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Journal Name:	<u>Journal of Advances in Medical and Pharmaceutical Sciences</u>
Manuscript Number:	2014_JAMPS_15296
Title of the Manuscript:	Interobserver agreement for Pap smear and visual inspection tests in southern Brazil
Type of the Article	Original Research Article

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This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound.

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PART 1: Review Comments

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
Compulsory REVISION comments	The abstract, title and parts of the Introduction should be revised for English. There are numerous examples of poor English. Examples: Title should read: <i>Interobserver agreement between Pap smear and visual inspection tests in southern Brazil</i> rather than <i>Interobserver agreement for Pap smear and visual inspection tests in southern Brazil</i> In regards to the title, since this was only done in one facility, the title should be revised to read 'a location' or 'a facility' in Southern Brazil rather than 'in southern Brazil, since the results do not apply to all of southern Brazil The abstract needs a rehaul to flow better and provide a more complete picture of the study,	A language revision was made. Actually, the agreement is not between the tests but between observers within each test. To clarify this, we changed the title to "Agreement between observers for Pap smear and visual inspection tests in Florianópolis, southern Brazil". We followed the suggestion. More details were added within the word limit. The authors believe that the



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	why it was done, what it revealed and what might be the implications. For example, the Aim should refer not only to testing the agreement between the tests, but why – to inform national policy makers on potential uses to incorporate VIT into CECAP programs in Brazil. Study design should be a full sentence: a prospective cross sectional study was conducted among consenting clients attending cervical cancer screening services at a facility in southern Brazil. Methodology should include who the clients were, how they were sampled, what was inclusion and exclusion criteria, and relation to HIV services (were clients recruited from care and treatment?) Methodology section is very unclear. Please detail how specimens were taken, where analysed, who did the analysis of each, what quality control measures were in place, how were the results of the specimens and VIT linked or analysed, and if applicable what inter rater reliability measures were conducted to make sure that these are gold standard	agreement is the main objective of the study, although it may be further used to inform policy makers in this area. However, the latter is more an implication of study results than an aim in itself in this paper. Done. All these elements are present in the methods section, now with new subheadings (e.g. Inclusion/Exclusion criteria), cf. lines 72-80). The information required is now clearly divided within subheadings of the methods section. The methods section describes in great detail who the observers were, the years of their work experience in the screening and the training they had for the purpose of the study. We also provided the information on the diagnostic criteria they followed for Pap smear and VIT.
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	measurements being compared. Results section: it is impossible to interpret the results if we do not understand the methodology. This kappa measures agreement between who and who, or between which measurement and which measurement? How do we know that these observers were standardized? Conclusion: the agreement between observers was good or the agreement between PAP and VIT was good? How did this compare with Kappas / agreement between PAP and VIT in other countries? Once this is clarified, the recommendation should be made more specific and realistic. This study was in one facility. The recommendation could be that the facility starts to employ VIT in conjunction with PAP, or that the facility and others start using both screening tests, or broader, like the MOH should consider further studies and incorporation of VIT in national strategy. Introduction: first sentence needs a reference. Not clear if that assertion is supported.	The agreement is always between observers within each method (Pap, VIT) as clarified in the study title and the section on study methods. The recommendation was followed (lines 306-309). Policy recommendations were made at the end of discussion. We substituted “most” with “many” to avoid the impression of having done an exhaustive counting of the countries worldwide.
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	In first paragraph, I do not agree that the major problem with PAP is errors associated with specimen collection and histopathology, rather availability of service (human resource and labs) and cost. Again, maybe because of English, it is not clear from the Introduction why this study was conducted. Is it to provide input to address national policy in regards to screening methods for CECAP programs nationally? To look at feasibility of changing this facility's screening program? Why did the study team embark on this study, and what relation does that have to INCA policy? Similarly, in regards to the final sentence of the Introduction: The aim of this study was to verify the interobserver agreement (IOA) in screening for cervical cancer by Pap test and VIT. Please state why the study was conducted. Why did the study team want to establish the IOA and what are the intended applications of the knowledge?	Actually, the authors did not state that the cited errors are major ones, only that these are among those often cited regarding Pap. A reference supporting this view has also been provided. The lack of human and laboratory resources is also mentioned as an obstacle to Pap screening. As explained earlier, the study aimed at examining the interobserver agreement as stated already in the title. The authors would be happy to provide wider policy implications but that would be another paper. Brazilian (INCA) recommendations do not include VIT, although we referenced another paper [12] which showed it would be a valuable addition to Pap screening in Brazil. In the penultimate paragraph of the introduction, we added that “Although interobserver agreement is an important component of diagnostic accuracy, there are very few studies on agreement between health professionals involved in cervical cancer screening with VIT, thus limiting the wider application of this method, particularly in the countries with limited resources” before formally stating the aim in the next paragraph.
