PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Predictors of postpartum glucose intolerance in women with gestational diabetes mellitus: A prospective cohort study in Ethiopia based on the updated diagnostic criteria
AUTHORS	Muche, Achenef Asmamaw; Olayemi, Oladapo; Gete, Yigzaw

VERSION 1 – REVIEW

REVIEWER	Deidré Mason Tygerberg Academic Hospital, Cape Town, South Africa
REVIEW RETURNED	27-Feb-2020

GENERAL COMMENTS	1. This paper presents important information that adds to the GDM knowledge pool, especially in the African and resource-limited setting. 2. Grammatically I found some areas of duplication and also some paragraphs where the intended meaning is unclear. I will list some examples but recommend that a formal language review be considered. Examples: document pg 3 lines 16-17; 29 document pg 4 lines 1-2, 11, 16-18 document pg 5 line 11 document pg 7 line 14 document pg 12 line 7-12, line 15 (spelling) document pg 13 line 5-9, line 17 BGL (abbreviation not used elsewhere, not explained) document pg 14 line 8-10 3. Study Limitations: Although justified in the text as acceptable when circumstances dictate, the use of capillary blood samples and point of care testing (rather than laboratory-based plasma glucose levels) needs to be acknowledged as a possible limitation. 4. Fasting plasma glucose and 2-h plasma glucose is used throughout the text although capillary glucose testing was performed. For the sake of veracity, consider changing the terminology to accurately reflect the methods (eg fasting capillary glucose). 5. Consistency in findings: When referring to the predictive value of antenatal factors to predict development of glucose intolerance 6-12 weeks postpartum, inconsistent terms are used for this in different places. i) Abstract (pg 2 line 16) "significant predicting factors" ii) Abstract (pg 2 line 24) "factors were modestly)

	iii) Strengths and limitations (pg 3 line 5) "can be easily predicted" Decide what your statistics are showing about the predictability and state so consistently in all areas of the text. 6. "updated diagnostic criteria" Although clinicians in the field will understand the implied meaning, I think it is important to define this in the text at least once. (I see it was done in the previous article that the authors often refer to in the methodology, but readers of this text also need clarity). 7. Discussion: i) General comment: there seems to be a lack of depth in the interpretation of the results found. Each result is compared to the known literature, but what does the results mean for practice in Ethiopia / Africa? ii)Reference is made in the Discussion to insulin sensitivity and beta-cell dysfunction not being significantly different between the two groups. (pg 12 line 24-28). This sounds like a specific statement rather than a general statement. If this was tested in your cohort, how was it tested? No comment is made of this in the methods or results sections. iii) page 13 line 23 "we strongly believe that appropriate prevention as well as..." - It is unclear what prevention is referred to here. Please review intended meaning and language. 8. Conclusions i) pg 14 line 18-20 "a risk score calculation based on a combination of antenatal factors was effective but had a lower accuracy than the model-based approach." I find no reference to this in the results or discussion and am unsure what this refers to. ii) The one objective was to develop a model, but the implications of the risk factors identified as significant are not explored or the utility of the 'model' not discussed.

REVIEWER	Costantino Di Carlo University of Catanzaro "Magna Graecia", Italy
REVIEW RETURNED	27-Feb-2020

GENERAL COMMENTS	Post partum oral glucose testing (pptOGTT) is a crucial point for the early detection of glucose intolerance in women who suffered GDM during pregnancy. There is a high percentage of these women that will develop Type Two Diabetes (T2D), an important medical condition. To predict which women are at a higher risk to result positive at the pptOGTT is important in view of the attention to pay for the execution of the test during the 6-12 weeks post partum. Indeed, previous literature has shown a worldwide low adherence to this test for women diagnosed with GDM during pregnancy. This study demonstrates that conditions such as maternal age, high fasting plasma glucose level at diagnosis, overweight/obesity and, surprisingly antenatal depression were predicting factors for positive PPT OGTT. I consider the examined topic relevant and interesting. In comparison to the previously published literature this paper gives a significant analysis of the main risk factors for the development of type two diabetes. Moreover, it adds antenatal depression as a

	condition that strongly expose women to postpartum glucose impairment. The paper is well written, with a clear text, easy to read. Tables are useful to immediately understanding the paper results. The only limit of this study is the limited number of examined cases. Unfortunately this number is too little to lead to strong conclusive considerations. This should be more clearly stated by the authors.

