Author's response to reviews

Title: Under-utilization of health care services for infectious diseases syndromes in rural Azerbaijan: A cross-sectional study

Authors:

Danielle V Clark (dvclark@gmail.com)
Afrail Ismayilov (afrail42@rambler.ru)
Sevinj Bakhishova (sevinc.baxishova@gmail.com)
Huseyn Hajiyev (xactaun@mail.ru)
Tahir Nuriyev (nuriyev_tahir@mail.ru)
Saleh Piraliyev (apsbaku@gmail.com)
Sadigulla Bagirov (apsbaku@gmail.com)
Afag Aslanova (aaslanowa@yahoo.de)
Maqsud Qasimov (azchum@mail.ru)
Matthew J Hepburn (Matthew.hepburn@amedd.army.mil)

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Editorial Office

Dear Dr. Smith,

The authors would like to express their gratitude to the reviewers and the editorial board for their comments and suggestions. Please find our responses below in bold.

Yours Sincerely,

Danielle Clark, MPH

1. Sampling Frame Demographics (Table 1). As currently presented, it was difficult to understand why the authors listed their sampling frame (rural villages sampled from 3 regions in Azerbaijan) as a variable in their Table 1 Demographics. Certain of the descriptive statistics were confusingly presented in Table 1. For instance, what is the statistic that is being reported at the intersect of their row variable Region under the column National Rural. Here is a suggestion for more clearly presenting their descriptive statistics of their Study Sample Demographics in Table 1: The authors should remove Region as a row variable, and instead place it as a sub-sample column header; And then describe the demographics (age, gender, ethnicity, education, household size) for (1) the entire study sample, (2) the sub-sample Guba, (3) Gusar, (4) Xachmaz, and (5) National Rural Averages for comparison. Re-working the presentation of descriptive statistics in their Table 1 Demographics-by-SamplingFrame, will make more sense to the reader, and it will also highlight possible differences in important demographic characteristics between the sampled Regions (e.g. proportionately higher Lezgi ethnic group in Gusar). Once the authors re-work their presentation of the descriptive statistics in Table 1 as suggested above, then this may reveal to them possible additional reasons to explain certain of their other findings of significant differences related to Region that would merit further discussion. (Note: for the remaining Tables 2,3,4, keep Region as it is, presented as a row variable that makes sense, for those Tables presenting bivariate and multivariate results).

We are appreciative of the Reviewer’s suggestion, and we have revised in response to this suggestion.

2. Methods -- The report needs more detailed reporting of the methods, within the methods section (some of the methods details are scattered throughout later sections of the paper and need to be moved to the methods section). In the Methods section, after the subsection reporting the sampling frame or Study Subjects?, and before the subsection reporting the bivariate and multivariate Data Analysis?, insert one or more subsections to explain more clearly the study design. For instance: How did the investigators operationalize each of their study variables (apparently some of the survey queries are based on 5-year recall, others are two-week recall?
Or, were the study subjects repeatedly surveyed over a 5-year timeframe, using 2-week recall for the queries?; How did the investigators develop their data collection instrument (e.g. were some of the query items prevalidated from other prior work or were all of the queries developed new by this investigative team for this study? Were the queries close-ended quantitative checkboxes? or open-ended qualitative narrative responses that were then later recoded by the study team?); How was the survey administered (e.g. the Discussion section mentions that the interviewers were local health dept epidemiologists, etc, -- that fact should be moved up to this methods section; was all of the data collected by interviewers or were literate subjects allowed to self-administer a questionnaire? Were the interviews structured or semi-structured?).

The Methods section was revised according to the reviewer’s suggestions:

Study subjects

A two-stage, probability proportional to size sampling design [9] was used to select 40 villages in three regions in Northern Azerbaijan with populations <500 people. Village registries served as the sampling frame for the selection of households; 20 households were selected in each village. The study was designed to be representative of rural adults in the Guba, Gusar and Xachmaz regions in Northern Azerbaijan. The clinical protocol was reviewed and approved by the Institutional Review Boards at the United States Army Institute of Infectious Diseases, Walter Reed Army Institute of Research, and the Azerbaijan Anti-Plague Station. All respondents provided informed consent.

