neurological departments.. Is mechanical thrombectomy in Japan performed only by neurosurgeons? What about interventional radiologists? p 6: You describe „mean and median“. For these data, arithmethic mean values seem not suitable and too little robust Student´s T Test requires normally distributed data. Non parametric test like Wilcoxon or Kruskal Wallis are more suitable Did you perform correction for multiple testing? You did not explain it in the methods section. Results in table 3, p 8 are weakly significant..could you explain the effects? p 7 . p for trend < 0.001 . You did not describe in the methods section the model that you use to model this trend… could you explain the relationsship between „hospital size“ and „number of physicians“? It is not quite clear why less than 7 physicians and more than 9 did not show a difference?

REVIEWER	Ruth Hall, Staff Scientist ICES, Canada
REVIEW RETURNED	15-Oct-2019

GENERAL COMMENTS	This paper looks at comprehensive stroke centers (CSCs) in Japan using a survey used to designate comprehensive stroke centers, to examine whether CSC capabilities changed between 2010 to 2018 and whether any recorded changes in hospital capability score (CSC score) were influenced by hospital characteristics. The focus is on the 323 hospitals that completed all three surveys. Hospital acute stroke care capability was assessed with a validated scoring system (CSC score), based on 25 items capturing 5 domains recommended by the Brain Attack Coalition. Hospital characteristics examined included: bed size, annual stroke hospitalizations, stroke physicians, academic status, adoption of the Diagnosis Procedure Combination (DPC)-based payment system and geographic location. CSC scores increased over the 3 periods and improvements occurred in 14/25 items. CSC hospital capabilities improved over time in Japan and hospital characteristics associated with improvement include annual hospital volume, hospital size and more stroke physician. This manuscript could be improved by: 1. The 4th sentence seems orphaned. 2. Provide a brief summary of the J_ASPECT study and stroke registry 3. Provide some context about Japan, mostly urban population. Is health care publicly funded? 4. The study design needs to be articulated 5. All tables require a title. 6. If the paper is focused on the 323 hospitals that participated in all three, table 1 should compare the 323 hospitals to the hospitals that did not participate in all 3 not the entire sample. 7. Consider the need for Table 2 as does not relate to your aim. Your aim did not indicate exploring impact of geography on

	specific CSC items. 8. You refer to **intermediate** number of stroke physicians in results. Either include descriptor in Table 3 and 4 OR state the actual value in the results 9. Conclusion needs to be revised to be clearer, particularly the last sentence. 10. Consider examining stroke physician to bed ratio. 11. Discussion needs further work to improve readability and ensure focuses on study aims and results.

REVIEWER	ken cheung columbia university
REVIEW RETURNED	15-Dec-2019

GENERAL COMMENTS	This study provides potentially useful information to understand association between the capability of Comprehensive Stroke Centers in Japan and the hospital characteristics. The methodology is appropriate, although the article will benefit from clarification of some background information and interpretation of the study endpoints. specifically, it may be useful to describe how a hospital would be designated a CSC. Would some of the capabilities on the scale be met by being a CSC? In addition, the primary endpoint is defined as temporal improvement on a CSC score from 2010 to 2018 by at least 1 point. Some discussion on the practical significance of a 1-point improvement would be useful. How is the data collected in 2014 factored into the analysis? This endpoint also does not differentiate CSC that stay the same from those with decline in score. The main analysis focus on hospitals responding to all three surveys. as the authors appropriately noted as limitations, it could cause an upward bias in the scores, and hence limited room for improvements over time. To understand the nature of bias, it might be useful to look at the association between hospitals that dropped out and their characteristics. Additional detailed comments: 1. Middle of Page 7. "p for trend". What statistical test was used for testing trend? 2. Table 4. Interpretation of the p values is sensitive to the choice of the reference group. For hospital location, while there is statistical difference with MEA central. Would there be a difference between MEA outlying vs McEA. An omnibus test (e.g. LRT with 2 degrees of freedom) may be more appropriate to evaluate the overall location effect. For some other characteristics, it may make sense to view them as ordinal (e.g. stroke case volume).