REVIEWER	A/Prof Alice Richardson Australian National University, Australia
REVIEW RETURNED	29-Mar-2020

GENERAL COMMENTS	In this paper, the authors have conducted a cohort study of women with GDM. The research question was: what are the predictors of post-partum glucose intolerance in this cohort? The protocol for this study has already been published and so the imperative to publish the results is strengthened. Below I will elaborate on the two items in the Review Checklist where my response was “No”. They are of a largely minor nature and so I recommend that the paper undergo minor revision before resubmission. Q7: The statistical analysis is a classic series of univariate tests followed by a multivariate logistic regression. However the authors should explain the multiple images in Figure 1, going into more detail than is currently in place on page 10 lines 12 – 14. It looks odd to see probabilities presented as numbers larger than 1 in Table 3. The authors should either declare these to be percentages or write the probabilities as numbers between 0 and 1. I find the construction of the “easily applicable postpartum glucose intolerance prediction score” (page 7 line 14) to be unclear and possibly introducing unacceptable rounding error into the construction of the score. The risk score is referred to again in the Conclusion but it hasn’t really been fully teased out in the paper. The authors should consider providing an example of the score and/or an equation with the coefficients used clearly indicated. A similar equation for the regression model already appears in the caption of Figure 1. Q10: Page 15, line 2, the authors need to consider carefully the use of the word “chance” here. Do they mean chance or odds or indeed odds ratio, bearing in mind that the outcome here is not rare (about 20%) and so odds cannot be conflated with chances in these circumstances. Finally, minor typos and items requiring clarification: Page 4 line 4. The term “introduced” does not seem to make sense. Should it be “predicted”? Page 4 line 15. “Literature” needs to be cited here. Page 4 line 29. “presently” not “present”. Page 13 line 15: should “Brazilin” be “Brazil”? Page 6 line 29-30. Variables are not parametric or non-parametric, the statistical methods used to analyse them are. Please replace with “Normally distributed and non-normally distributed variables”. Thankyou for the opportunity to be part of the academic referring system in this way.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1 (Deidré Mason)
Comment 1: This paper presents important information that adds to the GDM knowledge pool, especially in the African and resource-limited setting.
Response: Thanks for the appreciation.
Comment 2: Grammatically I found some areas of duplication and also some paragraphs where the intended meaning is unclear. I will list some examples but recommend that a formal language review be considered.
Examples:
document pg 3 lines 16-17; 29
document pg 4 lines 1-2, 11, 16-18
document pg 5 line 11
document pg 7 line 14
document pg 12 line 7-12, line 15 (spelling)
document pg 13 line 5-9, line 17 BGL (abbreviation not used elsewhere, not explained)
document pg 14 line 8-10
Response: We thank you for your comments. All the above addressed. We have made major revision on language issue. We have also avoided duplication and managed syntax errors.
Comment 3: Study Limitations: Although justified in the text as acceptable when circumstances dictate, the use of capillary blood samples and point of care testing (rather than laboratory-based plasma glucose levels) needs to be acknowledged as a possible limitation.
Response: We agreed to your comment without any reservation. We have added sentence as follows " Though, WHO recommends that in settings where laboratories or proper storages and transport of blood samples is not guaranteed, which is the case in resource-limited countries like Ethiopia, the use of point of care tests may influence the result (Hod et al., 2015). However, we used plasma-calibrated hand-held glucometers because of convenience and acceptable reliability." (see page 14 lines 24-29 and page 15 lines 1-2)
Comment 4: Fasting plasma glucose and 2-h plasma glucose is used throughout the text although capillary glucose testing was performed. For the sake of veracity, consider changing the terminology to accurately reflect the methods (eg fasting capillary glucose).
Response: We found out that your question is very interesting. Although we do respect your comment, Blood glucose level was analyzed using 5μl capillary whole blood with HemoCue Glucose B-201+ (A¨ngelholm AB, Sweden). It was recommended taking into consideration the difference between whole blood and plasma reference values. The HemoCue Glucose 201 DM Analyzer with blood plasma conversion multiplies the measured whole blood glucose value by a factor of 1.11 and displays a plasma equivalent glucose result. The whole blood capillary values were converted to plasma venous values by multiplying a constant factor of 1.11 (D'Orazio et al., 2005). I have added a sentence in the method section as follows "After capillary blood samples were taken the whole blood capillary values were converted to plasma venous values by multiplying a constant factor of 1.11 (D'Orazio et al., 2005)". (see page 5 line 17-18). For more clarity here are the specifications of the HemoCue Glucose B-201+ glucometer (see the attached file)
Comment 5: Consistency in findings:
When referring to the predictive value of antenatal factors to predict development of glucose intolerance 6-12 weeks postpartum, inconsistent terms are used for this in different places.
i) Abstract (pg 2 line 16) "significant predicting factors"
ii) Abstract (pg 2 line 24) "factors were modestly)
iii) Strengths and limitations (pg 3 line 5) "can be easily predicted"
Decide what your statistics are showing about the predictability and state so consistently in all areas of the text.
Response: We thank you for your valuable comment. All the above comments have been accepted and corrected. We have managed such terms to be consist, as we are referring to predictive value of

