Knowledge, attitudes and practices regarding antibiotic use in Maputo City, Mozambique

Inocência Mate, Charlotte Elizabeth Come, Maria Patrícia Gonçalves, Julie Cliff, Eduardo Samo Gudo

1 National Institute of Health, Ministry of Health, Maputo, Mozambique, 2 Community Health Department, Faculty of Medicine, Eduardo Mondlane University, Maputo, Mozambique

* esamogudojr@gmail.com

Abstract

Background
Irrational use of antibiotics is a major driver of antimicrobial resistance (AMR) worldwide. Sub-Saharan Africa, where the risk of spread of AMR is highest, lacks data on the knowledge, attitudes and practices regarding antibiotic prescription and use. This is the first study in Mozambique to address this gap.

Methods
A cross-sectional study was conducted in 2016 in 1091 adults (age ≥18 years) living in five districts in peri-urban areas of Maputo City. Three stage cluster sampling was used to select the households. A semi-structured questionnaire was used to collect information on the knowledge, attitudes and practices regarding antibiotics and their use and socio-demographic data.

Results
Of the 1091 participants, 20.9% (228/1091) had used non-prescribed antibiotics. Most of the non-prescribed antibiotics were purchased in pharmacies (199/228; 87.3%). The proportion of use of non-prescribed antibiotics was higher in those who purchased from informal markets (82.6%; 14/17) and home stores (66.7%; 12/18), compared to pharmacies (24.6%; 199/810) (p = 0.000). Variables significantly associated with use of non-prescribed antibiotics were male gender (p = 0.004), living in the Central A (p < 0.001), Aeroporto B (p < 0.001) or 25 de Junho (p < 0.001) neighborhoods, purchase of antibiotics in informal markets (p < 0.002) or obtaining from home stores (p = 0.026), not completing the course (p < 0.001) and having poor knowledge on the use of antibiotics (p < 0.001). Main reasons for use of non-prescribed antibiotics were a perception that there was no need to attend a health facility (26.8%), followed by someone else’s advice (7.7%), symptoms similar to a previous episode (6.2%) and poor quality of care in health facilities (6.7%).
Conclusions

Our study shows for the first time that knowledge regarding antibiotics is poor in Maputo City. Purchase of non-prescribed antibiotics is a common practice and most are sold in pharmacies, indicating deficient inspection. Interventions to reinforce adherence by pharmacies to current legislation for dispensing antibiotics, combined with community education are urgently needed.

Introduction

Antibiotic resistance (AMR) is expanding at an alarming pace worldwide and represents a serious public health threat [1, 2]. Due to this rapid growth, the available options for treatment of some bacterial pathogens are almost exhausted [2, 3].

AMR is responsible for an estimated 700,000 deaths annually. By 2050, deaths may increase to 10 million deaths per year, making AMR the leading cause of death[3].

The irrational use of antibiotics, including self-medication, sub-optimal dosage, overuse, and prescription/use of inappropriate antibiotics, is considered as a major driver of the emergence and spread of AMR worldwide [4–6]. A rapid and unprecedented increase in the consumption of antibiotics has been reported globally over the last decade [7]. This increase has been greatest in low income countries, where antibiotics are more frequently dispensed without prescription [5, 8–10].

In developing countries, which bear more than 90% of the global infectious diseases burden, inappropriate use of antibiotics, including their use without prescription, is of great concern [3, 9–11]. In particular in sub-Saharan Africa, where the number of deaths attributed to AMR each year is higher than in other parts of the world [3], irrational use of antibiotics is more common [10]. In this region, legislation on antibiotic use and dispensing is often absent, and when laws do exist, they may be poorly enforced. Access to health care is often difficult and public awareness on the risk of overuse of antibiotics is limited. Within health facilities, diagnostic capacity to inform treatment is poor [8, 9, 12].

In Mozambique, current legislation prohibits the use of non-prescribed antibiotics[13]. While in the public sector, prescription of antibiotics is guided by a National Drug Formulary [14], in the private sector prescription of antibiotics often does not follow the national guidelines. However, no study has been conducted so far to assess the use of non-prescribed antibiotics as well as its associated factors.