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Comment 1: Please state any competing interests or state ‘None declared’: no conflicts of interests
Authors’ Response :
(p20, A competing interests statement)

We thank Reviewer 1 for this comment. We stated “None declared” in the Competing interests statement. Please refer to that.

Comment 2 : Just wondering, why no neurologist is in the authors list. stroke units are usually located in neurological departments..
Author’s Response:
(p21, Acknowledgements, lines 2-5; Supplemental Appendix 1)
We thank Reviewer 1 for this comment. Prof. Takanari Kitazono, one of the authors, is an expert in stroke medicine. Additionally, there are many neurologists in our study collaborators. We added a list of the J-ASPECT Study Collaborators in Supplemental Appendix 1.

Comment 3 : Is mechanical thrombectomy in Japan performed only by neurosurgeons? What about interventional radiologists?
Author’s Response: We thank Reviewer 1 for this valuable comment. More than 95% of the Japanese Society of Neuro-Endovascular Treatment (JSNET) specialists, who perform almost all acute EVT cases in Japan, are neurosurgeons.

Comment 4 and 5 :
p 6: You describe „mean and median“. For these data, arithmethic mean values seem not suitable and too little robust
Student´s T Test requires normally distributed data. Non parametric test like Wilcoxon or Kruskal Wallis are more suitable
Authors’ Response :
(p10, 2nd para, lines 1-4; Table 1)
We thank Reviewer 1 for this valuable comment. We agree that a non-parametric test, as suggested by the reviewer, is more suitable. Thus, we re-analysed data using Wilcoxon rank sum test and revised the explanations and results in the revised manuscript.

Change to Text: Accordingly, the sentence “Hospital characteristics were compared between the two groups with means or medians for continuous variables and proportions for categorical variables, using Chi-square tests for categorical variables and a Student’s t-test for continuous variables.” in the Statistical analysis was changed to the sentence “We used a chi-squared test to detect differences between consecutively participating hospitals and other hospitals in the number of each hospital item. We did not perform multiple tests. Wilcoxon rank sum test was used to compare total CSC scores between consecutively participating hospitals and other hospitals.”

Comment 6 :
Did you perform correction for multiple testing? You did not explain it in the methods section. Results in table 3, p 8 are weakly significant. could you explain the effects?
Authors’ Response :
(p10, 2nd para, lines 1-4; p13, 1st para, line 2)
We thank Reviewer 1 for this comment. We did not perform multiple tests in this study. Regarding this point, we added explanations in the revised manuscript.
Additionally, as the reviewer pointed out, the explanations regarding results in table 3 were not suitable. Thus, we revised the explanations as follows in the revised manuscript.

Change to Text: The term “significant” was changed to “weakly significant”.

Comment 7 :
p 7 . < 0.001 . You did not describe in the methods section the model that you use to model this trend…

Authors' Response :
(p10, Statistical analysis; p4, Results in Abstract, line2; p11, 2nd para, lines 3)
We thank Reviewer 1 for this comment. As pointed out, the explanation was not suitable. Thus, we revised the explanation in the revised manuscript.

Change to Text : Accordingly, the term "p for trend < 0.001" was changed to "p < 0.001"

Comment 8 :
could you explain the relationship between „hospital size" and „number of physicians"?
Authors' Response :
(p10, 2nd para, line 4-6; p13, 2nd para, line 9-10)
We thank Reviewer 1 for this valuable comment. As the reviewer suggested, we examined the relationship between "hospital size" and "number of physicians" using chi-squared tests, and found a significant relationship between "hospital size" and "number of physicians" (P<0.001).
Thus, we added the following sentence to the revised manuscript.

Change to Text:
The following sentences were added in the Methods.
"We also examined the relationship between "number of physicians" and "hospital size", and the relationship between "number of physicians" and "CSC score" using chi-squared tests."
We added the following sentences in the Results.
"Additionally, there was a significant relationship between hospital size and number of physicians (P<0.001),"

Comment 9 : It is not quite clear why less than 7 physicians and more than 9 did not show a difference?
Authors' Response :
(p10, 2nd para, line 4-6; p13, 2nd para, line 9-11; p17, 2nd para, line 5-10)
We thank Reviewer 1 for this valuable comment. We examined the relationship between "CSC score" and "number of physicians". Additionally, there was a significant relationship between "CSC score" and "number of physicians". (P<0.001).
This means that institutions with more physicians tend to have higher baseline CSC scores in 2010. The reason that a physician volume of more than 10 did not affect the improvement of the CSC score may be explained by the ceiling effect of a high baseline CSC score in 2010.
Thus, we added the sentences as follows in the revised manuscript.