antenatal factors to predict postpartum glucose intolerance, we use the word " predictors" thorough out the manuscript.
Comment 6: "updated diagnostic criteria" Although clinicians in the field will understand the implied meaning, I think it is important to define this in the text at least once. (I see it was done in the previous article that the authors often refer to in the methodology, but readers of this text also need clarity).
Response: We agreed on your comment without any reservation. We have added sentences regarding the meaning of updated diagnostic criteria for more clarity. (see page 5 lines 19-31) see page 5, paragraph 2, line 19-25).
Comment 7: Discussion:
i) General comment: there seems to be a lack of depth in the interpretation of the results found. Each result is compared to the known literature, but what does the results mean for practice in Ethiopia / Africa?
Response: We agreed on your comment without any reservation. We have made a major revisions in the discussion section. (see the entire discussion section).
ii) Reference is made in the Discussion to insulin sensitivity and beta-cell dysfunction not being significantly different between the two groups. (pg 12 line 24-28). This sounds like a specific statement rather than a general statement. If this was tested in your cohort, how was it tested? No comment is made of this in the methods or results sections.
Response: Thank you for your valuable comment. We did not test the insulin sensitivity and beta-cell dysfunction in our cohort. We have re written this sentence to avoid confusion. (see page 13 line 13-16)
iii) page 13 line 23 "we strongly believe that appropriate prevention as well as..." - It is unclear what prevention is referred to here. Please review intended meaning and language.
Response: Thank you for your comments. We have accepted the comment and revised the sentences accordingly. (see page 13 line 27-29 and page 14 line 1-2)
Comment 8: Conclusions
i) pg 14 line 18-20 "a risk score calculation based on a combination of antenatal factors was effective but had a lower accuracy than the model-based approach." I find no reference to this in the results or discussion and am unsure what this refers to.
Response: We found out that your question is very interesting. Though it was not stated this in the result section, we investigated whether simplified risk score calculation representing the optimum prediction or a prediction model by original β coefficients. We found that the AUC of the simplified risk score prediction model was 0.808 (95% CI: 0.705 to 0.90) and the final reduced model by original β coefficients was 0.884 (95% CI: 0.822 to 0.937). We have also checked the calibration test which indicates indicating the reduced model using original β coefficients more represented represent the data than the simplified risk score prediction model. As the AUC of both model greater than 50%; we believed both are effective but the simplified risk score prediction model had lower accuracy than a prediction model by original β coefficients. For more clarity, we have added sentences for the value of the simplified risk score prediction model. (See page 9 line 12-19 and Figure 1A and 1B)
ii) The one objective was to develop a model, but the implications of the risk factors identified as significant are not explored or the utility of the 'model' not discussed.
Response: We agreed on your comment without any reservation. We have made a major revisions on the discussion section to more explored the prediction model and its implications. (see the entire discussion section).

Reviewer: 2 (Costantino Di Carlo)
Comment 1: Postpartum oral glucose testing (pptOGTT) is a crucial point for the early detection of glucose intolerance in women who suffered GDM during pregnancy. There is a high percentage of these women that will develop Type Two Diabetes (T2D), an important medical condition. To predict which women are at a higher risk to result positive at the pptOGTT is important in view of the attention to pay for the execution of the test during the 6-12 weeks post-partum. Indeed, previous literature has shown a worldwide low adherence to this test for women diagnosed with GDM during pregnancy.

