Reviewer's report

Title: Mortality after Inpatient Treatment for Diarrhea in Children: a Cohort Study

Version: 0 Date: 24 Oct 2018

Reviewer: Matthew O. Wiens

Reviewer's report:

This study examined post-discharge mortality among children who were admitted with diarrhea from a single hospital in Kilifi, Kenya. This is an important study in an area of pediatric global health, and one that has received relatively little attention over the past several decades. Despite and excellent rational, what appears to be high quality data and a strong methodology, I have several comments that may improve the overall quality of this manuscript.

Intro:

Overall, the introduction reads well and makes a logical argument to justify the study.

There is a claim that diarrhea is "reported to be associated with increased risk of post-discharge mortality in several settings in resource poor countries". This is not referenced. Increased compared to what group? Perhaps the relevant reference can be added in here. This is important since the results of this study show diarrhea not to be associated with an increase in risk compared to a "reference" population of hospitalized children. The SLR that is referenced mentions 3 studies, reporting only 1 study which shows diarrhea as a risk factors for post-discharge mortality (compared to malaria).

The introduction also states that "This review also identified 5 papers examining diarrhea as one of several risk factors for mortality after general pediatric admissions: 3 from Kenya, one from Guinea Bissau and one from Uganda.[1, 2, 9-11]" I'm not sure I'm following this exactly. Reference 1 is not included in the review, but does address diarrhea as a risk factor. Reference 11 is not a study on post discharge mortality. Of reference 2, 9 and 10, only reference 10 shows diarrhea as a risk factor (but in this case compared to Malaria). There is no study from Uganda showing diarrhea as a risk factor

Methods:

This study is examining first and foremost post-discharge mortality. All analyses of this outcome include only the KHDSS population. Why then do you even include the non-KHDSS children in this analysis?
This study almost reads like it was designed as a prospective cohort, yet it appears to have been a retrospective cohort analysis, using what appears to be routinely collected clinical data, linked to a community surveillance program. Perhaps more clarity can be provided as to what exactly subjects were consented for and how this particular analysis fits into the broad Kilifi Surveillance program. How was quality assured?

It is clear that non-KHDSS subjects fared much worse than KHDSS subjects (nearly double in-hospital mortality). Since all the post-discharge outcomes are in the KHDSS populations it thus makes sense to keep this population the focus of both pre and post-discharge analyses (including non-diarrhea comparisons).

Does it not make sense to compare diarrhea as a risk factor against other sensible disease groups, rather than a mix of all other subjects who did not have diarrhea? Since this is meant to inform practice and research in other areas, many of which have different underlying populations (i.e. different prevalence of other illnesses), I think that the authors should consider categorizing the non-diarrhea admissions for the purposes of comparison.

Several continuous variables were analysed as a dichotomous variable (like SpO2, Temperature, RR, HR, etc.). I think that perhaps it may make sense to utilize all the available data by analyzing these as continuous variables (age adjusted if necessary). For the variable of hypoxemia, for example, there were only 2 cases (in the post-discharge analysis), but if measured continually, this will increase the power of this analysis.

**Results:**

With the stark effect of KHDSS status on in-hospital outcomes, it really does not appear to make sense to include the non-KHDSS group in this analysis given the lack of post-discharge information (which is the ultimate purpose of this paper). It is possible that being a resident of the KHDSS population may have an interacting factor on other variables, making the entire in-hospital analysis difficult to interpret when these groups are combined, as they are. While it does add numbers, and statistical power, it also makes this paper a little more confusing to read and interpret.

Is the location of death available in this dataset? Several studies have shown that most post-discharge deaths occur outside of health facilities/hospitals and it would be interesting to see this data presented here if it is available.

As mentioned earlier, the comparison of diarrhea vs no diarrhea may not be the most ideal comparison. Consider have diseases specific comparisons. Related to this, Table 1 contains no data on diagnoses (other than HIV and malaria testing). Is this data available? What about co-morbidities?

The statement that post-discharge mortality was associated with SAM, but not MAM, is perhaps a little misleading. Categorizing children as SAM or MAM automatically reduces the analytic power of the analysis of anthropometry, compared to utilizing continuous data. In fact, in the
multivariate model, MUAC, as a continuous variable, was highly significant. This suggests a continuum of increasing risk as MUAC decreases. While I have no objection of the supplemental table, perhaps focusing on the primary results (i.e. those reporting MUAC) is ideal.

This study developed a predictive model for assessing risk for post-discharge mortality among children admitted with diarrhea. It would be helpful to include the regression equation for this model so that others can utilize this work from a validation perspective.

Discussion:

When was the rotavirus vaccine introduced in the Kilifi area? This was thought to be a factor in the relatively low rate of post-discharge mortality.

The concluding paragraph included the statement about SAM, but it was MUAC that was included in the main multivariable analysis, so consider rewording to include MUAC.

If the non KHDSS area is to be included in this analysis some discussion as to why the in-hospital outcomes were so different should be included.

The fact that this analysis developed a predictive model is important and should be reflected in the discussion. Validation is needed if this is to be used clinically. Also a practical method of risk stratification would be needed. Also, some discussion around the kinds of work needed to develop an effective intervention should be discussed.

Thank you for allowing me to review this interesting manuscript.

Sincerely,
Matthew Wiens, PhD

Are the methods appropriate and well described?  
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?  
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?  
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