Change to Text:
Accordingly, we added the following sentences in the Methods.
"We also examined the relationship between "number of physicians" and "hospital size" and the relationship between "number of physicians" and "CSC score" using chi-squared tests."
We added the following sentences in the Results.
"Additionally, there was a significant relationship between hospital size and number of physicians (P<0.001), and between CSC score and number of physicians (P<0.001). "
We added the following sentences in the Discussion.
"We also found a significant relationship between CSC score and number of physicians. This means that, in 2010, institutions with more physicians tended to have higher baseline CSC scores. The reason that a physician volume of more than 10 did not affect the improvement of the CSC score may be explained by the ceiling effect of a high baseline CSC score in 2010."

Reviewer: 2

Comment 1 : Please state any competing interests or state ‘None declared’: None declared
Authors’ Response :
(p20, Competing interests statement)
We thank Reviewer 2 for this comment. We stated “None declared” in the Competing interests statement. Please refer to that.

Comment 2 : Tables need titles
Authors’ Response :
We thank Reviewer 2 for this valuable comment. As the reviewer noted, we added the title of each table. We also changed Table 1 itself; please refer to Response of Comment 4 for Reviewer 3.

Change to Text: Accordingly, we added the following title for each Table:
The title of Table 1 is “Number (percentage) of the responding hospitals fulfilling the recommended items of comprehensive stroke care capabilities”.
The title of Table 2 is “Characteristics of comprehensive stroke care capabilities according to geographical differences”.
The title of Table 3 is “Hospital characteristics those with/without temporal improvement of the CSC capabilities”.
The title of Table 4 is “Multivariable analysis of the impact of hospital characteristics on one-point increases of the CSC score”.

Comment 3 : Did not see a supplementary report – STROBE
Authors’ Response :
We thank reviewer 2 for this valuable comment. As the reviewer noted, we added a supplementary report.

comments in the attachment

Comment 4 :The 4th sentence seems orphaned.
Authors’ Response :
(p6, 1st para, line6-7)
We thank Reviewer 2 for this comment. As suggested, we changed the sentence as follows:

Change to Text:
From “Previous studies showed that patient outcomes associated with stroke and cardiovascular diseases are influenced by the hospital case volume, 5, 6 number of physicians, and geographical locations of the facility7.” to “In addition to the influence of this process, previous studies have shown that patient outcomes associated with stroke and cardiovascular diseases are influenced by the hospital case volume, 5, 6 number of physicians, and geographical locations of the facility.7”

Comment 5 :Provide a brief summary of the J_ASPECT study and stroke registry
Authors’ Response :
(p7-8, 3rd para, line1-7)
We thank Reviewer 2 for this comment. As suggested, we added the following sentence:

Change to Text:

Participation in the J-ASPECT Study was voluntary. Of the 1369 training institutions certified by the Japan Neurosurgical Society, the Japanese Society of Neurology, and the Japan Stroke Society, 621 agreed to participate in this study. The J-ASPECT Study group analysed the Diagnosis Procedure Combination (DPC) database to gain new clinical insights on ischaemic and haemorrhagic stroke, an approach we applied again for this cross-sectional survey.

Comment 6 : Provide some context about Japan, mostly urban population.
Is health care publicly funded?
Authors' Response :
(p9, 1st para, line5-6)
We thank Reviewer 2 for this valuable comment. In 2015, 86.4% of the Japan's population lived in urban areas. Health care is publicly funded. Accordingly, we added the following sentence:

Change to Text:
"Details of UEAs, such as total population or total land area, have been previously described."

Comment 7 : The study design needs to be articulated
Authors' Response :
(p3, Design; p7,3rd para, line 1-2)
We thank Reviewer 2 for this valuable comment. We mentioned the study design as a hospital-based cross-sectional study in the Design section of the ABSTRACT. Please refer to that. Additionally, we added the following sentences in the Methods.