Response: Thank you for your comment. Currently literatures revealed that there is high subsequent diabetes mellitus after GDM. Regarding the adherence for post-partum glucose test, off course there is poor adherence in other literature however, it was good for our study. It was happening due to frequent contact and closely following of study participants from pregnancy to postnatal period and sending a reminder for postpartum oral glucose testing.
Comment 2:This study demonstrates that conditions such as maternal age, high fasting plasma glucose level at diagnosis, overweight/obesity and, surprisingly antenatal depression were predicting factors for positive PPT OGTT.
Response: Yes, we found antenatal depression was a predictor for postpartum glucose intolerance. Thus, it highly recommends getting more attention for GDM patients with a comorbid situations of antenatal depression.
Comment 3: I consider the examined topic relevant and interesting. In comparison to the previously published literature this paper gives a significant analysis of the main risk factors for the development of type two diabetes. Moreover, it adds antenatal depression as a condition that strongly expose women to postpartum glucose impairment.
Response: Thank you for appreciation regarding our paper.
Comment 4: The paper is well written, with a clear text, easy to read. Tables are useful to immediately understanding the paper results.
Response: Thank you for appreciation regarding our paper.
Comment 5:The only limit of this study is the limited number of examined cases. Unfortunately, this number is too little to lead to strong conclusive considerations. This should be more clearly stated by the authors.
Response: Thank you for your comment. We described as limitation. (see page 14 lines 24-29 and page 15 lines 1-2)

Reviewer: 3 (A/Prof Alice Richardson)
Comment 1: In this paper, the authors have conducted a cohort study of women with GDM. The research question was: what are the predictors of post-partum glucose intolerance in this cohort? The protocol for this study has already been published and so the imperative to publish the results is strengthened. Below I will elaborate on the two items in the Review Checklist where my response was “No”. They are of a largely minor nature and so I recommend that the paper undergo minor revision before resubmission.
Response: We thank you for your comments. All comments have been accepted and corrected accordingly.
Comment 2: Q7:
i. The statistical analysis is a classic series of univariate tests followed by a multivariate logistic regression. However, the authors should explain the multiple images in Figure 1, going into more detail than is currently in place on page 10 lines 12 – 14.
Response: Thank you for your comment. In Addition to we fitted the multivariate logistic regression to identify the risk factors, we have also fitted the model accuracy of by combined each significant variable and each independent significant variable separately to predict postpartum glucose intolerance. We believed this prognostic risk prediction approach was very important to predict the future occurrence of the outcomes. For this reason, the discriminative power of predictable variables for postpartum glucose intolerance and to check model accuracy, we computed the area under the ROC curve (discrimination) and calibration plot (calibration) and estimated as the area under the curve (AUC) with 95% confidence interval.
Regarding the multiple images in Figure 1, it is R software output during ROC curve analysis.
The ROC curve (left up described the area under the ROC curve (AUC) of the model (discrimination performance), all other images indicated the model accuracy. It has been described in the method and result section. Additionally, based on your comment below about the risk score prediction model; we have revised Figure 1 by complied the area under the ROC curve (AUC) of the model (discrimination performance) selected the AUC curve only (to avoid redundancy of multiple images).

Therefore, we revised figure 1 as final reduced prediction model (Figure 1A) and the simplified risk score prediction model (Figure 1B). We have also revised the sentences as follows " The area under the ROC curve (AUC) of the final reduced model was 0.884 (95% CI: 0.821 to 0.939). The calibration test had a p-value of 0.759, indicating the model does not misrepresent the data (Figure 1A). Rounding of all regression coefficients in the reduced model to 1 point resulted in a simplified prediction score presented in table 2. The AUC of the simplified risk score prediction model was 0.808 (95% CI: 0.705 to 0.90). The calibration test had a p-value of 0.044, indicating the model less represent the data (Figure 1B). Since the simplified score had a lower prediction accuracy than the model that used the results of the original β coefficients, we prefer to use the original β coefficients." (see Method section page 6 line 16-24, result section page 9 line 12-19 and Figure 1A and 1B)

ii. It looks odd to see probabilities presented as numbers larger than 1 in Table 3. The authors should either declare these to be percentages or write the probabilities as numbers between 0 and 1.

Response: Thank you for your comment. To avoid confusion, we have added the % (95% CI) in the first row of the Table 3. (See page 11, Table 3)

iii. I find the construction of the "easily applicable postpartum glucose intolerance prediction score" (page 7 line 14) to be unclear and possibly introducing unacceptable rounding error into the construction of the score. The risk score is referred to again in the Conclusion but it hasn't really been fully teased out in the paper. The authors should consider providing an example of the score and/or an equation with the coefficients used clearly indicated. A similar equation for the regression model already appears in the caption of Figure 1.

