

PEER REVIEW HISTORY

BMJ Paediatrics Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Use of the ReSVinet scale for parents and health care workers in a pediatric emergency service: a prospective study
AUTHORS	Camacho-Cruz, Jhon Briñez, Shirley Alvarez, Jorge Leal, Victoria Villamizar Gómez, Licet Vasquez-Hoyos, Pablo

VERSION 1 – REVIEW

REVIEWER	Reviewer name: Dr. Eirini Koutoumanou Institution and Country: University College London, 30 Guilford Street, London, WC1N 1EH, United Kingdom of Great Britain and Northern Ireland Competing interests: None
REVIEW RETURNED	13-Jan-2021

GENERAL COMMENTS	<p>This study analyses data relating to an existing questionnaire (ReSVinet, originally designed for adults) but applied in a new setting (emergency paediatric patients). Three different sources of data collection are utilised, parents and two types of doctors (professors and specialists). Data entries from the two groups of doctors (also referred to as Health Care Workers) are mostly consistent but the same does not apply when compared to the parent data. Below I have listed some questions/comments/recommendations which I think will make certain areas clearer and more transparent for the readers.</p> <p>Does ReSVinet stand for something? If so, please add it in the abstract and introduction. Also, it should be referenced correctly in the introduction section as soon as it's first mentioned, start of 4th paragraph which should incorporate (otherwise should be additional) references about the Galician Pediatric Research Network and the FIVE research group.</p> <p>In the abstract, does the term faculty relate to health care workers group? And what about residents? Which group is that? This becomes later on in the paper but needs to be clear in the abstract too. Also, it is not immediately clear to me how the two different types of doctors (pediatric doctor-professors vs specializing in pediatrics) are different in practical terms, i.e. are they more experienced, have been serving longer, more specialist? It might be worth adding some comments about this.</p> <p>I believe the following statement is confusing "Parents who wished to participate by completing the scale were included.", as it nearly implies that it was up to the parents to approach the researchers. But it is later made clear that this was not the case..."Patients were identified by physicians..."</p>
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	<p>How were the 10 parents that tested the Colombian version of the questionnaire chosen? Also, what was the specific explanation of the term apnea? This might be relevant clinically as it might inform readers of potential bias? (It could be included in an appendix for further reading. It could also include a plain English translation)</p> <p>How were the time points of 10 and 30 days chosen?</p> <p>Means and SDs have been used for a lot of measures on Table 1 but it's obvious that most of these (all?) are non-symmetrically distributed, e.g. age: mean\pm2*sd leads to negative values, similarly for the rest. These should be replaced by medians and IQRs.</p> <p>I recommend that the correlation coefficients and Cronbach's alphas are presented with confidence intervals too.</p> <p>I recommend that the authors include in the study's limitations, potential biases introduced via included only workers with mandatory insurance and only those that speak Spanish.</p> <p>Minor:</p> <ul style="list-style-type: none"> - Spacings between numbers in the Tables need to be reviewed (on my version, there are spaces between the dots and the following decimal points, making it difficult to read the numbers) - Reference Stata accordingly - Move Figure 1 after Figures 2-4 as it's cited after the latter in the text
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REVIEWER	<p>Reviewer name: Dr. Federico Martín-Torres Institution and Country: Hospital Clínico Universitario de Santiago, Pediatrics, A choupana s.n., Santiago de Compostela, La Coruña, 15701, Spain Competing interests: None</p>
REVIEW RETURNED	01-Jan-2021