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	Methods: the Methods section should more clearly state how measurements regarding suspect cancer were handled. Were clients presenting suspect cancer included in the analysis or dropped? Materials and Methods section: provide a bit more detail about the setting. This was a facility which had been providing PAP-based screening for how many years? Average client flow per year? Scheduled appointments or drop in? Regional hospital or small facility? Associated with HIV services? Useful to know more about the setting especially since this study was only conducted in one facility. Also, were all clients read the consent script and offered to be in the study? Only clients over 18? Notices about the study posted? Provide a bit more detail about the consent process and study recruitment. It was not clear to me from the Abstract and the Intro what was being compared (it should be). From the Methods, I understand that PAP was collected by a nurse and the comparison, with outcome negative and positive, is between 3 laboratory-based readers. For the VIT, it is conducted by a nurse followed by a gynecologist, also comparing negative to	No, they were not included. See the new subheadings on inclusion/exclusion criteria. More details were added (lines 58-61, 63). This is a low risk population as mentioned in the 1st paragraph of the methods and repeated on lines 69-71. We believe that previous comments have clarified the issue. Specimen collection and diagnostic procedures have been re-organized. A comparison of diagnostic performance of both Pap and VIT regarding histological examination as gold standard has already been published and referenced in the text
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	positive (no reference to findings of suspect cancer or large lesions). If I understand correctly, then, this analysis does not compare Pap classifications to VIT classifications. This significantly reduces the relevance of the analysis. For policy importance (depending on the orientation of this article, which is not clearly articulated) the reader would want to be provided with a comparison of PAP versus VIT, or at least have a table which looks into the sensitivity and specificity of PAP vs. VIT in this setting. This could then be expanded in the Discussion to talk about scale up in this facility or policy-wise. In the Methods, be more specific about data management: data from client individual records was abstracted and entered into STATA? Were study forms used or normal hospital records? Were any data quality measures conducted, such as double data entry?	[12] but is not the object of this paper. Done (line 148). No double data entry was performed but all suspicious values were double-checked. No other sources of patient information were used beyond those cited in the text.
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<u>Minor</u> REVISION comments	Introduction: Does INCA have a policy on screening which is different than every 3 years for women with HIV infection? Please define the ALTS study, where it was conducted and state why it is being presented – did it have similar aims of the current study? This sentence needs a reference: Visual inspection techniques (VIT) have been amply piloted in Asian and African countries with limited resources where the access to Pap test screening is often difficult and women health prevention programs are precarious. Consider Sangvi for Thailand, Grosskurth for Zambia. Also, change to ‘access to Pap test is limited.’ In addition to the references on agreement between tests, please include Sue Goldie’s comparison of the agreement between visual inspection and PAP In regards to this sentence...medical professionals of varying background in order to capacitate them for cervical screening, which is an important shortcut in places with the lack of	Yes, INCA recommends annual Pap test for people with HIV. However, these were excluded from the present study as stated in the exclusion criteria. This paragraph was removed as suggested by another referee. Done (line 46). Included as reference [4]
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	trained screening professionals... most programs in developing countries are using nurses, please refer to this directly. And it is not a shortcut, it is a health systems approach which is both effective and appropriate in countries with a human resource shortage and constraints on histopathology infrastructure...is this not the case in Brazil? In regards to this sentence... However, intensive initial training and periodic refreshment and/or upgrade courses are necessary to ensure effectiveness of this strategy... a reference was provided to one example in Asia. I do not believe that the literature provides ample examples of the need for refresher / upgrade courses for CaCx screening compared to other public health interventions. Either make this clear that this is one example from one country or find more examples to support this statement from the literature.	The authors fully agree, this is the case in Brazil. Another reference was added under [9]. Other studies [8] conclude along these lines and the authors of the present study share this view.
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<u>Optional/General</u> comments	The abstract of this paper must be re-written. Most readers will only go as far as the abstract and so it must be concise and well-written – the abstract as it currently stands is not publishable. Please refer to comments above. Overall, it is very hard to get a sense of why this study was conducted. What were the researchers hoping to achieve by conducting the study? A change in hospital policy? National policy? How do the results fit into the context of Brazil's cervical cancer screening efforts? How do they fit in with issues of integration, such as human resources, responses to HIV, health system capacity? Without this context, the results are interesting only to a very few readers. I would not recommend publishing this article if the authors cannot articulate the purpose of the study and its importance to cervical cancer prevention in Brazil and other settings.	The abstract was revised. The authors state explicitly the motivation and the aims of the study in the introduction. The focus is on a well known problem of interobserver agreement which has been much more frequent with Pap than VIT tests. It may seem a narrow focus but we explain in the first paragraph why it is an important component of validity. Policy implications are beyond the scope of this paper, although the main idea has been mentioned in the introduction and in the conclusion: if a satisfactory validity (of which interobserver agreement is an important component) of VIT can be confirmed, these tests could be more widely used in low-resource countries.
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