Data Collection

The data collection instrument was developed by the study team and pilot tested in one of the selected villages in Guba. The information collected during pilot testing was used to revise the questionnaire, but was not used in the analysis. The questionnaire was administered in structured interviews by trained local epidemiologists who were periodically observed by study investigators throughout the course of the study.

Respondents reported their date of birth, gender, and ethnicity. Socioeconomic indicators included highest level of education achieved, occupation, and number of household residents. Respondents were asked about their infection related health utilization history in the last five years, including hospitalization, outpatient visits, illness resulting in bed rest during the day, and over-the-counter antibiotic use for an infection. Follow-up questions regarding the frequency of occurrence of the utilization practice, duration of illness and diagnosis were administered for affirmative answers. Respondents who responded that they had taken non-prescription antibiotics in the last five years were also queried regarding the number of separate illness episodes for which antibiotics were taken, where the antibiotics were obtained, and the name of the antibiotic(s). All questions were closed-ended with the exception of follow-up questions on disease diagnosis and antibiotic name.
The infectious syndromes under study included influenza-like illness (ILI), gastrointestinal illness (GI), and fever occurring in the last five years. These syndromes were selected to represent three broad categories of infectious diseases syndromes that were likely to be prevalent in this population. More infectious syndromes could not be included due to the need to limit the length of the questionnaire. ILI was defined as fever with generalized aches and/or fatigue. GI included nausea, vomiting, and/or diarrhea. Non-specific complaints included depressed mood, sleep disturbances, and arthritis. These symptoms/complaints were selected as capturing a wide range of potential non-specific clinical issues. Due to limits in questionnaire length, additional complaints could not be added. Follow-up questions regarding the frequency of occurrence of the symptoms were administered for affirmative answers.

3. What was the response rate to the survey? (The authors mention that there were 796 respondents but how many adults did they approach? This would give the reader a better indication if self-selection bias was an issue.).

The following has been added to the results section: “Of the 780 selected households, 146 did not have anyone at home on 2 separate visits, and 113 refused to participate.”

4. Use of health services, Self-medication / Antibiotics --? These are very important variables in this study, and need to be explained more clearly. In their report, the authors use the terms ?antibiotic use? and ?self-medication? interchangeably (in the narrative text, as well as in the Tables). This is very confusing to the reader/reviewer. Does the variable ?antibiotic use? capture prescriptions by doctors, or are these antibiotics being obtained and used ?over the counter? without a doctor?s prescription, or both?? Does self-medication refer to an individual self-medicating by purchasing antibiotics from pharmacies without a prescription; or to differentiate those antibiotics that are administered in a doctor?s office from those that patients administer at home following a doctor?s prescription? This is a very important variable, and needs to be more clearly explained in the methods section (how was this variable operationalized; length of recall; was the antibiotic use queried for specific illness episodes, or just for general use over some timeframe,etc).

Please see the revised methods section above. The question was designed to query about non-prescribed, over-the-counter antibiotic usage. Per the reviewer’s suggestion, we edited the manuscript so that the term ‘over-the-counter antibiotic use’ is the phrase to describe our observations.

5. An interesting and important aspect of health services use, is whether people have symptoms that should require they see a physician, such as what is the reported use of health services among those with ILI or GI conditions?

The health services use among the general study population answers a slightly different question than the health services use among those reporting an illness. We report the
demographic distribution of health utilization in the general study population in order to
describe who is utilizing the health system in the rural adult population in these three
regions. By looking at table 2, we can see that 1.6% of females saw a physician for an
infection compared to 0.9% of males. These demographic trends are important from a
health program planning perspective. The multivariate model of antibiotic use in effect
provides the comparison suggested by the reviewer; we can see in table 4 that respondents
reporting a fever in the last 5 years were 8.4 times more likely to use antibiotics than those
who did not report a fever in the last 5 years. Similar multivariate models were not
provided for hospitalization or outpatient visits due to the low prevalence of use in this
population.

Other Issues with this manuscript that should be addressed (minor essential revisions):

1) Use consistent language for reporting results. On page 6 and 7, study participants are referred
to as study population?, volunteers, people, respondents and residents. For a survey such as this
study, respondent is probably the most appropriate term and should be used consistently
throughout the paper.

