PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Comparative effectiveness of injectable penicillin versus a combination of penicillin and gentamicin in children with pneumonia characterised by indrawing in Kenya: A retrospective observational study.
AUTHORS	Malla, Lucas; Perera, Rafael; McFadden, Emily; English, Mike

VERSION 1 – REVIEW

REVIEWER	Tor Strand Innlandet Hosptial Trust Norway No competing interest
REVIEW RETURNED	27-Sep-2017

GENERAL COMMENTS	The updated version reads well.

REVIEWER	Lilliam Ambroggio Cincinnati Children's Hospital Medical Center
REVIEW RETURNED	29-Sep-2017

GENERAL COMMENTS	Malla et al. present a statistically robust study investigating IV penicillin versus penicillin plus gentamicin for treatment of indrawing pneumonia in two slightly different groups. A few minor considerations for the authors to consider to strengthen the manuscript: 1. The dataset used from the study seems to be from a registry and thus would indicated this a retrospective cohort study (a type of observational study). The methods discuss that data are collected prospectively post discharge which is not accurate. The data for the hospital visit is collected retrospectively if it is collected post discharge, once again making this a retrospective cohort study (please change in manuscript and title accordingly). 2. PS Weighting, PS trimming and instrumental variable analysis all answer slightly different questions and deal with confounding in different ways. Although the authors explain these methods well, it is important to note in the interpretation that comparing these three methods to each other is not entirely accurate. A bit more delineation of the interpretation should occur in the first paragraph of the discussion section. 3. Figure 2 and 3, please change the icons for each method so it is easier for someone to read the graph if printed in black and white.

VERSION 1 – AUTHOR RESPONSE

2) Reviewer 2 requests:

• The dataset used from the study seems to be from a registry and thus would indicated this a retrospective cohort study (a type of observational study). The methods discuss that data are collected prospectively post discharge which is not accurate. The data for the hospital visit is collected retrospectively if it is collected post discharge, once again making this a retrospective cohort study (please change in manuscript and title accordingly).

Action:

Thank you for this clarification. We have revised the type of the study to indicate it was a retrospective observational study (see lines 1 – 3). Also we have revised the wording in the methods section to indicate that we implemented improved data collection processes at the start of the observation period while making it clear that the data are collected post discharge (see line 172-175).

• PS Weighting, PS trimming and instrumental variable analysis all answer slightly different questions and deal with confounding in different ways. Although the authors explain these methods well, it is important to note in the interpretation that comparing these three methods to each other is not entirely accurate. A bit more delineation of the interpretation should occur in the first paragraph of the discussion section.

Actions:
Thank you and we do acknowledge this and an explanation has been included in the first paragraph of the discussion:
We undertook two formal approaches to sensitivity analysis. First, we employed PS trimming to exclude 10% of the analysis populations in experiments 1 and 2. Effect estimates in this case are based on analyses of 90% of cases that PS suggest are best matched. Second, we used an instrumental variable. These techniques employ different approaches to account for possible confounding that might contribute to estimated treatment effects. Both these forms of analysis provided results that support the suggestion that poor outcome in this population is not associated with the antibiotic regimen received.
See lines 373 - 385.

• Figure 2 and 3, please change the icons for each method so it is easier for someone to read the graph if printed in black and white.

Actions:

Thank you for the suggestion. This has been revised – see figures 2 and 3.
Sincerely,
Authors:
1. Mr. Lucas Malla (lmalla@kemri-wellcome.org) - *Corresponding Author
2. Prof. Rafael Perera-Salazar
3. Dr. Emily McFadden
4. Prof. Mike English

VERSION 2 – REVIEW

REVIEWER	Lilliam Ambroggio Assistant Professor of Pediatrics Cincinnati Children's Hospital Medical Center
REVIEW RETURNED	23-Oct-2017

GENERAL COMMENTS	The authors addressed previous concerns adequately.