GENERAL COMMENTS	<p>I found the paper interesting and profitable for your readers, as it adds information on the reliability and usability of a clinical respiratory scale that, as the authors have explained, has been used by both parents and physicians in hospitalized children suffering from bronchiolitis. The scale can also be completed using information obtained from medical records. The availability of a clinical scoring tool that could be used in a similar way by healthcare providers and non-professionals alike, and that offers the possibility of being completed reviewing medical records, could make close monitoring required by clinical trials more feasible.</p> <p>I must remark two issues no other paper has ever addressed before the present one: Investigators have applied the ReSVinet Scale in the Emergency Room, and they did not limit its use to a unique specific entity causing respiratory distress. At the moment, we have many different clinical scoring tools for children presenting with respiratory difficulty, but they have been validated in only one specific setting (Emergency Room or wards or PICU) and address only one cause of respiratory distress (PRAM is intended for bronchiolitis, Westley's Score for croup, etc...).</p> <p>Maybe the main flaw affecting this paper is the lack of interpretability of the results for different subgroups of patients: i.e,</p>
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	<p>I would have appreciated that investigators provided mean scores and standard deviation for clinical relevant subgroups – and a cut-off value in the ReSVinet Scale for safe discharge or for PICU admission for both professional and parental raters. Also, we still lack publications dealing with the lack of data on measurement error and responsiveness of the ReSVinet Scale, and this should be mentioned in the main text.</p> <p>Lastly, I would like that the authors could give me some feedback on the following particular points:</p> <p>Page 2, line 32 - The following sentence - “ but when used by HCW compared to when used by parents in the pediatric emergency setting” seems to be incomplete. Please clarify it.</p> <p>Page 7, line 16 – sample size consideration. Did you set beforehand a maximum drop-out rate/lost to follow-up to consider the data viable?</p> <p>Page 8, line 23. “ Hospital Length of Stay was 4.5□ 5.1 days”. I would recommend using median and interquartile range in this specific line.</p> <p>Page 8, line 41 - “no significant differences were found” and p-values are provided. How did you obtain these p-values?</p> <p>Page 9, line 11 – The same issue with the p-values, “analysis by individual items showed statistical differences between**** on medical intervention, respiratory difficulty, and frequency, p<0.01”. What statistics tests were run?</p> <p>Page 10, line 29 _ “Finally, it may be necessary to use technical devices such as automatic respiratory counters...”. As stated in the paper by Justicia-Grande et al describing the first use of the ReSVinet Scale, one of the main aims when developing the parental tool was to avoid the use of technical devices, or at least those not universally available in most households.</p> <p>Page 10, line 41 - “on the subject of medical intervention, most parents choose no treatment in our study” – but on Figure 4 (Page 24) I can see they usually marked the “basic” intervention. Could you further clarify this point?</p> <p>Page 10, line 53 – “ This suggests that this scale may require more explanation or training... in greater detail how to score individual points on the scale in the parents’ version”. Authors could have a point on this. But something else may be happening when assessing the area of medical intervention, and it is related with parental and patient education and perceptions. Some patients will not even consider being assessed by a physician a kind of medical “intervention”, despite the act being described in the original ReSVinet Scale.</p> <p>It is possible that, in the original paper, the differences of appreciation in medical intervention between Healthcare providers and non-professional raters were not so evident as it included only children admitted to wards or to PICUs, and therefore they actually required more aggressive interventions.</p>
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	<p>Page 11, line 50 - “ Since the initial design was only for bronchiolitis, the result may be lower when various disease with different symptoms are assessed”. This is an interesting hypothesis to labour on, but can you back this assumption offering the internal consistency of the different subgroups after classifying the patients for a specific entity (pneumonia, bronchiolitis, pharyngitis...)?</p> <p>Page 11, line 53 – “A universal scale for all ARIs is, in our opinion, a far better option than individual scales for each respiratory disease”. Maybe this interesting, but personal, opinion may be better backed by literature showing that most scales that comply with Cornbach’s alpha requirements are homogeneous and that they assess patients suffering only one specific cause of respiratory distress.</p> <p>Page 12 , line 27 - “ (patients with gastroenteritis and food intolerance) were not excluded”. Should you have done that, your results could have been flawed, as “Feeding Intolerance” is, as you have explained in methods, one of the items measured by the scale. I am suggesting you should re-write this statement.</p> <p>REFERENCES -</p> <p>References 28 and 30 are the same. Please erase one of them and rearrange your citations accordingly. References 29 and 31 are the same. Please correct this issue and rearrange your citations accordingly.</p>
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REVIEWER	<p>Reviewer name: Dr. James M. Gerard Institution and Country: St Louis Univ, United Kingdom of Great Britain and Northern Ireland Competing interests: None</p>
REVIEW RETURNED	22-Dec-2020

