Author’s response to reviews

Title: Compliance with Referrals for Non-acute Child Health Conditions: Evidence from the Longitudinal ASENZE Study in KwaZulu Natal, South Africa

Authors:

Omolara T Uwemedimo (omolara.thomas@gmail.com)
Stephen M Arpadi (sma2@columbia.edu)
Meera K Chhagan (chhaganmeera@gmail.com)
Shuaib Kauchali (kauchalis@gmail.com)
Murray H Craib (asenze.director@gmail.com)
Fatimatou Bah (fb2201@columbia.edu)
Leslie L Davidson (lld1@columbia.edu)

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Author’s response to reviews: see over
We are pleased to re-submit the revised manuscript entitled “Compliance with Referrals for Child Health Services: Evidence from the Longitudinal ASENZE Study in KwaZulu Natal, South Africa” for consideration for publication in BMC Health Services Research. We have included a point by point response to the comments posed by each reviewer on the following pages.

In this paper, we report the relationship between compliance with referrals to child health services for sub-acute, chronic conditions and socio-demographic factors within the ASENZE study, a longitudinal study conducted in KwaZulu Natal, South Africa.

Within sub-Saharan Africa, there has been a notable increase in the burden of chronic conditions among pediatric populations. An effective referral system is an integral component to ensuring improved health outcomes for these conditions. While many studies have evaluated factors associated with referral compliance for acute, life threatening conditions affecting young children in sub-Saharan Africa, no studies, to our knowledge, have evaluated referral compliance for sub-acute chronic conditions in this population. This is of great importance, since management of chronic conditions is heavily reliant on well-functioning referral systems that allow a child to move from screening to treatment with ease, thereby resulting in improved quality of care, decreased healthcare expenditures and most importantly, better health outcomes. In this study, referral compliance was high for HIV infection and anemia, but lower for vision problems, hearing or ear problems, anemia and developmental delay. After controlling for significant socio-demographic factors, referral compliance increased with higher household educational attainment and stable caregiving.

The BMC Health Services Research audience will benefit greatly from these findings and may be able to integrate this information to support further research investigating other potential determinants of compliance with child health services, such as caregiver knowledge and attitudes about the health system and infrastructure of the health system. This study may also highlight possible at-risk groups for poor compliance with referrals in disadvantaged African communities, although further research is needed to explore these relationships.

The contents of this research are the sole responsibility of the authors and do not represent the official views of the funding agency. This research study was approved by the Columbia University Medical Center Institutional Review Board and the Biomedical Research Ethics Committee of University of KwaZulu-Natal, Durban, South Africa. Each of the authors has contributed to development of the concept/design, data analysis, interpretation of data, drafting and/or revising this manuscript. Additionally, all authors have reviewed and approved the manuscript as submitted. The authors have no conflicts of interest or financial disclosures. This manuscript has not been published nor is being considered for publication elsewhere.

Thank you for your time and consideration. Please contact me by telephone (212-305-6227) or electronic mail (Ouwemedimo@nshs.edu) if you have any questions.

Sincerely,

Omolaru Thomas Uwemedimo, MD, MPH
Assistant Professor of Pediatrics
Division of General Pediatrics, Hofstra North Shore-LIJ School of Medicine
Responses to reviewer comments

Reviewer 1 (Ogunlesi)
(a) "Child Health Conditions" in the title should be replaced with "Childhood Disorders"
   - Due to the fact that not all of the medical problems that were assessed would fall under a clear diagnosis, we chose to use the less rigid term of conditions rather than disorders.

(b) Authors need to harmonise the nomenclature used in the manuscript: "sub-acute" is NOT the same as "non-acute"
   - The term sub-acute was replaced with non-acute in the Background section.

(c) Abstract: In the conclusion, "...Household education level and stability .......may be associated with referral....." 'be associated with' should be replaced with 'influence'
   - The term may be associated was replaced with influenced in the conclusion section of the abstract.

(d) Methods: Grading of educational qualification should be described. It may be confusing to generally accept "anaemia" as a non-acute condition. Severe anaemia is definitely an emergency. Therefore, authors need to specify what severity of anaemia is under focus in the manuscript.
   - The term “mild” was used to categorize the anemia, to clarify its categorization as a non-acute condition

(e) Discussion: For this manuscript to be useful to clinicians and health policymakers, authors need to suggest practical ways of tackling the identified impediments to compliance with referral. Although, the research did not apparently seek to find out why respondents did not comply with referrals but issues like distance, cost, stability of health services particularly in terms of closures during industrial disputes should be highlighted. This should provide a guide for subsequent studies of this nature.
   - We have alluded to our plan for future work regarding these very important factors in the conclusion section of the abstract and the manuscript. We agree with the reviewer that this is extremely important and are planning on putting these analyses forward in a subsequent paper.

(f) In Table 3, why was "Child gender" include in the logistic regression model since bivariate analysis didn't suggest any relationship with gender.
   - The authorship team apologizes for the oversight, as the row with child gender in Table 3 was not omitted although it as not included in our analysis.

Reviewer 2 (Simba)
ABSTRACT
1) The abstract will be informative if authors will outline the sampling method.
   - The sampling method is now clearly outlined in the results section of the abstract.

