Author's response to reviews

Title: Trends in antibiotic use among outpatients in New Delhi, India

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Authors: Anita Kotwani and Kathleen Holloway

Reply to comments of Reviewer 1

General

Thanks for appreciating the methodology and its wider use

Methods (major compulsory revisions)

1. Rationale for conducting 30 exit interviews at private retail pharmacies and public facilities is based on an adaptation of the INRUD methodology - WHO, 1993, “How to investigate drug use in health facilities,” WHO/DAP/93.1. As suggested we have incorporated the rationale of 30 exit interviews in Methods section, under Sample size sub-heading.

   The rational for conducting these number of exit interviews is from the WHO manual, “How to investigate drug use in health facilities” which recommends 600 encounters (20 facilities and 30 patients/prescriptions per facility) for one survey [10]. Therefore, for both public facilities and private retail pharmacies we conducted 30 exit interviews per month over one year. However, in private sector clinics, the amount of time to get this ideal number of interviews was too long and so we had to reduce the number of interview to 10-12 per facility per month due to resource constraints. Data collectors’ schedules were randomly prepared for the day and time (two hour) of each visit. During each facility visit, all patients receiving any antibiotic were interviewed. During their stay in the facility for that particular day all patients who visited were interviewed if they got any antibiotic.

2. We have included the year for ATC/DDD index in Outcome measures section. Also included in the same section how to calculate the DDD. To calculate the total DDDs for each exit interview, the strength of dosage form (tablet/capsule etc.) and total units of tablet/capsules of each antibiotic received or purchased was noted. Multiplying the strength and total units of antibiotic received followed by dividing the amount by DDD of that antibiotic gave the total DDDs that patient received. Antibiotics for local use, like creams or any drops prescribed or dispensed were not included for calculating the DDDs consumed. Consumption in terms of DDDs per population per day was not used since complete data (covering all patient attendees) could not be collected from any facility nor could all private facilities in the concerned areas be included.
The methodology that we are using is for out-patient and expresses the consumption as DDD/1000 patients attending the facility. You cannot include all the pharmacies and not collecting data for all patients visiting these pharmacies for the entire period. However, for surveillance, it should not matter provided the same method is used each month and over a period. At the end of the day, this surveillance system has been set up to assess trends and evaluate the impact of future interventions, not to try and assess accurately exposure of the population to antibiotics. Therefore, DDD/1000 inhabitants were not used. This point is clarified in the discussion section as well.

3. Total number of public facilities and private retail pharmacies has been included in the Method section. Reasons for enrolling 20 pharmacies and about sampling have been clarified with reference as mentioned above and in the text at suitable place.

4. Primary aim of the surveillance was to study the antibiotic use in the community. Primary care health facilities reflect community use of antibiotics. Therefore, for private clinics we mainly wanted to do surveillance at GPs and pediatricians, few physicians were included. Dermatologist included in the study was very keen to participate in the study and was practicing as GP as well. There was selection bias but it was unavoidable. We got a convenience sample of private practitioners, so not all specialties were included but this was the best that could be done because many doctors do not tolerate continued data collection processes. Moreover, we wanted to include clinics with sufficient number of patients per day. Total number of private sector doctors practicing in the surveyed area is not known.

   Antibiotics for local use, like creams or any drops prescribed or dispensed were not included for calculating the DDDs consumed. This statement is included under sub heading, Outcome measures.

5. Method section is now clearer. As suggested the statement which was later in the method section is put in the beginning in Setting and Facility sub heading of Methods section.

Language (minor compulsory revisions)

(1) The words “a” and “the” are added wherever required in the results and discussion sections.

(2) The word antimicrobials are changed to antibiotics in the introduction except for antimicrobial resistance as the term antimicrobial resistance is generally used instead of antibiotic resistance. Antimicrobial resistance is also now mentioned as AMR.

(3) Adverse side effects changed to side effects in the background section.
Clavulanate is changed to clavulanic acid.

ATC codes for all antibiotics have been mentioned in the text as well as in Table 1 and Table 2.

