Author’s response to reviews

Title: Non Prescribed Sale of Antibiotics in Riyadh, Saudi Arabia: A Cross Sectional Study

Authors:

Aref A Bin Abdulhak (aref146@gmail.com)
Mohamad A Altannir (maltannir@kfmc.med.sa)
Mohammed Almansor (drmohd002@gmail.com)
Mohammed Almohaya (dr.mohamed15@gmail.com)
Attallah Onazi (ataonazi@kfmc.med.sa)
Mohammed Marei (Dr_marei@hotmail.com)
Oweida Aldossary (dr.oweida@hotmail.com)
Sadek Obeidat (Sadek.Obeidat@gmail.com)
Mustafa Obeidat (mustafa.Obe@gmail.com)
Muhammed Riaz (MORIAZ@kfmc.med.sa)
Imad M Tleyjeh (itleyjeh@kfmc.med.sa)

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Author’s response to reviews: see over
Dear Editor,

We appreciate your positive evaluation of our manuscript. All the comments made by the reviewers were seriously considered leading to a more clear and articulated paper for the readership of the BMC-Public Health. Herein, we provide a point by point response. We look forward to seeing our work published in the journal

Reviewer: Pauline Norris:

How common is it for pharmacy customers to buy products on behalf of family members? This is important in assessing how plausible the simulated patients would have been to the pharmacy staff. Were the simulated patients women or men? In some countries it would be much more common for women to seek help on behalf of men, but I understand that in Saudi Arabia it may be the other way round.

It is very common in Saudi Arabia and most of Middle East countries for a relative to buy products on behalf of a family member. All the actors were men and we have clarified this fact in the revised methods section.

Were the staff who sold the antibiotics pharmacists or assistants? Was it possible for the simulated patients to know?

The staff who sold antibiotics were pharmacists. KSA regulations mandate that pharmacists post their licenses and pictures in the pharmacy.

How much information was provided by the simulated customers, and how much was given only on request? Did the patients ask any questions or did they take a passive role in the interactions? Did the patients use any medical jargon, or did they deliberately use lay language and ways of describing problems?

Only the information presented in the methods section was provided to the pharmacists without any questions. Any additional information was only provided if the pharmacist inquired about. The actors used lay language and refrained from using any jargon. We have revised the methods section to reflect this fact.
I am a bit confused about the levels of demand. Were these used sequentially, ie, if one didn’t result in an antibiotic being sold, the next one was used, etc. Or were different levels of demand assigned to different interactions?

The levels of demands were used sequentially. We have revised the methods section to reflect this fact.

It would be useful for readers to know about whether and how the regulations prohibiting non-prescription sale of antibiotics are enforced in Saudi Arabia. The authors’ suggestions about how to improve this enforcement would be useful.

Unfortunately, there is no active monitoring for the compliance with this specific national regulation in KSA. There is also lack of an electronic system to track prescriptions in community pharmacies.

Are limitations of the work clearly stated?
No, there is no section describing the limitations of the work. This needs to be included (compulsory revision). The limitations in my opinion include the use of doctors and medical students as simulated patients. It is likely that the pharmacy staff noticed the class and medical expertise of the patients, and may have provided less counselling because of this. Obviously the staff’s actions in selling antibiotics without prescription and without appropriate counselling is still completely inappropriate, but in terms of the generalizability of the study it would be useful to have used simulated patients who were not health professionals.

We have added a limitation section.

Our study findings may not be generalizable to other countries. Although the actors were medical professionals, they have not used medical jargon to avoid introducing bias in favor of antibiotic sale without prescription.

Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?
Yes, but I think it would be useful to refer to other studies that have used simulated patients in a community pharmacy setting, because this is quite a well-established methodology. A review of this methodology is provided in Watson M, Norris P, Granas A. A systematic review of the use of simulated patients and pharmacy practice research. International Journal of Pharmacy Practice, (2006) 14: 2 83-93.

We have included this important review about use of simulated patients and pharmacy practice research in our methodology section.
Is the writing acceptable?
The use of English could be improved somewhat. The Implications section is very good, but could be shortened and revised to make it clearer and easier for readers to follow. Dispensing should be dispensing, and dispended should be dispensed (minor essential revision).

The manuscript has been edited by a native English speaker with considerable experience in medical literature. Revisions have been made accordingly.

**Reviewer:** Daniel Morgan

**Major Compulsory Revisions**

1) the text is poorly written and makes the message difficult to infer. It needs extensive editing by a native English speaker to correct errors such as antibiotics being "dispended" instead of dispensed etc.

The manuscript has been edited by a native English speaker with considerable experience in medical literature. Revisions have been made accordingly.

2) the writing is not clear beyond the English. Authors go beyond the data for the adverse consequences of antibiotic use in their introduction & discussion... there is a new review on the subject in which we tried to achieve a balance... Morgan et al. Lancet Infectious Diseases, that may be helpful.

The review by Morgan et al. is very valuable. It has been published after submission of our manuscript. We have included important findings and quoted it in our discussion. We have deleted Table 4 and rewritten the section about (comparison to other studies) by using the findings summarized by Morgan et al.

In a systematic review by Morgan et al. of 35 community surveys from five continents, non-prescription use of antibiotics occurred worldwide and accounted for 19-100% of antimicrobial use outside of northern Europe and North America. Similar to our findings, Morgan et al observed that non-prescription use was common for non-bacterial disease. In 2 of the 35 surveys, > 80% of pharmacists did not inquire about drug allergy.

**The discussion was not clearly organized.**

Subheadings should be removed, they are distracting and not particularly helpful. Organizing the discussion into a more clear flow of ideas would help e.g.
summarize findings, discuss impact on resistance, potential adverse events including allergies and pregnancy, then conclusions.

