Author's response to reviews

Title: Antibiotic use and resistance in emerging economies: a situation analysis for Viet Nam

Authors:

Nguyen V Kinh (kinhvaac@yahoo.com)
Do TT Nga (thuynga2806@yahoo.com)
Arjun Chandna (ariunchandna@gmail.com)
Nguyen V Trung (nvutrun@fpt.vn)
Pham V Ca (caphamyan@yahoo.com)
Doan M Phuong (doanmaiphuong@yahoo.com)
Nguyen Q An (anguyenthuong5@gmail.com)
Nguyen TK Chuc (ntkchuc020234@gmail.com)
Mattias Larsson (mlarsson@oucru.org)
Socorro Escalante (escalantes@wpro.who.int)
Babatunde Olowokure (olowukureb@wpro.who.int)
Ramanan Laxminarayan (ramanan@cddep.org)
Hellen Gelband (gelband@cddep.org)
Peter Horby (peter.horby@gmail.com)
Ngo TB Ha (bichhakcb@gmail.com)
Hoang T Mai (maicqld@gmail.com)
Jeremy Farrar (jfarrar@oucru.org)
Tran T Hien (hientt@oucru.org)
Heiman FL Wertheim (heiman.wertheim@gmail.com)

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Author's response to reviews: see over

Dear Professor Aslak Steinsbekk and BMC Public Health editorial team,

Thank you for arranging to have our manuscript reviewed. We found the reviewer’s comments most useful and have carefully considered each of their suggestions whilst revising our manuscript. We were pleased to note that overall the reviewer’s appeared to find our manuscript of high quality. I have resubmitted the revised manuscript along with this rebuttal letter. We have addressed each of the reviewer’s comments in turn below, in order to make it easier for your editorial staff to consider these alterations when reviewing our revised manuscript.

We hope you find the revised manuscript improved and worthy of inclusion in your journal. We firmly believe that it will be of interest and use to your readership.

We look forward to hearing from you.

Yours Sincerely,

Dr. Arjun Chandna
Oxford University Clinical Research Unit,
Hanoi,
Viet Nam

Reviewer 1
“The manuscript is a well written description of how available data at the national level were compiled and used to formulate public health policies towards antimicrobial resistance. The presentation is clear and consistent, and I have no specific suggestions for improvement.”

Reviewer 1 did not have any specific areas of concern for us to address.
Reviewer 2

"In the section on Infection Control, the authors highlight the challenges with poor handwashing facilities yet make no mention about availability of alcohol hand rub, especially using the in-house WHO formulation. Considering the WHO initiatives in recent years, I believe it is essential to highlight this in the situation analysis"

We have now included a sentence referring to Viet Nam’s involvement in the WHO Clean Hands campaign. We acknowledge that specific data regarding the compliance with alcohol gel usage (and other infection control initiatives) is needed. We mention this in the recommendations in table 3. Unfortunately we do not have any specific data on use of WHO-formulation gel.

“No mention could be found about any educational initiatives to the public. The authors quote an adult literacy rate of 92% which would therefore offer possibilities of educating the consumers, especially when over the counter use is so high.”

Thank you for bringing this to our attention. We have included this as a key recommendation in the summary section of the results and findings. We have also alluded to it in table 2.

Reviewer 3

“I am not convinced whether this is a genuine ‘systematic review’. It is perhaps also not feasible to perform a ‘systematic review on everything with regards to antibiotic use and resistance’ in a country. The search terms mentioned are rather limited and do not guarantee that everything has been found. One would expect also a clear break-down of n papers searched, found, classified, excluded,... which is lacking here. Also, I think the antibiotic resistance section brings up rather limited information for a systematic review. If the authors’ aim was to provide a genuine systematic review of white and grey literature, then it would be better to summarize more in detail resistance data in tables etc... I would suggest to remove the statement ‘systematic review’ and rather have the aim to give a good (though not exhaustive) overview of the most relevant issues.”

We agree with the reviewer’s comments, and a situation analysis is the more appropriate approach to assess key aspects of antibiotic use and resistance in one country. With the reviewer’s comments in mind, we feel that a ‘situation analysis’ is the most accurate description of the work. We have therefore removed the term ‘systematic review’ throughout the manuscript. We feel that this is an improvement and hope that it also serves to address the reviewer’s later comments with regards to the slight methodological differences between our work and a typical systematic review.