No routine surveillance system exists to assess the profile and trends of AMR in Mozambique. However, recent publications from small studies show that AMR is increasing [8, 15, 16], with a high prevalence of multi-drug resistance [17].

A National Action Plan to Combat AMR is currently under development. Pillars of this plan include increased public awareness regarding antimicrobial resistance and rational use and prescription of antibiotics, through effective communication, education and training [2]. Evidence on the current knowledge and practices regarding use and dispensing of antibiotics is urgently needed to guide the design of these interventions. Studies in other continents have shown heterogeneous results, with few studies in sub-Saharan Africa. Lack of evidence in Mozambique stimulated this study, which aimed to investigate for the first time the knowledge, attitudes and practices towards antibiotic use among adults living in peri-urban areas of Maputo City. The study will also provide baseline data for comparison with post-intervention studies.
Methods

Study design and setting

A cross sectional and semi-quantitative study was conducted in peri-urban areas of Maputo City between August and November 2016. The peri-urban areas consist of large slums surrounding the urban area of the city. Most roads are unpaved, sanitation is poor, and most houses are built from rudimentary materials.

Eligibility criteria

Eligibility criteria were: individuals aged 18 years and over, with permanent residence (> 1 year) in the selected household, who accepted to participate in the study. To mitigate recall bias, only individuals with a history of use of antibiotics for their own health or for their children’s health in the 90 days prior to the study were eligible.

Ethics statement

This study was approved by the Institutional Bioethics Committee of the Faculty of Medicine of Eduardo Mondlane University (Ref #: CIBS FM&HCM/89/2016). Written and informed consent was obtained from each eligible individual prior to enrolment.

Household sampling

For selection of households, we used three stage cluster sampling. In the first stage, we selected all districts of Maputo City, except Ka Tembe and Ka Nhaca, which were excluded for logistic reasons. From each district, we randomly selected neighborhoods as the second stage. In the third stage, we randomly selected at each neighborhood an imaginary center to identify the first household. From this household, consecutive households were selected one every three in a clockwise direction until the number of households for the corresponding neighborhood was reached.

In each household, only one eligible individual was interviewed according the criteria of eligibility for the study. In households with more than one eligible individual, the interviewer selected the main caretaker of children in the household.

Sample size calculation and sampling

For sample size calculation, we used the probability proportionate to size of districts of Maputo City. Sample size was calculated using the following assumptions: i) population of Maputo City of 1,094,315 inhabitants, according to 2007 population census (CMM 2010), ii) expected frequency of use of non-prescribed antibiotics of 50%, iii) an error of the estimate of 5% and iv) a confidence interval of 95%. Based on these assumptions, our sample size was 1,111 people. We assumed a refusal proportion of 10%, giving a final sample size of 1,222 people.

To define the number of individuals to be recruited per district and neighbourhood we first obtained the weight of each district. The estimated number of people living in Maputo City (1,094,315) was divided by the estimated number of individuals living in each district. We calculated the number of individuals to be recruited in each district by multiplying our sample size (n = 1,222) by the corresponding proportion (See S1 Table).

Since we excluded two districts (Ka Nhaca and Ka Tembe), the number of individuals expected to be recruited in these two districts (n = 28) was allocated to the other five districts, according the proportion to be recruited in each of these five districts. (See S2 Table).
Data collection
A semi-structured questionnaire (See S1 File and S2 File) was used to collect socio-demo-
graphic data and information on the knowledge, attitudes and practices regarding the use of
antibiotics. The questionnaire was administered by trained interviewers. A pilot study of 60
individuals (5% of the sample size) to test all study tools was conducted. Information on
monthly income is presented in Meticais (MT), the Mozambican currency. The exchange rate
from US dollar to meticais during data collection was 60 (1 US dollar = 60 MT).

Information about the completeness of the course of the antibiotic was determined by com-
paring the course reported by the participant with that described in the National Drug
Formulary.

Identification of the antibiotic
The antibiotic used by the participant for his/her and/or their child’s health was identified by
self-reporting the name and/or by showing other evidence, such as any remaining antibiotic, a
medical prescription, or the antibiotic container. Participants who didn’t know the name of
the antibiotic and were not able to show any evidence, were excluded from the study.