GENERAL COMMENTS	<p>The manuscript entitled, "Reliability of the ReSVinet scale for parents and health care workers in a pediatric emergency service" describes a prospective study conducted to determine whether or not the ReSVinet scale for acute respiratory infection in infants is reliably used by health care workers and parents in an emergency room setting.</p> <p>General comments:</p> <p>Overall, the study appears appropriately designed to address this objective. The statistical analyses seem appropriate and the results of the study support the conclusions drawn by the authors.</p> <p>Overall, the manuscript is clear and well-written, however, there are a large number of minor grammatical errors in the manuscript. It would be good to thoroughly review the manuscript and correct these errors.</p> <p>It is interesting that the parents disagreed to the extent that they did regarding the "medical intervention" metric, especially given that the parents completed these surveys while still in the ED. The authors state that more training of parents on the scale and its components may be needed. The authors might want to expand a little bit more on this sub-component of the scale.</p>
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VERSION 1 – AUTHOR RESPONSE

We thank the editor and reviewers for their time in evaluating our article. Below we attach the article with all the suggestions highlighted in red letter and a letter responding point by point to the reviewers. We have worked hard this month to be able to have all the corrections and suggestions at the level of your prestigious journal, so we implore you to keep it in mind for publication.

Thank you again.

Reviewer: 1

General comments:

Overall, the manuscript is clear and well-written, however, there are a large number of minor grammatical errors in the manuscript. It would be good to thoroughly review the manuscript and correct these errors.

Answer: A grammar check was performed again by a certified translator English native

It is interesting that the parents disagreed to the extent that they did regarding the "medical intervention" metric, especially given that the parents completed these surveys while still in the ED. The authors state that more training of parents on the scale and its components may be needed. The authors might want to expand a little bit more on this sub-component of the scale.

Answer: we agree with the reviewer, medical intervention was a striking point on the scale. We tried to discuss why the medical intervention was undervalued by the parents (page 10, line 41). An interesting finding is that the first time the scale was designed was at the end of the hospitalization, in order to avoid this memory bias we tried to apply the scale after the evaluation and medical decision making, this could affect the final result .

Reviewer: 2

General comments:

Maybe the main flaw affecting this paper is the lack of interpretability of the results for different subgroups of patients: i.e, I would have appreciated that investigators provided mean scores and standard deviation for clinical relevant subgroups – and a cut-off value in the ReSVinet Scale for safe discharge or for PICU admission for both professional and parental raters. Also, we still lack publications dealing with the lack of data on measurement error and responsiveness of the ReSVinet Scale, and this should be mentioned in the main text.

Answer: thanks for the comment, As the initial objective was reliability, no cut-off points were set for safe discharge or for PICU. When we evaluate pneumonia that could have a more aggressive behavior, the sample (n = 3) is insufficient to carry out these analyzes, the same for admission to PICU (n = 5). But that is very interesting for new studies.

Particular points:

Page 2, line 32 - The following sentence - " but when used by HCW compared to when used by parents in the pediatric emergency setting" seems to be incomplete. Please clarify it.

Answer: The sentence was adjusted according to the Editor in Chief.

Page 7, line 16 – sample size consideration. Did you set beforehand a maximum drop-out rate/lost to follow-up to consider the data viable?

Answer: Yes, it was calculated with a 10% loss of follow-up.

Page 8, line 23. " Hospital Length of Stay was 4.5 5.1 days". I would recommend using median and interquartile range in this specific line.

Answer: The sentence was adjusted

Page 8, line 41 - "no significant differences were found" and p-values are provided. How did you obtain these p-values?

Answer: The sentence was completed. Mann-Whitney U test.

Page 9, line 11 - The same issue with the p-values, "analysis by individual items showed statistical differences between**** on medical intervention, respiratory difficulty, and frequency, $p < 0.01$ ". What statistics tests were run?

Answer: We add in the text, "The comparison between total scores was performed using the Mann-Whitney U test".

Page 10, line 29 - "Finally, it may be necessary to use technical devices such as automatic respiratory counters...". As stated in the paper by Justicia-Grande et al describing the first use of the ReSVinet Scale, one of the main aims when developing the parental tool was to avoid the use of technical devices, or at least those not universally available in most households.

Answer: We agree with the reviewer, the sentence was modified

Page 10, line 41 - "on the subject of medical intervention, most parents choose no treatment in our study" - but on Figure 4 (Page 24) I can see they usually marked the "basic" intervention. Could you further clarify this point?