Change to Text:
"This cross-sectional survey used the DPC discharge database from participating institutions in the J-ASPECT Study."

Comment 8 : All tables require a title.
Authors' Response : We thank Reviewer 2 for this valuable comment. As Reviewer 2 noted, we added a title for each table. Please refer to the Response of Comment 2. We also changed Table 1 itself, please refer to the Response of Comment 4 for Reviewer 3.

Comment 9 : If the paper is focused on the 323 hospitals that participated in all three, table 1 should compare the 323 hospitals to the hospitals that did not participate in all 3 not the entire sample.
Authors' Response: We thank Reviewer 2 for this valuable comment. As suggested by Reviewer 2, Table 1 has been changed. Please refer to Response of Comment 4 for Reviewer 3.

Comment 10 : Consider the need for Table 2 as does not relate to your aim. Your aim did not indicate exploring impact of geography on specific CSC items.

Authors' Response: We thank Reviewer 2 for this valuable comment. As Reviewer 2 noted, Table 2 described the impact of geography on specific CSC items. However, as we described in the original manuscript and title, one of the main aims of this study was to determine rural/urban differences in CSC capabilities. We believe that our study identified some differences; hence, we prefer not to change our table.

Comment 11 : You refer to intermediate number of stroke physicians in results. Either include descriptor in Table 3 and 4 OR state the actual value in the results

Authors' Response :
(p13, 2nd para, line 6-11; table3; Supplementary table 1.)

We thank Reviewer 2 for this valuable comment. As Reviewer 2 suggested, we added the characteristic of “the number of stroke physicians tertile to Table 3. We also performed logistic regression analysis, adjusting for tertile instead of quartile, of stroke physician volume in addition to the other adjusting factors. Except for Q3 of stroke physician volume, we found very similar results.

Change to Text: The following statement in the Results was changed to
“We also performed the logistic regression analysis adjusting tertile, instead of quartile, of stroke physician volume in addition to the other adjusting factors. Except for Q3 of stroke physician volume, we found very similar results (Supplementary Table 1).

Accordingly, we made the following changes in Table 3 and Table 4:

Table 3. Hospital characteristics those with/without temporal improvement of the CSC capabilities
Hospital-related factors in 2010 all Consecutively participating Hsps. (n=300) Improvement Hsps. No improvement Hsps. p value#
(n=198) (n=102)
Hospital locations 0.478
MEA central 186 (62.0) 121 (61.1) 65 (63.7)
MEA outlying 79 (26.3) 56 (28.3) 23 (22.6)
McEA 35 (11.7) 21 (10.6) 14 (13.7)

CSC score in 2010
median (IQR) 16 (13, 19) 16 (13, 18) 17 (13, 20) 0.032

Academic hospital 58 (19.3) 42 (21.2) 16 (15.7) 0.251

DPC* hospital 225 (75.0) 145 (73.2) 80 (78.4) 0.325

Number of hospital beds 0.016
1-99 17 (5.7) 9 (4.6) 8 (7.8)
100-299 68 (22.7) 37 (18.7) 31 (30.4)
300-499 96 (32.0) 62 (31.1) 34 (33.3)
≥500 119 (39.7) 90 (45.5) 29 (28.4)

Annual stroke case volume 0.915
0-99 34 (11.3) 21 (10.6) 13 (12.8)
100-199 73 (24.3) 47 (23.7) 26 (25.5)
200-299 67 (22.3) 45 (22.7) 22 (21.6)
≥300 126 (42.0) 85 (42.9) 41 (40.2)

Number of stroke physician volume
median (IQR) 6 (3, 9) 6 (3.8, 9) 5 (3, 9.3) 0.139
Number of stroke physicians, quartile
Q1 (0-3) 82 (27.3) 49 (24.8) 33 (32.4)
Q2 (4-6) 68 (22.7) 43 (21.7) 25 (24.5)
Q3 (7-9) 80 (26.7) 61 (30.8) 19 (18.6)
Q4 (≥10) 70 (23.3) 45 (22.7) 25 (24.5)