Spelling of cotrimoxazole is corrected wherever wrong.

For references normal script between brackets is done.

Changes made.

Modified the sentences.

“WHO” is written in full in Background section
Sentence changed as suggested.
“Percentage” is changed to “percent”

Background section (discretionary revisions)

We have done the suitable change.

Results section (discretionary revisions)

This section is made clearer and now it is easy to read.

Discussion (minor compulsory and discretionary changes)

Repetition is deleted.
The mentioned statement is deleted as suggested and this was already mentioned in the limitation of the study.
Sentence is changed as suggested.
Sentence modified and added “than measuring the DDD/1000inhabitants”
As suggested ‘Thus’ is replaced with ‘For example’
The area wise analysis was not mentioned in the results. We have mentioned in the Results section that, “The pattern and consumption of various groups of the antibiotics appeared similar in all the four areas studied.” The detail analysis of area wise is discussed in the Discussion section. The text is slightly modified to make it clear.
No, we could not confirm this (mentioned in the text) but it is a known fact that there are at times irregularities in supply of medicines in public facilities.
A survey for antibiotic use in diarrhea in primary care was conducted simultaneously with this study. Results of the survey showed that fluoroquinolones were the main antibiotics prescribed for diarrhea and diarrhea cases increased during rainy season (humid summer months). This reference and statement is added in the discussion.
Suitable changes are done and it blends with strength and weakness of the study.
We have included the concern of DDD/1000 inhabitants just before the strength and weakness section.

We did not measure DDD/1000 inhabitants as is generally done by the European countries. In our settings this is not an accurate measure of exposure of the population to antibiotics because we have not included all the facilities of our catchment area and complete data (covering all patient attendees) could not be collected from any enrolled facility. The objective was not to measure accurately population exposure to antibiotics, rather to measure trends in use as part of a surveillance system. Provided the same methodology is used each month, then the same degree of error occurring each month will be the same and the data collected will be sufficient for trend measurement even though it is not accurate for a one-off exposure measurement. Since the exit interview data only measures use in some of the patients attending some of the health facilities, the total number of DDDs per population would be much less than would be the case if all the facilities were included.

This is now clarified in the Methods section.

**Conclusion (minor compulsory revisions)**

1. This section is shortened.
2. As suggested one sentence from conclusion is shifted to study limitation section.

**Tables and Figures (minor compulsory revisions)**

1. Figure 1 is deleted. Table 2 and 3 are combined. Figures 2-7 can be put in one panel and designated as Figure 1 (A)-(F) as they are depicting the monthly trend of consumption of each group of antibiotic over a year.
2. Title is changed and Table 2 and 3 are combined.
3. Corrected the typing errors in the Tables
4. Figure 1 is deleted and Table 1 is modified.

**Reply to comments of Reviewer 2**

Thanks for appreciating the importance of the paper.

Following are our answers and edits done as suggested

- Included in the discussion about appropriateness of antibiotics like amoxicillin and other first generation antibiotics included in the Delhi state EML for dispensaries as these antibiotics are the first choices for treating most common infections in the community.
- We have discussed the use and availability of antibiotics in the public sector with the list of Delhi state list of essential medicines list (Discussion section, page 14).
- We have deleted Figure 1; modified Table 1 on the suggested pattern and on similar pattern to the second Table.
- As suggested the percentage of total DDD/1000 patients is reported in Table 2 (previously Table 3). With percentage of different members of each class of antibiotics now it is easy to follow the extent of use of different members of each class of antibiotic in the community in different sector.

Minor essential revisions

- Figures 2-7 can be shown in one panel on one page and we have numbered them as Figure 1 (A) – (F). These figures show monthly trend of each class of antibiotics in three different types of facilities and average consumption of each class of antibiotic in the community. These are important figures and have shown some variation in antibiotic consumption during winter and humid summer season. This data can be referred by other researchers for reference.
- Spelling of cotrimoxazole is corrected throughout the paper.
- ATC codes of penicillins, tetracyclines and cotrimoxazole are added in the Table.