Answer: We agree with the reviewer, the sentence was modified to some parents. On Figure 4 (Page 24), some parents choose no medical treatment and this causes a significant disagreement

Page 10, line 53 - " This suggests that this scale may require more explanation or training... in greater detail how to score individual points on the scale in the parents' version". Authors could have a point on this. But something else may be happening when assessing the area of medical intervention, and it is related with parental and patient education and perceptions. Some patients will not even consider being assessed by a physician a kind of medical "intervention", despite the act being described in the original ReSVinet Scale.

It is possible that, in the original paper, the differences of appreciation in medical intervention between Healthcare providers and non-professional raters were not so evident as it included only children admitted to wards or to PICUs, and therefore they actually required more aggressive interventions.

Answer: is a very interesting comment, the phrase was adjusted and we request your permission to use part of your explanation as a way to clarify our text in the article.

Page 11, line 50 -" Since the initial design was only for bronchiolitis, the result may be lower when various disease with different symptoms are assessed". This is an interesting hypothesis to labour on, but can you back this assumption offering the internal consistency of the different subgroups after classifying the patients for a specific entity (pneumonia, bronchiolitis, pharyngitis...)?

Answer: We agree with the reviewer, the sentence was modified

Page 11, line 53 - "A universal scale for all ARIs is, in our opinion, a far better option than individual scales for each respiratory disease". Maybe this interesting, but personal, opinion may be better backed by literature showing that most scales that comply with Cornbach's alpha requirements are homogeneous and that they assess patients suffering only one specific cause of respiratory distress.

Answer: Again the comment opens the panorama and completes the meaning of the sentence, sincerely we request that you allow us to use your phrase to incorporate it into the text.

Page 12 , line 27 - " (patients with gastroenteritis and food intolerance) were not excluded". Should you have done that, your results could have been flawed, as "Feeding Intolerance" is, as you have explained in methods, one of the items measured by the scale. I am suggesting you should re-write this

statement.

Answer: According to the comment, we prefer to delete that paragraph

REFERENCES:

Answer: The references were adjusted

Reviewer: 3

Comments to the Author

This study analyses data relating to an existing questionnaire (ReSVinet, originally designed for adults) but applied in a new setting (emergency paediatric patients). Three different sources of data collection are utilised, parents and two types of doctors (professors and specialists). Data entries from the two groups of doctors (also referred to as Health Care Workers) are mostly consistent but the same does not apply when compared to the parent data. Below I have listed some questions/comments/recommendations which I think will make certain areas clearer and more transparent for the readers.

Does ReSVinet stand for something? If so, please add it in the abstract and introduction. Also, it should be referenced correctly in the introduction section as soon as it's first mentioned, start of 4th paragraph which should incorporate (otherwise should be additional) references about the Galician Pediatric Research Network and the FIVE research group.

Answer: We agree with the reviewer, the sentence was modified. The reference was added and corresponds to number 15.

In the abstract, does the term faculty relate to health care workers group? And what about residents? Which group is that? This becomes later on in the paper but needs to be clear in the abstract too. Also, it is not immediately clear to me how the two different types of doctors (pediatric doctor-professors vs specializing in pediatrics) are different in practical terms, i.e. are they more experienced, have been serving longer, more specialist? It might be worth adding some comments about this.

Answer: Thanks for the comment, indeed "faculty" are pediatricians who do teaching and also have more experience. "resident" general practitioners who are doing their first specialty in pediatrics

I believe the following statement is confusing "Parents who wished to participate by completing the scale were included.", as it nearly implies that it was up to the parents to approach the researchers. But it is later made clear that this was not the case..."Patients were identified by physicians...".

Answer: Thanks for the comment, the sentence was adjusted

How were the 10 parents that tested the Colombian version of the questionnaire chosen? Also, what was the specific explanation of the term apnea? This might be relevant clinically as it might inform readers of potential bias? (It could be included in an appendix for further reading. It could also include a plain English translation)

Answer: Thanks for the comment, the choice of the 10 parents was a randomization by convenience of parents who met inclusion criteria in the emergency department.

The specific explanation of the term apnea, an episode of respiratory pause, "the child stopped breathing. It may have been necessary to stimulate him/her in order to regain normal breathing rate. This clarification was added in writing to the parents' format. We attach the English version for parents <https://journals.plos.org/plosone/article/figure?id=10.1371/journal.pone.0157665.t002>

How were the time points of 10 and 30 days chosen?

Answer: They were chosen due to the natural history of the disease. On day 10 after the onset of the disease, the highest incidence of respiratory failure, admission to PICU and mechanical ventilation has been described. And on the 30th when there is histological recovery of the majority of patients with lower respiratory infection.