Number of stroke physicians, tertile
T1 (0-4) 114 (38.0) 72 (36.4) 42 (41.2)

T2 (4-8) 96 (32.0) 63 (31.8) 33 (32.4)
T3 (≥9） 90 (30.0) 63 (31.8) 27 (26.5)

Table 4. Multivariable analysis of the impact of hospital characteristics on one-point increases of the CSC score
Hospital-related factors in 2010 Odds 95%CI P value
Hospital locations
MEA central ref.
MEA outlying 1.42 0.76-2.65 0.269
McEA 0.82 0.36-1.86 0.632

CSC score in 2010 0.82 0.75-0.90 <0.001

Academic hospital 1.37 0.54-3.48 0.506

DPC hospital 0.77 0.41-1.42 0.397

Number of beds
1-99 ref.
100-299 1.16 0.37-3.66 0.794
300-499 1.68 0.56-5.10 0.358
≥500 3.9 1.17-13.00 0.027

Annual stroke case volume
1-99 ref.
100-199 1.62 0.64-4.07 0.305
200-299 2.41 0.89-6.49 0.083
≥300 2.74 0.99-7.54 0.051

Number of stroke physicians, quartile
Q1 (0-3) ref.
Q2 (4-6) 1.77 0.81-3.88 0.153
Q3 (7-9) 2.63 1.10-6.27 0.030
Q4 (≥10) 1.58 0.57-4.38 0.380

We also added the following table as Supplementary Table 1.
Hospital-related factors in 2010 Odds 95%CI P value
Hospital locations
MEA central ref.
MEA outlying 1.35 0.36-2.48 0.339
McEA 0.78 0.35-1.75 0.549

CSC score in 2010 0.83 0.76-0.91 <0.001

Academic hospital 1.29 0.52-3.24 0.582

DPC hospital 0.72 0.39-1.34 0.302

Number of beds
1-99 ref.

100-299 1.1 0.36-3.41 0.868
300-499 1.82 0.60-5.48 0.285
≥500 3.81 1.16-12.54 0.028

Annual stroke case volume
1-99 ref.
100-199 1.68 0.67-4.18 0.267
200-299 2.47 0.92-6.61 0.072
≥300 3.17 1.16-8.66 0.024

Number of stroke physicians, tertile
T1 (0-4) ref.
T2 (4-8) 1.12 0.58-2.16 0.745
T3 (≥9） 1.35 0.57-3.21 0.492

Comment 12 : Conclusion needs to be revised to be clearer, particularly the last sentence.
Authors' Response :
(p4, Conclusion, line3-4; p19, 2nd para, line 2-4)
We thank Reviewer 2 for this valuable comment. As Reviewer 2 suggested, we changed the sentence as follows in the Conclusion.

Change to Text:
We changed the sentence "Hospital characteristics may be considered to further improve systems of stroke care in light of limited medical resources in a defined area." to "Our findings may be useful to determine which hospitals should be targeted to improve CSC capabilities in a defined area."

Comment 13 : Consider examining stroke physician to bed ratio.
Author's Response: We thank Reviewer 2 for this valuable comment. We have examined the relationship between "hospital size" and "number of physicians". Please refer to our Response of Comment 8 for Reviewer 1.

Comment 14 : Discussion needs further work to improve readability and ensure focuses on study aims and results.
Author's Response: We thank Reviewer 2 for this valuable comment.
A native English editor (Editage) revised our manuscript to improve readability in the discussion.

Reviewer: 3

Comment 1 : Specifically, it may be useful to describe how a hospital would be designated a CSC.
Authors' Response :
(p18, 1st para, line 6-12)
We thank Reviewer 3 for this comment. In Japan, the official certification process for PSCs (primary stroke centres) just began in 2019. The criteria for CSC certification is now under discussion by the Japan Stroke Society. The results of this study could have a significant impact on the recommended items and criteria for the designation of official CSCs in Japan. After the official certification process for CSCs is implemented, we plan to reassess the effect of CSC capabilities on AIS patients.