2) Author reports high referral compliance for HIV infections. Authors need to explain why children with HIV infections required referral if they did not have AIDS complex.
   - The results section of the abstract also explains that children received a positive HIV test and were referred for further evaluation (which would include HIV staging and assessment of need for antiretroviral therapy).
3) In the conclusion part of the abstract the authors recommend for further research to examine whether other factors such as caregivers knowledge are determinants of referral compliance. Authors need to explain why these important factors were not studied and in the absence of these factors what is the validity of multivariate models they presented in the findings?

The conclusion of the abstract also notes that the study team is in the midst of ongoing analyses to assess the impact of other possible determinants as outlined.

METHODS

The authors state in page 3 line number 45/46 that, ‘a door to door survey of all households in five contiguous isiZulu tribal areas was conducted’. The authors need to explain how this area was selected since this has serious implication on the generalization of the findings. Page 3 line number 46 states that ‘all 4-6 year old were invited to a comprehensive medical and developmental assessment’. Authors need to state how they established the age of the children.

The methods section now includes information regarding the reasoning behind the selection of the cohort in paragraph 1(pg5 lines 20-22) and age determination techniques, found in paragraph 2(pg6 lines 3-4)

In addition, inviting all children from a household would result into clustering effect in which households with more children are overrepresented. How was this effect addressed by the authors? Author need to also explain how this limitation might influence their results because poorer households are more likely to have more children.

We did not control for the clustering effect, so we report this as a limitation on page 14 line 11-13. We did conduct bivariate analyses to look at any associations between number of children in household and referral compliance and number of children in a household and poverty. Neither of these relationships were significant, so we felt slightly reassured by these findings. Although to truly be sure, we should have run a generalized random effects model.

About 12% of the children/caretakers did not consent for Phase 1. In the African setting the proportion is quite high. Authors need to explain the reasons for and the implication on generalization of the findings.

Lastly, in most research settings a rate of up to 15%, while not ideal, is tolerated for many studies performed in Africa. A simulation study by Kristman, et.al. in 2004 was the first that compared the bias associated with varying degrees of loss to follow-up across different missing data mechanisms. Considerable bias associated with non-random loss to follow-up was only found once loss to follow-up rates approached 20% or more (Kristman V., Manno M, Cote P. European Journal of Epidemiology 19: 751–760, 2004.)

In page 4 line 9 / 10 authors report of ‘HIV counseling … to all participants.’ Since participants were of children aged 4-6 years. Authors need to explain how the consent was administered and the ethical implication.

Line 13-14 on page 6, discusses the procedure of signed parental consent for HIV testing since the children were too young for consent or assent.

RESULTS

Page 6 line number 7 / 8 authors state that children were referred to local health clinics and a third to regional hospitals. Studies have reported different referral patterns (factors) level of care provision (primary level facilities versus hospitals). Authors need to explain how this limitation influenced the findings from their research.
This issue regarding possible effects on compliance by place of referral was not taken into consideration and is now identified as a limitation in our analyses in the final paragraph of the discussion. (pg14, line8-9)

**DISCUSSION**

The cut-off point for referral of conditions such as anaemia was Hb <10 g/dL. Authors need to discuss this in the context of the general population because the level might be perceived to be too high for caretakers to comply with referral and for referral facilities to take action.

South Africa standard treatment guidelines for primary health care (PHC EDL) recommend treating this age group at PHC if Hb below 10 and otherwise asymptomatic and following up in 2 weeks. We referred to a PHC for basic treatment rather than a referral to higher level of care, which we have addressed.

Page 4 line 16/18 authors report giving instructions to caregivers on the referral. However, chronic conditions that were referred are normally asymptomatic. Caregivers required health education on the conditions rather than instructions prior to referral. Health education was certainly performed during the Phase 1 referral and not just instructions for referral. It is now documented on page 6, lines 20-21.

Authors need to also discuss how the referral process might have influenced the compliance rate..

The artificial nature of referring from a research facility and the influence on compliance rates as a limitation to our study was addressed in the final paragraph of the discussion. (pg 14 lines 13-16)

Reviewer 3 (Peterson):

1) The recruitment and Phase 1 (n=1581) and Phase 2 (n=1078) is not clear to me after reading twice. Please make this clearer

   We have attempted to clarify the methodology of recruitment and the sampling on pg 7, lines 9-11.

2) Also where did the assessment take place - at household level, or at some later point in a facility??

   The Methods section and Figure 1 now clarifies the site of assessment on pg 6, lines 4-10. The Phase 1 assessment took place at our study facility within 2 weeks of an initial household visit (n=1581) and the phase 2 assessment occurred 18-24 months later at our study facility (n=1078).

3) Relatedly, is this therefore a community to First level facility-referral, or a facility to hospital/corresponding referral.??

   The place of referral by type of referral has now been added to pg 8, lines 17-22

4) In Table 2 the ORs seem to be alternatively expressing "compliance" or "non-compliance", as judged by comparing Percentages and ORs between reference category and comparator (eg. first section on age where >5 years has lower completion proportion, and yet OR=1.32. Yes "same caregiver" shows the opposite pattern
Table 2 has been fixed to show concordance between percentages and ORs between reference category and comparator. It was typed incorrectly.

5) Please clarify timeframe to assessment - is this completion within X months of first referral? Paragraph 5 of the METHODS section, states that the timeframe between referral from phase 1 assessment and phase 2 follow-up is 18-24 months. (pg 7, lines 10-11)