Means and SDs have been used for a lot of measures on Table 1 but it's obvious that most of these (all?) are non-symmetrically distributed, e.g. age: mean \pm 2*sd leads to negative values, similarly for the rest. These should be replaced by medians and IQRs.

Answer: Thanks for the comment, the suggestions were made in red font

I recommend that the correlation coefficients and Cronbach's alphas are presented with confidence intervals too.

Answer: Thanks for the comment, the suggestions were made in red font

I recommend that the authors include in the study's limitations, potential biases introduced via included only workers with mandatory insurance and only those that speak Spanish.

Minor:

- Spacings between numbers in the Tables need to be reviewed (on my version, there are spaces between the dots and the following decimal points, making it difficult to read the numbers)
- Reference Stata accordingly
- Move Figure 1 after Figures 2-4 as it's cited after the latter in the text

Answer: Thanks for the comment, the suggestions were made

Associate Editor

Comments to the Author:

Kindly take note of the feedback to clarify on the scores relevant to specific diagnostic groups to enrich the discussion, translation and applicability of your findings.

Answer: thanks for the comment, As the initial objective was reliability, no cut-off points were set for safe discharge or for PICU. When we evaluate pneumonia that could have a more aggressive behavior, the sample (n = 3) is insufficient to carry out these analyzes, the same for admission to PICU (n = 5). But that is very interesting for new studies.

According to the comments of the reviewers, we make all adjustments in the way of presenting the scores, so you will find a more organized text, which makes the discussion more applicable

Editor in Chief

Please include the ReSVinet scale scoring system as a table (reproduce from reference 15. This is acceptable as long as you cite the source as PlosOne is open access). This will make your paper easier to comprehend.

Answer: Thanks for the comment, the suggestions were made

Title add "a prospective study" and replace "Reliability" with "Use". Reliability is not the correct term for your study. You have studied correlation. To evaluate reliability, you would have to compare scores with clinical outcomes

Answer: Thanks for the comment, the suggestions were made

Abstract Conclusion amend to "There was a good correlation in ReSVinet scores by health professionals when used in the pediatric emergency area. Agreement between parents and health professionals was found to be more variable. Future studies should focus on finding ways to improve its reliability when used by parents before the scale is used in the emergency room."

Answer: Thanks for the comment, the suggestions were made

What this study adds replace with "There was good correlation of scores between health professionals.

There was more variation between scores by parents and health professionals"

Answer: Thanks for the comment, the suggestions were made

Discussion para 2 delete the last sentence "This is the first published study using..." Journal style is for authors NOT to claim their study is the first. This for others to decide (see instructions to authors)

Answer: Thanks for the comment, the suggestions were made. Please, excuses for the mistake.

Conclusions again delete the sentence "This tool was used for the first time in" (page 13, line 10)

Answer: Thanks for the comment, the suggestions were made. Please, excuses for the mistake.

Sincerely,

Authors

VERSION 2 – REVIEW

REVIEWER	Reviewer name: Dr. Eirini Koutoumanou Institution and Country: University College London, 30 Guilford Street, London, WC1N 1EH, United Kingdom of Great Britain and Northern Ireland Competing interests: None
REVIEW RETURNED	09-Mar-2021

GENERAL COMMENTS	<p>The authors have addressed successfully the reviewers' comments. However, may I suggest that some of their answers are actually incorporated into the revised version? The answers are mostly satisfactory but they should also be reflected in the revised version. For example (just picking one), the reference to the 10 parents that were chosen to test the Colombian version of the questionnaire, should be re-written to say "a convenience random sample of 10 parents was chosen..." or similar. Could the authors please review all the responses and incorporate the answers in the manuscript where appropriate/not done already?</p> <p>Minor: The following phrases do not read well:</p> <ul style="list-style-type: none"> - "...was done of patients under..." – change to: was done on patients...? - "...by completing the scale were included." – rewrite - "...Cronbach's alpha was done with..." – change to: was calculated...? - The days between first symptoms and consultation is still reported as mean and SD – I believe this might be an oversight as it should be changed to median and IQR. - Is it an overstatement to say that the ReSVinet scale was highly reliable at the start of the discussion section? Maybe rephrase to "...was found to have very good reliability..."? "Highly reliable" might be interpreted as an alpha a lot higher than 0.6-0.7. - Finally, I recommend that the following sentence is re-written to be clear that it does not reflect the aim of this current study: "The question to be evaluated was if this scale required any previous training (prior to using it) or a specific guide that explained in greater detail how to score individual points on the scale in the parents' version." This might be ultimately another goal and another interesting point but this study and the data collected did not focus on the training provisions. Therefore, this point should
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	not be blurred with the original research question addressed by the collected data.
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REVIEWER	Reviewer name: Dr. Federico Martín-Torres Institution and Country: Hospital Clínico Universitario de Santiago, Pediatrics, A choupana s.n., Santiago de Compostela, La Coruña, 15701, Spain Competing interests: None
REVIEW RETURNED	19-Mar-2021