Change to Text:
Accordingly, we added the following sentences in the Limitation.
"Fourth, the CSC score is a self-reported questionnaire rather than the result of any formal certification process. In Japan, the official certification process for PSCs (primary stroke centres) just

began in 2019. The criteria for CSC certification is now under discussion by the Japan Stroke Society. The results of this study could have a significant impact on the recommended items and criteria for the designation of official CSCs in Japan. After the official certification process for CSCs is implemented, we plan to reassess the effect of CSC capabilities on AIS patients."

Comment 2 : Would some of the capabilities on the scale be met by being a CSC?
In addition, the primary endpoint is defined as temporal improvement on a CSC score from 2010 to 2018 by at least 1 point. Some discussion on the practical significance of a 1-point improvement would be useful.

Authors' Response :
(p9-10, 2nd para, line 5-10; p22, reference no. 11)
We thank Reviewer 3 for this comment. To assess the effect of the CSC capabilities on being a CSC, further studies are needed in the future. We described the reason for this in our response to your Comment 1 above.
Additionally, "one point" was set based on our previous report on the CSC score. In that study, we showed that even a small preceding improvement of the CSC score was associated with reduced in-hospital mortality, reduced poor outcomes, and higher use of acute reperfusion therapy in AIS patients; our findings also suggested the difficulty in improving the CSC score in a relatively short time period.

Change to Text:
Accordingly, we added the following sentences in the Statistical analysis.
The increase of "one point" was set based on our previous report on the CSC score. In that study, we showed that even a small preceding improvement of the CSC score was associated with reduced in-hospital mortality, reduced poor outcomes, and higher use of acute reperfusion therapy in AIS patients; our findings also suggested the difficulty in improving the CSC score in a relatively short time period.

Accordingly, the following reference was included in the revised References list.
10. Kada A, Ogasawara, K, Kitazono, T, et al. National trends in outcomes of ischemic stroke and prognostic influence of stroke center capability in Japan, 2010-2016. Int J Stroke. 2019.

Comment 3 : How is the data collected in 2014 factored into the analysis? This endpoint also does not differentiate CSC that stay the same from those with decline in score.
Authors' Response :
(p18, 1st para, line 13-15)
We thank Reviewer 3 for this comment. As the reviewer noted, we did not use 2014 data in this analysis because of the small number of participants in 2014. Further research is required to examine the effect of 2014 data.

Change to Text:
Accordingly, we added the following sentences in the Limitation.
"Finally, the 2014 data did not factor into this analysis because of the small number of participants in that year. Further research is required to examine the effect of 2014 data on the analysis."

Comment 4 : The main analysis focus on hospitals responding to all three surveys. As the authors appropriately noted as limitations, it could cause an upward bias in the scores, and hence limited room for improvements over time. To understand the nature of bias, it might be useful to look at the association between hospitals that dropped out and their characteristics.
Authors' Response :

(p11, 2nd and 3rd para, line 2,4,7; p14, 1st para, line 2-4)
We thank reviewer 3 for this valuable comment. As the reviewer suggested, we changed Table 1 to compare the hospitals that consecutively participated in all 3 surveys to those that did not.

Change to Text: Accordingly, we changed the terms “Table1a” and “Table1b” to “Table 1” in “Trends in the CSC capabilities from 2010 to 2018” in the Results.

In addition, the following statement in the Results was added:
“Selection bias”
“We found that a selection bias did exist; in fact, the total CSC scores and most of the implementation rates of each item were significantly higher for the consecutively participating hospitals than for the others in all three surveys (Table 1).”