“There is an imbalance between discussion and conclusions. Rather have either separate discussion section, or move discussion points towards relevant paragraphs, and keep a genuine synthetizing conclusion. Many paragraphs contain interesting and relevant information, but the ‘narrative line’ throughout the paragraphs could be improved. Several paragraphs are collections of stand-alone sentences, and several re-iterations are being made. This makes it difficult for the reader to absorb the content and remain concentrated with the content.”
We have addressed these comments throughout the manuscript in attempt to make the narrative line clearer and the information more succinct. We have paid particular attention to the conclusion section and removed redundant text and stand-alone sentences where appropriate.

“It is not clear why Nguyen Van Kinh is the first author of this paper if he/she did not contribute to the drafting, which one would expect from the first author?”

Dr. Kinh is the lead author of this paper. He was the key person for the whole study and in drafting the paper. We have adjusted the author contributions to reflect this.

“It is unusual for an abstract to contain literature references, but I would leave this upon the editor’s decision”

We have removed the references.

“Please provide a little bit of background information on recent political, economical and social evolutions within Vietnam. For instance, referring to ‘the 1986 market reforms’ may not be clear enough for the average reader unfamiliar with recent evolutions in Vietnam.”

We have contextualised the increased access to antimicrobials related to the Vietnamese economic reforms.

“In addition, the background should provide information on the n of physicians and pharmacists in the country.”

We have added this information with the appropriate reference. However as the information was published during the period of the situation analysis (1/1/1990 – 31/08/2012) we felt it was more appropriate for the results and discussion section, and have included it there.

“The link between this sentence and the 2 other of this paragraph is not clear. It is also not necessarily bad that newer antibiotics don’t find their way easily to the market.”

We agree with the reviewers comments and have removed this sentence to aid clarification.

“Last sentence (‘we believe it can be useful…’): this seems rather appropriate for the discussion or conclusions, not for the background.”

We have moved this sentence to the discussion section.

“Please explain all abbreviations (e.g. WHO)”

We have endeavoured to ensure that all abbreviations are explained. The example cited by the reviewer was already defined in the introduction so we have not re-defined it in the methodology section.

“Why was this particular period chosen (1-1-1990-31-8-2012)?”
This reflects the period immediately after the economic reforms up until the date that the manuscript was being prepared for submission.

“There has been a substantial increase in healthcare costs’: please situate this statement: e.g. from which to which order of magnitude”

After careful consideration we have removed this sentence.

“Please explain also who is legally allowed to prescribe and dispense drugs”

We have clarified that antibiotics can only be dispensed by a pharmacist if the patient has a prescription issued by a doctor.

“Please provide a reference to this ‘GPP’. “

We have provied the reference.

“Paragraph 4 (on DTC): please provide a reference for these statements.”

We have provied the reference.

“Please mention if there is any information available on quality of drugs (substandard drugs), counterfeit. If this information is not available, please mention so in the discussion or limitations section”

Substandard or counterfeit antibiotics (except antimalarials) are not recognised as a major problem in Viet Nam however we do not have specific data reporting on drug quality. We have mentioned this in the limitations section.

“What is meant exactly with ‘bulk injectable antibiotics’?”

We have removed the word bulk.

“High price of injectable cephalosporins: please provide evidence, as these drugs are often rather cheap in emerging economies…”

The costs are of course all relative as most antibiotics are often cheap. However, as compared to oral drugs the costs are significantly higher (source: IMS Health data, Vietnam). We have included the reference in the manuscript for readers who may be unfamiliar with this.

“Last sentence (‘As the risk of resistance…’): connection between, this sentence and the rest of the paragraph is not clear.”

We have tried to clarify this by explaining that using more expensive antibiotics will increase the percentage of the hospital budget spent on antibiotics (already a high proportion).

“Please provide reference to ‘CDC best practice guidelines’”
We have provided the reference.

“Please provide URL to national stewardship website”

The website is an ongoing project. We have adjusted the text to clarify this. We have also provided the URL in the text.

