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Journal Name:	International Journal of TROPICAL DISEASE & Health
Manuscript Number:	2013_IJTDH_5724
Title of the Manuscript:	MODS culture for primary diagnosis of tuberculous meningitis and HIV-associated pulmonary tuberculosis in Indonesia
Type of the Article	Short Communication

General guideline for Peer Review process:

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.

To know the complete guideline for Peer Review process, reviewers are requested to visit this link:

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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	This kind of practical studies are important and this specific study seems to be well performed. However, the reviewer has a number of comments: 1. Methods: With the volumes of CSF obtained it seems as if this study was done in adults rather than children? It is important to include detail on inclusion criteria, especially age of the patients, in the study method, as TB in children is even more often paucibacillary and may yield different results 2. Results: The results are mostly presented as percentages only. This is confusing and inaccurate despite the fact that the authors state that this will be done in the methods section. The problem is that the denominator is NOT clear, especially taking into account Figure 1, which shows data only of 160 HIV-infected pulmonary TB cases and 85 TB meningitis cases, while there should be 167 and 88, respectively. With some calculations and interpretation the reviewer understands that this reflects the contaminated MODS	1. The reviewer is right that this study was done in adult TB meningitis patients. We have now added this information in the method section (line 78), which now reads "The second group consisted of adult patients (≥ 18 years old) with suspected TB meningitis." 2. Following the reviewer's comments about the presentation of the positivity rate of diagnostic tests we have now modified the second paragraph of the result section. We now present the exact number of positive results as well as the denominator (line 121-134). We also put additional information related to this issue in the legend of figure 1 (line 142-144).



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	cultures, but it should not be necessary for the reader to figure this out – data should be correctly presented. The reviewer recommends that in the results the exact numbers (of patients with positive cultures) and denominators should be provided (as the authors have done for the smear microscopy negative cases). It should be clear to the reader if any patients were not included in the final results – both number and reason for exclusion should be provided. The legend in Figure 1 should also explain how many and why patients were excluded. 3. The authors present stats for the time to culture positivity, but why not any statistical comparison between culture types' positive yields? 4. Lines 126-127: This statement, that cultures were done only on a single specimen from each HIV-infected patient suspected of having pulmonary TB, while microscopy for acid-fast bacilli by ZN method was done on all specimens should be clearly stated in the method section - it	3. We have added the statistical comparison of diagnostic methods compared in both group of patients in the result section in paragraph two (line 126, 132-133). 4. We understand this question. We have now clarified this issue in the method section line 71-72: "Direct smears were prepared from each sputum specimen for Ziehl-Neelsen (ZN) staining." and line 74-75: "For each patient,
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	should not surface the first time in the discussion! Currently the methods state that all remaining specimens were cultured. 5. Lines 129-134: This belongs in the methods section – the fact that the authors tried to make the methods concise now leads to explanations in the discussion which should definitely form part of the methods section	one sputum culture was made. Sputum specimens from patients who had provided ≥ 1 specimen were mixed before decontamination.” 5. Following the reviewer’s suggestion, we have now replaced this information from the discussion section and put it in the method section with slightly modification (line 85-91).
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<u>Minor</u> REVISION comments	1. Abstract: - First line: From the title it seems that the authors studied two patient groups – HIV-associated pulmonary TB and TB meningitis (not specifically associated with HIV). The reviewer was confused reading the aim in the abstract, as here it seems as if both groups were HIV-infected, which, from reading the aim in the manuscript, seems not to be the case. Maybe better to mention TB meningitis first as in the title? - MODS should be written in full before using abbreviation - It is not Ziehl-Neelsen microscopy, but microscopy of Ziehl-Neelsen stained smears 2. Methods: - Dates of study – which months of 2010-2012? - With the volumes of CSF obtained it seems as if this study was done in adults	1. Abstract We agree with the reviewer's suggestions: - First line (and also the second sentence in discussion section): we have now mentioned TB meningitis first as in the title, which now reads: "...for diagnosis of TB meningitis and HIV-associated pulmonary tuberculosis (TB)." - We have added " the microscopic observation drug susceptibility culture" before "MODS culture" - We have changed "Ziehl-Neelsen microscopy" to "microscopy of Ziehl-Neelsen (ZN) stained smears" 2. Methods We also agree with the reviewer's suggestions: - We have now added: "...February 2010 and January 2012..." (line 62) - We have added this information in the method section line 78
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	rather than children? It is important to include detail on inclusion criteria, especially age of the patients, in the study method, as TB in children is even more often paucibacillary and may yield different results - Line 53: a very minor point: if 5-10ml of fluid obtained, first tube 0.5-1ml, then second tube 4-10 ml, not 8-10ml? - Line 63: EQA – write out before abbreviating 3. Results: - line 77: Up to this point, authors use HIV-infected, but now use HIV-positive – it is best to use same terminology throughout the manuscript, unless difference is implied in which case both terms should be defined - line 78: “Most patients came with advanced HIV,...” Suggest adding “infection” to HIV (or disease), because HIV = virus only. - Line 81: 11% HIV-infected – please add exact number - Line 89: “and 3 respectively 8 patients were MODS-negative/Ogawa-positive” –	- We have corrected the volume from “8-10 ml” to “4-10 ml” (line 81) - We have written “external quality assurance” before “EQA” (line 100) 3. Results - The reviewer rightly points towards some inconsistency in the terminology. We have now used “HIV-infected” throughout the manuscript. - We have added “-infection” to HIV (line 116-117) - We have added the exact number: “9 patients (11%) were HIV-infected” (line 120) - We have changed the sentence to “...., and 3 and 8 patients, respectively, were MODS-
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	do they mean: “and 3 and 8, respectively, were ...”? - Figure 1: Change HIV-positive to HIV-infected PTB (as there are also HIV-infected patients in the TBM group, most likely not included here?) - Line 96: Using sputum from HIV patients (change to “HIV-infected”) - Line 98: “TB meningitis suspects”- this terminology is no longer “politically correct” – suggest change to “suspected TB meningitis patients” 4. Discussion: - line 110: ZN-microscopy not a method, rather microscopy of Ziehl-Neelsen stained smears - Line 117: MGIT – write in full and give company details, as this is a specific registered product - lines 121-122: compared with 2.4% respectively 0% using Ogawa solid culture – please change to: compared with 2.4% and 0%, respectively, using Ogawa solid culture - line 124: as shown by a study from Peru	negative/Ogawa-positive” (line 136-137) - We have changed “HIV-positive” to “HIV-infected” (line 141) - We have changed “HIV patients” to “HIV-infected patients” (line 146) - We have changed “TB meningitis suspects” to “suspected TB meningitis patients” (line 149-150) 4. Discussion - We have changed “ZN-microscopy” to “microscopy of Ziehl-Neelsen stained smears” (line 164-165) - We have written “Mycobacterial growth Indicator tube (MGIT, Becton Dickinson)” (line 173-174) - We have changed “...,compared with 2.4% respectively 0% using Ogawa solid culture.” with “..., compared with 2.4% and 0%, respectively, using Ogawa solid culture.” (line 180-181) - We have changed “..., as shown by the group in Peru.” with “...,as
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	(changed from “the group”)	shown by a study from Peru.” (line 183-184)
<u>Optional/General</u> comments		