In addition, we changed the following table into Table 1

Components Items 2010 2014 2018
All participating Hsps.
(n=749) Consecutively participating Hsps.
(n=323) Other Hsps.
(n=426) p value All participating Hsps.
(n=532) Consecutively participating Hsps.
(n=323) Other Hsps.
(n=209) p value All participating Hsps.
(n=786) Consecutively participating Hsps.
(n=323) Other Hsps.
(n=464) p value
Personnel Neurologists 358 (47.8) 176 (54.5) 182 (42.7) 0.001 283 (53.2) 177 (54.8) 106 (50.7) 0.357 452 (57.5) 210 (65.0) 242 (52.2) <0.001
Neurosurgeons 694 (92.7) 314 (97.2) 380 (89.2) <0.001 515 (96.8) 317 (98.1) 198 (94.7) 0.03 754 (95.9) 317 (98.1) 437 (94.2) 0.006
Endovascular physicians 272 (36.3) 146 (45.2) 126 (29.6) <0.001 280 (52.6) 196 (60.7) 84 (40.2) <0.001 428 (54.4) 211 (65.3) 217 (46.8) <0.001
Emergency medicine 162 (21.6) 96 (29.7) 66 (15.5) <0.001 207 (38.9) 146 (45.2) 61 (29.2) <0.001 427 (54.3) 205 (63.5) 222 (63.5) <0.001
Physical medicine and rehabilitation 113 (15.1) 61 (18.9) 52 (12.2) 0.011 143 (26.9) 95 (29.4) 48 (23.0) 0.102 313 (39.8) 137 (42.4) 176 (37.9) 0.206
Rehabilitation therapy 742 (99.1) 321 (99.4) 421 (98.8) 0.435 529 (99.4) 321 (99.4) 208 (99.5) 0.832 779 (99.1) 321 (99.4) 458 (98.7) 0.354
Stroke rehabilitation nurses 102 (13.6) 48 (14.9) 54 (12.7) 0.388 157 (29.5) 116 (35.9) 41 (19.6) <0.001 285 (36.2) 146 (45.2) 139 (30.0) <0.001
Diagnostic CT 742 (99.1) 322 (99.7) 420 (98.6) 0.122 527 (99.1) 322 (99.7) 205 (98.1) 0.061 763 (97.1) 322 (99.7) 441 (85.0) <0.001
MRI with diffusion 647 (86.4) 291 (90.1) 356 (83.6) 0.01 504 (94.7) 311 (96.3) 193 (92.3) 0.047 732 (93.1) 314 (97.2) 418 (90.1) <0.001
Digital cerebral angiography 602 (80.3) 288 (89.2) 314 (73.7) <0.001 476 (89.4) 305 (94.4) 171 (81.8) <0.001 638 (81.2) 299 (92.6) 399 (73.1) <0.001
CT angiography 627 (83.7) 289 (89.5) 338 (79.3) <0.001 492 (92.5) 305 (94.4) 187 (89.5) 0.034 701 (89.2) 309 (95.7) 392 (84.5) <0.001
Carotid duplex ultrasound 257 (34.3) 126 (39.0) 131 (30.8) 0.018 219 (41.2) 153 (47.4) 66 (31.6) <0.001 343 (43.6) 169 (52.3) 174 (37.5) <0.001

TCD 121 (16.2) 70 (21.7) 51 (12.0) <0.001 123 (23.1) 87 (26.9) 36 (17.2) <0.010 162 (20.6) 95 (29.4) 67 (14.4) <0.001
Specific Expertise Carotid endarterectomy 603 (80.5) 292 (90.4) 311 (73.0) <0.001 458 (86.1) 288 (89.2) 170 (81.3) 0.011 613 (78.0) 284 (87.9) 329 (70.9) <0.001
Clipping of intracranial aneurysm 685 (91.5) 314 (97.2) 371 (87.1) <0.001 504 (94.7) 315 (97.5) 189 (90.4) <0.001 706 (89.8) 314 (97.2) 392 (84.5) <0.001
Hematoma removal/draining 689 (92.0) 315 (97.5) 374 (87.8) <0.001 505 (95.0) 315 (97.5) 190 (90.9) <0.001 718 (91.3) 314 (97.2) 404 (87.1) <0.001
Coiling of intracranial aneurysm 360 (48.1) 192 (59.4) 168 (39.4) <0.001 332 (62.4) 223 (69.0) 109 (52.2) <0.001 448 (57.0) 223 (69.0) 225 (48.5) <0.001
Intra-arterial reperfusion therapy 498 (66.5) 245 (75.9) 253 (59.4) <0.001 398 (74.8) 261 (80.8) 137 (65.6) <0.001 510 (64.9) 247 (76.5) 263 (56.7) <0.001
Infrastructure Stroke unit 132 (17.6) 74 (22.9) 58 (13.6) <0.001 202 (38.0) 136 (42.1) 66 (31.6) 0.015 342 (43.5) 171 (52.9) 171 (36.9) <0.001
Intensive care unit 445 (59.4) 214 (66.3) 231 (54.2) <0.001 362 (68.0) 224 (69.4) 138 (66.0) 0.422 467 (59.4) 220 (68.1) 247 (53.2) <0.001
Operating room staffed 24/7 451 (60.2) 230 (71.2) 221 (51.9) <0.001 339 (63.7) 239 (74.0) 100 (47.9) <0.001 487 (62.0) 243 (75.2) 244 (52.6) <0.001
Interventional services coverage 24/7 279 (37.3) 147 (45.5) 132 (31.0) <0.001 317 (59.6) 218 (67.5) 99 (47.4) <0.001 452 (57.5) 219 (67.8) 233 (50.2) <0.001
Stroke registry 235 (31.4) 133 (41.2) 102 (23.9) <0.001 260 (48.9) 172 (53.3) 88 (42.1) 0.012 349 (44.4) 164 (50.8) 185 (39.9) 0.003
Education Community education 369 (49.3) 188 (58.2) 181 (42.5) <0.001 144 (27.1) 91 (28.2) 53 (25.4) 0.476 204 (26.0) 98 (30.3) 106 (22.8) 0.018
Professional education 436 (58.2) 207 (64.1) 229 (53.8) 0.005 326 (61.3) 208 (64.4) 118 (56.5) 0.066 429 (54.6) 184 (57.0) 245 (52.8) 0.249
Total CSC score
median, (IQR) 14 (11, 18) 16 (13, 19) 13 (10, 17) <0.001 17 (13, 19) 18 (14, 20) 15 (12, 18) <0.001 17 (12, 20.3) 19 (15, 21) 15 (10, 19) <0.001

