



SDI FINAL EVALUATION FORM 1.1

PART 1:

Journal Name:	International Journal of TROPICAL DISEASE & Health
Manuscript Number:	2013_IJTDH_6809
Title of the Manuscript:	Bloodstream infections and malaria as causes of fever among adult medical patients at a referral hospital in Malawi

PART 2:

FINAL EVALUATOR'S comments on revised paper (if any)	Authors' response to final evaluator's comments
I raised a number of issues when I first reviewed the manuscript. Some of the issues I raised were methodological in nature. The authors' responses indicate that they were unable to carry out a number of important tasks that would contribute to the validity of the inferences they make in the manuscript. For example, there was no standardized protocol for what the investigating team should look for when examining patients that accepted to be enrolled into the study. It seems there was no standardized data collecting tool for collecting clinical data. This is repeated over and over in the responses from the authors of the manuscript. One would have wanted at a minimum the following information: - Duration of the fever - Associated symptoms with the fever e.g. dysuria, cough, weight loss, night sweats, constipation or diarrhoea, headache with photophobia etc - Physical findings on examining the patient - Comorbid conditions e.g. rheumatic heart disease, diabetes mellitus etc. these conditions influence the type of organisms that are likely to be - Provisional diagnosis on admission before the blood culture or malaria test results were known I did not look at data analysis when I last reviewed the manuscript. I was of the view that bringing in extra data would have affected the types of analyses that would be done. Unfortunately there are no improvements in this section. At least one would have expected analysis to include: - What was the effect of prior antibiotic use on culture results? In this regard the authors respond by saying that they needed to do blood levels. This need not be so. They could compare the positive blood culture yield between those that took antibiotics and those that did not. The same can be said about cotrimoxazole prophylaxis on blood culture and malaria test - What was the effect of prior antimalarial use on positive malaria tests? Was a positive malaria antigen test commoner in people that had taken antimalarials compared with the smear test?	We can only re-emphasize that in principal we agree with the reviewer. However, the main aim of our study was to determine the proportion of malaria and bloodstream infections among adult patients presenting with fever to a central hospital in Malawi. The main focus was therefore not the association of fever with other clinical conditions. We have explained what we were able to perform at KCH. At the time of the study it was not feasible to implement a standardized clinical data collecting tool. It was rather the intention of our operations research to underline the need for that and to start processes that would enable the department to answer the pertinent questions raised by the reviewer. The routinely captured information did not allow us to link in sufficient quality clinical data with the laboratory results. We may add that at the time of the investigation, there was a severe shortage of staff, no medical specialist, few experienced clinicians and nurses on the wards. Even regularly taking of temperature of patients on the wards was not done and/or documented for various reasons including lack of thermometers. That is why we focused on the laboratory part since this could be handled in a standardized way. We believe it is worth to report these data despite the admitted lack of corresponding clinical data. a) We would like to hold up the argument that in order to make firm conclusion on the effect of prior antibiotic use, blood levels of antibiotics would be necessary. We have however added the information on the proportion of patients with prior use of antibiotics among the patients with positive blood culture. (Three patients with bacteremia had taken antibiotics prior to hospital admission. One patient with <i>S. pneumoniae</i> took CPT, one with <i>Salmonella</i> Typhimurium took amoxicillin for six days and another one with <i>Salmonella</i> Typhimurium took an unspecified antibiotic for five days. See page 6, line 203) b) We added the information of the effect of prior use of antimalarials on the smear and antigen test results. (Among the 57 patients diagnosed with malaria twelve patients had reported prior use of a full course of antimalarial treatment. Seven patients took a full course of SP. Out of these four had both a positive smear and a positive RDT, two had a negative smear but a positive RDT and one had a positive smear but a negative RDT. Five patients took a full



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c. What was the effect of cotrimoxazole prophylaxis on a positive malaria test These issues and others raised earlier are very important if authors would like to make the inferences they have made in the paper. The discussion section of the paper dwells at length on the antibiotic and antimalarial practices at this hospital. Although these are important issue, the study is not an audit of these practices. One would really like to know the following: 1) If one is to work at Kamuzu Central Hospital in Lilongwe Malawi, and is faced with a patient with a febrile illness, what would be the likely diagnosis if they were HIV positive or negative? 2) What would be the likelihood that the patient in my consultation room with a fever has malaria or a blood stream infection? 3) If the patient has diabetes mellitus, rheumatic heart disease, HIV/AIDS what is the likely organism that will be isolated from the blood? 4) If a patient takes cotrimoxazole prophylaxis while on HAART, what is the likelihood that the patient will be suffering from malaria? 5) Which patients are likely to have dual pathology if they come with fever? 6) Does the duration of fever help in determining the likely diagnosis when considering blood stream infection or malaria. Unfortunately the paper is not able to address these in the current format.	course of LA. Out of these two had both a positive smear and a positive RDT. Another two had a negative smear but a positive RDT. One was smear positive but tested negative in the RDT. See page 5, line 170 and page 8 line 287). c) Only five patients were on CPT - a far too small number to draw any inferences. We added the following comment: The number of observations in patients using cotrimoxazole as prophylaxis was too small to allow any conclusion on the potential effect. See page 8 line 264. Out of these five patients on CPT one had a bloodstream infection with <i>S. pneumoniae</i>. The other four had neither a bloodstream infection nor malaria. We also believe that we are very cautious in making inferences from our data and remain mainly descriptive and therefore based on the available data we cannot answer the questions 1 to 6. Our current study has stimulated the process to start long term surveillance at KCH. That will eventually allow answering these important questions.
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