This change has been made.

2) The research question and study purpose could be clarified, i.e. the purpose is to determine the
prevalence of infectious syndromes, to characterize health utilization practices related to
infectious disease, and to describe associations between demographic characteristics, health
utilization, and infectious syndromes.

The purpose of the study was to characterize the health utilization practices related to
infectious disease and to determine the prevalence of infectious syndromes as stated. The
authors feel that demographic variation is an important component of a comprehensive
description of these utilization practices, and therefore the data presented supports the
primary purpose of the study.

3) Additional details need to be mentioned or clarified in the background, methods, and
discussion sections. Such as:
a. Why did the authors choose to focus on some infectious syndromes and non-specific
complaints over others?
These syndromes and complaints were selected as representing a broad range of infectious
diseases. We were also very conscious of the need to limit questionnaire length, and
therefore more syndromes and complaints could not be added. We have explained this
issue in the Methods section:

These syndromes were selected to represent three broad categories of infectious diseases
syndromes that were likely to be prevalent in this population. More infectious syndromes
could not be included due to the need to limit the length of the questionnaire.
These symptoms/complaints were selected as capturing a wide range of potential non-specific clinical issues. Due to limits in questionnaire length, additional complaints could not be added.

b. How was random selection incorporated into the study design?
Random selection is incorporated in the probability-proportional to size sampling methodology cited in the methods.

c. Why was income not included as a study variable and how might income be affecting the results as an unmeasured confounding variable?
Income was not a useful measure in this rural population, as very few respondents receive an income in the traditional sense. Instead, socioeconomic indicators such as household size, education, and occupation were used. Additional information on these indicators has been added to the methodology section.

d. Study limitations of over-representation of Lezgi ethnic group and larger than average household sizes?
The national rural averages are presented in order to give the reader an idea of how the study population compares to the national rural population, however the study is not designed to represent the country as a whole. Therefore the demographic differences between the study population and the national rural population is not really a limitation. Statements have been added throughout the manuscript to clarify the generalizability of the results.

e. What evidence from the literature supports the statement on page 11: The health-seeking behaviors we have described substantially increase the likelihood that drug-resistant pathogens are circulating in this population.
This sentence has been removed.

f. How do the antibiotic usage rates found in this study compare to expected rates? How are antibiotics accessed in rural Azerbaijan?
There are no reliable data to determine the expected rate. Information on antibiotic access over the counter was added to the discussion.

g. What did the authors find to support the statement better coordination with local health nurses may also be potentially helpful?
This sentence has been modified to indicate that the engagement of local health nurses is a possible future direction for programs to increase utilization of health services.

h. One of the two objectives of the paper is to estimate the prevalence of infectious disease syndromes. The prevalence among study subjects is reported but how might this translate to the entire country? Given the nationally-representative design of the sample is it possible to make some national estimates with SEs? If not, perhaps the authors could just discuss briefly what the national prevalence (cases) might be to give the reader a more complete picture and fully obtain
this study objective of estimating prevalence.

The sample was not designed to be nationally representative, but rather representative of rural villages in the three regions studied. The following statement was added to the methods section: “The study was designed to be representative of rural populations in the Guba, Gusar and Xachmaz regions in Northern Azerbaijan.” Clarification was also added to the results section.

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Editorial comments:

1) Please include the name of the ethics committee that approved your study.

* Ethics - Experimental research that is reported in the manuscript must have been performed with the approval of an appropriate ethics committee. Research carried out on humans must be in compliance with the Helsinki Declaration (http://www.wma.net/en/30publications/10policies/b3/index.html), and any experimental research on animals must follow internationally recognized guidelines. A statement to this effect must appear in the Methods section of the manuscript, including the name of the body which gave approval, with a reference number where appropriate.

This information has been added to the Methods section.

2) Two of the authors of this manuscript (Saleh Piraliyev and Sadigulla Bagirov) have the same email address in our system (both are using apsbaku@gmail.com). Please ensure that all authors have their own email address and update this on the Author Details page in the submission system.

These authors do not have their own email addresses. Email is not a common form of communication for people living outside of Baku. The email address given is for the institute, and can be used to communicate information to them.