Hsp, hospital; CT, computed tomography; MRI, magnetic resonance imaging; TCD, transcranial Doppler.

Additional detailed comments:
Comment 1. Middle of Page 7. "p for trend". What statistical test was used for testing trend?
Authors' Response: We thank Reviewer 3 for this valuable comment. As the reviewer noted, we added a title for each table. Please refer to Response of Comment 7 for Reviewer 1.

Comment 2. Table 4. Interpretation of the p values is sensitive to the choice of the reference group. For hospital location, while there is statistical difference with MEA central. Would there be a difference between MEA outlying vs McEA. An omnibus test (e.g. LRT with 2 degrees of freedom) may be more appropriate to evaluate the overall location effect. For some other characteristics, it may make sense to view them as ordinal (e.g. stroke case volume).
Authors' Response :
We appreciate Reviewer 3 comment on this point. We agree that additional analysis would be valuable. We are now investigating this point and intend to report it in a later paper.

VERSION 2 – REVIEW

REVIEWER	Julia Ferrari St. John´s of God Hospital Vienna, Austria
REVIEW RETURNED	09-Feb-2020

GENERAL COMMENTS	no more comments, all questions answered.

REVIEWER	ken cheung Columbia University USA
REVIEW RETURNED	12-Apr-2020

GENERAL COMMENTS	I have two remaining comments: 1. while there is a section on selection bias, it may be useful to note it again briefly under Limitations. 2. the tables are cropped. please reformat to make sure they appear on the whole page

VERSION 2 – AUTHOR RESPONSE

RESPONSE TO REVIEWER #3:

We wish to express our appreciation to Prof. Ken Cheung for his insightful comments, which have helped us significantly improve the paper.

Comment 1 : while there is a section on selection bias, it may be useful to note it again briefly under Limitations.

Authors' Response :
(p17, 2nd para, Limitation, lines 1-4)
We thank Reviewer 3 for this comment. Following the comment, we revised and added the explanations in the revised manuscript.

Change to Text:
First, since the total CSC scores and most of the implementation rates of each item were significantly higher for the consecutively participating hospitals than for the others in all three surveys, our findings may have included biased information.

Comment 2 : the tables are cropped. please reformat to make sure they appear on the whole page

Authors' Response :
(p24-p31, Tables 1-4)
We thank Reviewer 3 for this comment. Following the comment, we reformatted the tables in the revised manuscript.

Thank you again for your comments on our paper. We trust that the revised manuscript is suitable for publication.