Response: We found out that your question is very interesting. We have added more sentences and Figure 2 to show clearly the risk score prediction model. In addition to our response for comment 2i; the equation with the coefficients for both final reduced prediction model and the simplified risk score prediction model at the caption of figure 1 as follows "Figure 1. ROC curve for prediction of postpartum glucose intolerance using different models: A. Linear predictor model for estimated risk of postpartum glucose intolerance = 1/(1+exp-(-11.87007) +1.48 * age (≥35 years)+1.716*overweight and/or obesity (MUAC ≥ 28CM) + 0.081* FPG at diagnosis + 1.637* antenatal depression (yes) B. Simplified risk score predictor model for estimated risk of postpartum glucose intolerance = (age ≥35 years*4) + (overweight and/or obesity (MUAC ≥ 28CM)* 4) + (FPG at diagnosis*1) + (antenatal depression*5)"

(see page 9 line 12-29, and Figure 1A and 1B)

Comment 3: Q10: Page 15, line 2, the authors need to consider carefully the use of the word "chance" here. Do they mean chance or odds or indeed odds ratio, bearing in mind that the outcome here is not rare (about 20%) and so odds cannot be conflated with chances in these circumstances.

Response: Thanks for your comment. We do respect your comment. Though the outcome showed was 21.4% which was about 20% but the lower limit ranges 14.3% and the limited number of examined cases.

Comment 4: Finally, minor typos and items requiring clarification:

Page 4 line 4. The term "introduced" does not seem to make sense. Should it be "predicted"?

Response: The comment has been accepted and corrected.

Page 4 line 15. "Literature" needs to be cited here.

Response: The comment has been accepted and corrected. We have revised this sentence.

Page 4 line 29. "presently" not "present". Page 13 line 15: should "Brazilin" be "Brazil"?

Response: The comment has been accepted and corrected.

Page 6 line 29-30. Variables are not parametric or non-parametric, the statistical methods used to analyse them are. Please replace with "Normally distributed and non-normally distributed variables".

Response: The comment has been accepted and corrected.

FORMATTING AMENDMENTS (if any)

Required amendments will be listed here; please include these changes in your revised version:

- Split figures 1-3:

Kindly split your Figures 1-3 to have one single figure each and upload it under file designation "Image". Figures can be supplied in TIFF, JPG or PDF format (figures in document, excel or

powerpoint format will not be accepted), we also request that they have a resolution of at least 300 dpi and 90mm x 90mm of width.
Response: We have splitted all figures separately and we have used PDF format.
Additionally, all other technical issues, sentence and grammar errors have been addressed.
Thank you for your valuable comments!
The Authors

References

D'ORAZIO, P., BURNETT, R. W., FOGH-ANDERSEN, N., JACOBS, E., KUWA, K., KÜLPMANN, W. R., LARSSON, L., LEWENSTAM, A., MAAS, A. H. & MAGER, G. 2005. Approved IFCC recommendation on reporting results for blood glucose (abbreviated). Clinical chemistry, 51, 1573-1576.
HOD, M., KAPUR, A., SACKS, D. A., HADAR, E., AGARWAL, M., DI RENZO, G. C., ROURA, L. C., MCINTYRE, H. D., MORRIS, J. L. & DIVAKAR, H. 2015. The International Federation of Gynecology and Obstetrics (FIGO) initiative on gestational diabetes mellitus: a pragmatic guide for diagnosis, management, and care. International Journal of Gynecology & Obstetrics, 131, S173-S211.

VERSION 2 – REVIEW

REVIEWER	Dr Deidre Mason Tygerberg Hospital and University of Stellenbosch South Africa
REVIEW RETURNED	07-May-2020

GENERAL COMMENTS	I appreciate the lengths the researchers went to, to adjust the concerns raised in the previous review. However, there is still some editing necessary to bring the English language used, to a publication standard. Errors were found especially in the new additions to the articles. The science is sound and I think a formal language review will make this research publication-ready.