“Pneumococcal penicillin resistance: please specify whether this is ‘I’ or ‘R’, provide MIC’s where available, provide n of isolates (i.e. denominators) on which these figures are based and also whether these data come from invasive versus colonizing pneumococci. A table summarizing the available information, n of isolates tested, methods used etc... would be highly welcome.”

Only invasive pneumococci were studied – all sampled sites were usually sterile with the exception of lower respiratory tract samples, which were only included if the isolation of pneumococci corresponded with clinical and radiographic findings of pneumonia. CLSI breakpoints were used for interpretation. 71.4% R, 20.6% I. Number of isolates 64. We have included some of this information in the manuscript but feel that it is beyond the scope of a broad situation analysis to provide details regarding specific studies. If the reader is interested in this information, it is easily found in the referenced article.

“S. aureus: please mention the n of isolates that were studied.”

We have done this. The n number is 80.

“Gram-negative pathogens. Please be more specific than ‘an enterobacteriaceae study’. Clinical or environment, community or hospital, invasive or colonizing, number of isolates tested...?”

We have included this information. The n number is 71 and the organisms were isolated from hospitalized patients on ICU and non-ICU wards with complicated intra-abdominal infection, nosocomial pneumonia (including ventilator-associated pneumonia) and bloodstream infections.

“Enteric pathogens. The first sentence is too general (‘In Viet Nam MDR resistance is 50’), please mention the year, n of isolates tested, nuance with other available data etc.... Provide also information on what is meant with MDR for Salmonella, Vibrio and E. coli (not necessarily the same)”

We have included the study definitions for each of these in the manuscript.

“Too strong statement: Helicobacter has been associated with peptic ulcer disease, is not ‘the’ (only) cause of it.”

Thank you for drawing this error to our attention. We have corrected the manuscript.

“Are any of the Vietnamese hospitals connected to the WHO Clean hands campaign?”
Yes, Viet Nam is part of the WHO clean hands campaign. This is now mentioned in the text.

“Last sentence (on shrimp aquaculture): please provide reference”

This is unpublished data from our unit in Hanoi. We have referenced this in the text.

“Suggest to provide a summary in the text of the recommendations made in table 3.”

Thank you for this suggestion. We have incorporated a summary of the main points from table 3 into the text.

“This does not read as a genuine ‘conclusion’, rather a discussion on its own. This section would benefit from substantial shortening, restructuring and inserting a more clear narrative line. I would suggest to move some of the content to the results-discussion part, and keep only the main conclusions and plans here. There are also several re-iterations and generalizations which can be shortened or removed.”

Thank you for these comments. We have shortened and re-ordered the conclusion section. We hope that it is more focussed and a clearer narrative runs through it.

“Table 1: please provide URL and access date for the sources”

We have provided the relevant URLs and date of access. We have also taken this opportunity to update the data in the table.

“Table 2: please explain ‘DTC’. Suggest to mention also public campaigns as an intervention.”

We have defined DTC in the table. We have also added public campaigns as an intervention. We felt this was most relevant to increasing public awareness that anitbiotics are prescription-only medications and so have listed it in this section of the table.

“Table 3: if access to non-medicated animal feeds is a problem for farmers, please mention and reference this in the text.”

This information comes from a personal communication from a veterinanarian at our Ho Chi Minh City research unit. We have referenced it as such in the text.

“Flow chart behind table 3: is this figure 1?”

Yes

“Figure 2 is blurred (not readable), not convinced of their added value.”

We have decided to remove this figure after consideration of the reviewer's comments. We agree that in the context of a general overview that this situation
analysis is intended to provide this figure did not add sufficient value to warrant inclusion in the manuscript.

“Figure 3: please provide legends for the X and Y axis, and explain where the 4 common GNB come from (clinical isolates, blood cultures,...)”

We have provided legends. We have also explained where the specimens have been isolated from in the figure title.

“Please complete and/or provide URL and date accessed for the following incomplete references: 1, 6, 7, 10, 13, 14, 16, 17, 20, 22, 23, 25, 30, 40, 47, 50, 55”

We have completed the references. Please let us know if further clarification is required for any of them.