GENERAL COMMENTS	I would like to express my most sincere thanks to all authors for taking our review suggestions and comments into account.
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REVIEWER	Reviewer name: Dr. James M. Gerard Institution and Country: St Louis Univ, United Kingdom of Great Britain and Northern Ireland Competing interests: None
REVIEW RETURNED	07-Mar-2021

GENERAL COMMENTS	The Authors have done a commendable job of addressing the comments of the reviewers. Thank you for your contribution to the existing research on this topic.
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VERSION 2 – AUTHOR RESPONSE

Again, we thank the editor and reviewers for their time in evaluating our article. Below we attach the article with all the suggestions highlighted in red letter and a letter responding point by point to the reviewers.

Thank you again.

Associate Editor

Comments to the Author:

Thank you for working on all the changes requested. Please effect the changes in the manuscript specifically those pertaining to the Methods section:

- How the 10 parents were chosen
- Why the assessment was performed at Day 10 and Day 30

Answer: thanks for the comment, we make all adjustments.

Reviewer 1:

Dr. James M. Gerard, St Louis Univ

Comments to the Author

The Authors have done a commendable job of addressing the comments of the reviewers. Thank you for your contribution to the existing research on this topic.

Answer: thanks for the comment, we are glad that you liked the changes

Reviewer: 2

Reviewer: 2

Dr. Eirini Koutoumanou, University College London

Comments to the Author

The authors have addressed successfully the reviewers' comments. However, may I suggest that some of their answers are actually incorporated into the revised version? The answers are mostly satisfactory but they should also be reflected in the revised version. For example (just picking one), the reference to the 10 parents that were chosen to test the Colombian version of the questionnaire, should be re-written to say "a convenience random sample of 10 parents was chosen..." or similar. Could the authors please review all the responses and incorporate the answers in the manuscript where appropriate/not done already?

Answer: Thanks for the comment, all the suggestions have been reviewed and incorporated into the text

Minor:

The following phrases do not read well:

- "...was done of patients under..." – change to: was done on patients...?

Answer: We agree with the reviewer, the sentence was modified

- "...by completing the scale were included." – rewrite

Answer: We agree with the reviewer, the sentence was modified

- "...Cronbach's alpha was done with..." – change to: was calculated...?

Answer: We agree with the reviewer, the sentence was modified

- The days between first symptoms and consultation is still reported as mean and SD – I believe this might be an oversight as it should be changed to median and IQR.

Answer: We agree with the reviewer, the sentence was modified

- Is it an overstatement to say that the ReSVinet scale was highly reliable at the start of the discussion section? Maybe rephrase to "...was found to have very good reliability..."? "Highly reliable" might be interpreted as an alpha a lot higher than 0.6-0.7.

Answer: We agree with the reviewer, the sentence was modified

- Finally, I recommend that the following sentence is re-written to be clear that it does not reflect the aim of this current study: "The question to be evaluated was if this scale required any previous training (prior to using it) or a specific guide that explained in greater detail how to score individual points on the scale in the parents' version." This might be ultimately another goal and another interesting point but this study and the data collected did not focus on the training provisions. Therefore, this point should not be blurred with the original research question addressed by the collected data.

Answer: We agree with the reviewer, is an excellent suggestion, the sentence was re-written

Reviewer: 3

Dr. Federico Martín-Torres, Hospital Clínico Universitario de Santiago

Comments to the Author

I would like to express my most sincere thanks to all authors for taking our review suggestions and comments into account.

Answer: thanks for the comment, we are glad that you liked the changes

Sincerely,

Authors