We have taken Dr Morgan's comments in consideration and have revised the manuscript accordingly.

3) the methodology used by authors is close to that validated by others...see "simulated patients" in above review for reference. It would add significance to make it clear this is a validated approach despite using deceit etc.

We have added a statement and reference in this regard to the methods section

4) tables are not very helpful as they stand.
Table 1 needs better legend. "Percentage of pharmacies willing to sell antibiotics without medical prescription according to strength of patient demand".

Legend has been revised as suggested.

Table 1 could easily include information from Table 3 regarding appropriateness of antibiotic use for each diagnosis. This should be stated more simply than it is in table 3 though. Perhaps antibiotics appropriate? Yes, No, sometimes. See study from Wachter et al. in Nepal in above review for example of presentation.

Table 3 was combined with table 1 as suggested.

Table 2 is fine, but needs a better legend...one that better explains purpose of table. I think this is very important to present though.

Revised legend: Pharmacists’ Inquiries and Recommendations in Response to the Simulated Clinical Scenarios.

Table 3 -- make part of table 1
Table 3 was combined with table 1 as suggested.

Table 4--remove. This is limited--see review above for complete list of studies. This is better just mentioned in the discussion as it is not new data from this study.
Table 4 removed

- Minor Essential Revisions
Note, in Brazil and potentially other countries, nonprescription antibiotic sales were not against regulations at time of study "comparison to other studies" section is therefore inaccurate.

Comparison to other studies section was revised to include summary findings by Morgan et al. Describe better how levels of demand or request were used. Potentially ahve a sentence after describing each method in methods "Each was employed sequentially until an antibiotic was dispensed or denied."
Describe clinical scenarios better. e.g "Pharyngitis: A healthy young male relative was described as having sore throat, difficulties in swallowing with slight fever of 24 hours duration. Acute Bronchitis: An elderly male relative was described as having sore throat, cough with sputum production. Additional information provided upon request was the patient had multiple comorbid conditions and was using warfarin...."

Authors do not discuss what seems a key finding from this study... that pharmacists were more likely to provide antibiotics inappropriately than for indications that may be appropriate. Diarrhea commonly receiving an antibiotic, whereas UTI did not. In other words, pharmacists did not give antibiotics for the right indications.

This is an excellent observation. We have added this to the discussion section.

If authors could give potential reasons why antibiotics are used without a prescription it would be welcome... I'm sure they must have some hypotheses, such as it takes too long to see a doctor, or costs too much etc.

Our study objective was not to examine why patients seek treatment without physicians opinion. This is a study we are currently conducting as stated in the section about (future research: Future studies should examine reasons why patients seek non-prescribed medications directly from pharmacists despite the presence of public hospitals and primary care centers.

**Reviewer: Carl Llor**

**MAJOR COMPULSORY REVISIONS:**
I am in doubt about the number of ‘actors’ used and the standardization. In the present paper, the pharmacists had no contact with ‘simulating patients’, since the ‘patients’ did not attend the pharmacies. The authors state that a total of eight physicians participated and five different health problems were taken into account. I would like to know how they standardized these problems. It is important in this type of studies to homogenize the way they communicate and how the message was put across. According to the Methods section a pilot study was not undertaken and this aspect is therefore even more important.

We have elaborated more about this in the method section to make it clear.

Two sessions of standardization took place in the presence of all actors. Each group rehearsed simulating all the clinical scenarios to the senior investigator using the same complaints (terminology and statements). Rehearsal was repeated to ensure reliability of the simulated scenario.
One aspect to be discussed is how was the sample of pharmacies stratified? The authors say that pharmacies were stratified by five regions. I would like to know if they consider other variables, like deprivation status. Were pharmacies in deprived areas chosen and in this case, were the results similar? Another aspect, reported in other studies, is the size or the revenues of the pharmacies. Do those pharmacies with lower incomes or smaller pharmacies sell more antibiotics without prescription than those pharmacies with higher revenues?

All regions of Riyadh (Central, North, South, East, and West) were visited regardless of the deprivation level, or pharmacy size. We did not collect data about the other variable suggested by Dr. Carl since they were not necessary for the study objective.

MINOR ESSENTIAL REVISIONS:
The authors write that the actors were instructed in presenting five different clinical scenarios (5 different diagnoses of infectious diseases). However, I anticipate that they presented the symptoms only. Therefore I would prefer to use the term sore throat instead of pharyngitis (why could the case not be tonsillitis?)

Revised as suggested

Another aspect is if the ‘actors’ interacted only with pharmacists or not. A distinction between pharmacists or pharmacy clerks should have been considered. Could the authors explain this issue and if this distinction was considered were there any differences in the main results between both interactions?

The staff who sold antibiotics were pharmacists. KSA regulations mandate that pharmacists post their licenses and pictures in the pharmacy. All "actors" interacted only with pharmacists as per the posted licenses.

It is not clear if demographic information was or was not collected about the pharmacist or pharmacy clerk. For example, the age of the pharmacy representative was noted. Do the authors have this information?

Because the study objective was concealed from pharmacist, no demographic data were collected.

I would like that authors might discuss their results and compare them with the other few papers that have use a similar methodology and why these results differ.

We have added findings from a recent systematic review by Morgan et al that addressed this issue.
I also miss an in-depth discussion about the problem of the over-the-counter availability of some countries in which this practice is illegal as in Saudi Arabia. We are limited by the word count and previous reviewers have suggested shortening the discussion section. Therefore we have not addressed over-the-counter medication because it was outside the scope of this work.