REVIEWER	A/Prof Alice Richardson Australian National University, Australia.
REVIEW RETURNED	04-May-2020

GENERAL COMMENTS	The authors have satisfactorily addressed the points raised in my first review of this paper in regards to Figure 1 and Table 3 and i am recommending that the paper be acccepted for publicaiton subjec to the minor items referred to below. The authors have persisted with their rounded coefficients described on page 7, lines 20 - 22 to construct the "simplified risk prediction score model" (page 10 line 21) which unsurprisingly does not perform as well as the model that used the results of the original beta coefficients. I am content for the paper to be accepted for publication with the two models compared in this way and with this result. Nonetheless I still fail to see why the simplified model should be a realistic competitor to the original. A few minor typos remain: Page 3 line 6: should read "modestly predicted by postpartum …" Page 4 line 9: should read "It is anticipated that our setting …" Page 4 line 30: take out the comma after "Whereas …" Page 14 line 18: should read "two existing pieces of evidence …." Page 17 line 16: should read "cohort study involving …"

	Page 17 line 21: should read “Though WHO recommend that in settings where laboratories or proper storage and transport ...”

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1 (Deidré Mason)
Comment 1: I appreciate the lengths the researchers went to, to adjust the concerns raised in the previous review. However, there is still some editing necessary to bring the English language used, to a publication standard. Errors were found especially in the new additions to the articles. The science is sound and I think a formal language review will make this research publication-ready.
Response: We have made major revision on language issue and proofreads has been done on the manuscript.
Additionally, all other technical issues, sentence, and grammar errors have been addressed.
Thank you for your valuable comments!
The Authors

Reviewer: 3 (A/Prof Alice Richardson)
Comment 1: The authors have satisfactorily addressed the points raised in my first review of this paper in regard to Figure 1 and Table 3 and i am recommending that the paper be accepted for publication subject to the minor items referred to below.
Response: Thanks for your appreciation.
Comment 2: The authors have persisted with their rounded coefficients described on page 7, lines 20 - 22 to construct the “simplified risk prediction score model” (page 10 line 21) which unsurprisingly does not perform as well as the model that used the results of the original beta coefficients. I am content for the paper to be accepted for publication with the two models compared in this way and with this result. Nonetheless I still fail to see why the simplified model should be a realistic competitor to the original.
Response: We found out that your question is very interesting. As we already clearly respond in the previous review, we investigated whether the simplified risk score calculation representing the optimum prediction or a prediction model by original β coefficients. We found that the AUC of the simplified risk score prediction model was 0.808 (95% CI: 0.705 to 0.90) and the final reduced model by original β coefficients was 0.884 (95% CI: 0.822 to 0.937). We have also checked calibration test which model using original β coefficients indicating the model does not misrepresent the data (as the calibration test had a p-value of 0.759) than the model using simplified risk score indicating the model less represent the data (as the calibration test had a p-value of 0.044). As the AUC of both models greater than 50%; we believed both are effective but the simplified risk score prediction model had lower accuracy than a prediction model by original β coefficients. Thus; we more prefer to use the prediction model using the original β coefficients.
For more information about calibration of the area under the ROC curve; a calibration slope was interpreted as: non-informative (slope ≤ 0.5), poor calibration (0.5 < slope < 0.7) and good calibration (slope ≥ 0.7)(Pepe et al., 2008, Janes et al., 2008)
Comment 3: A few minor typos remain:
Page 3 line 6: should read “modestly predicted by postpartum …”
Response: The comment has been accepted and corrected.
Page 4 line 9: should read “It is anticipated that our setting …”
Response: The comment has been accepted and corrected.
Page 4 line 30: take out the comma after “Whereas …”
Response: The comment has been accepted and corrected.
Page 14 line 18: should read “two existing pieces of evidence ….”
Response: The comment has been accepted and corrected.

Page 17 line 16: should read “cohort study involving …”
Response: The comment has been accepted and corrected.
Page 17 line 21: should read “Though WHO recommend that in settings where laboratories or proper storage and transport ...”
Response: The comment has been accepted and corrected.

References

JANES, H., PEPE, M. S. & GU, W. 2008. Assessing the value of risk predictions by using risk stratification tables. Annals of internal medicine, 149, 751-760.
PEPE, M. S., FENG, Z., JANES, H., BOSSUYT, P. M. & POTTER, J. D. 2008. Pivotal evaluation of the accuracy of a biomarker used for classification or prediction: standards for study design. Journal of the National Cancer Institute, 100, 1432-1438.
PEPE, M. S., FENG, Z., JANES, H., BOSSUYT, P. M. & POTTER, J. D. 2008. Pivotal evaluation of the accuracy of a biomarker used for classification or prediction: standards for study design. Journal of the National Cancer Institute, 100, 1432-1438.