Statistical analysis
Data from questionnaires were double entered by two separated data clerks into a data base
developed using the Epidata software package version 3.1 (Epidata Association Denmark).
The two datasets were then matched and all discrepancies were cleaned. Data analysis was per-
formed using SPSS Software package version 20 (IBM, USA).

Several variables on knowledge, attitudes and practices were re-categorized and recoded.
Factorial analysis was used to compare different groups after categorization of the variables.
Variables related to the knowledge about antibiotics were re-categorized using the following
classification “Good/Adequate if > 75%; Reasonable/Regular if ≤ 75% and > 50%, and Bad/
Insufficient if ≤ 50%.

The chi-square test (Pearson) and logistic regression analysis were used to assess the associ-
ation between socio-demographic characteristics and knowledge, attitudes and practices
regarding antibiotics.

Results
Socio-demographic characteristics and association with use of non-
prescribed antibiotics

Table 1 shows that 1091 individuals were enrolled in the study, of whom 73.1% (797/1091)
were female. The median age was 33 years (IQR: 25–47). Most participants were aged 18–39
years (61.9%; 675/1091). More than 50% of the participants lived with a partner (officially mar-
ried or in a de facto relationship) and 30.5% (333/1091) were single. Smaller proportions were
widowed (7.2%; 79/1991) and divorced (3.0%; 33/1091). In terms of education, 50.9% (555/
1091) had attained secondary level. More than 50% had a low monthly income level (less than
5,000 MT per month).

Table 1 also shows that, out of 1091 participants, 20.9% (228) had purchased antibiotics
without a prescription. In the bivariate analysis, socio-demographic characteristics associated
with use of non-prescribed antibiotics were gender, marital status and place of residence. A
higher proportion of males (26.2%) versus females (18.9%) (p = 0.009) used them. Use of non-
prescribed antibiotics was also more frequent (p = 0.027) in single (26.7%) and divorced par-
ticipants (24.2%) as compared to other marital status. A higher proportion of participants
(49.4%) living in the Central A neighborhood had used non-prescribed antibiotics compared to residents in other neighborhoods (p<0.001)

Age, educational level and monthly income were not associated with use of non-prescribed antibiotics.

Knowledge and practices regarding antibiotics and association with use of non-prescribed antibiotics

Table 2 shows that the antibiotics were mostly obtained from pharmacies (74.2%; 810/1091), with only 3.2% obtained from informal markets (1.6%) and home stores (1.6%). Most

Table 1. Socio-demographic characteristics by use of prescribed and non-prescribed antibiotics.

| Characteristics | Total n (%) | Use of prescribed antibiotics n (%) | Use of non-prescribed antibiotics n (%) | p-value |
|-----------------|-------------|------------------------------------|----------------------------------------|---------|
| Gender          |             |                                    |                                        | 0.009   |
| Male            | 294(26.9%)  | 217(73.8%)                         | 77(26.2%)                              |         |
| Female          | 797(73.1%)  | 646(81.1%)                         | 151(18.9%)                             |         |
| Age, median (IQR) | 33(25–47)  | 33(25–46)                          | 33(23–49)                              | 0.340   |
| Age (years)     |             |                                    |                                        | 0.236   |
| 18–39           | 675(61.9%)  | 534(79.1%)                         | 141(20.9%)                             |         |
| 40–59           | 299(27.4%)  | 244(81.6%)                         | 55(18.4%)                              |         |
| ≥60             | 112(10.3%)  | 81(72.3%)                          | 31(22.7%)                              |         |
| No information  | 5(0.5%)     | 4(80.0%)                           | 1(20.0%)                               |         |
| Marital status  |             |                                    |                                        | 0.027   |
| Single          | 333(30.5%)  | 244(73.3%)                         | 89(26.7%)                              |         |
| Married (officially) | 166(15.2%) | 134(80.7%)                         | 32(19.3%)                              |         |
| Married (de facto) | 446(40.9%) | 371(83.2%)                         | 75(16.8%)                              |         |
| Widowed         | 79(7.2%)    | 64(81.0%)                          | 15(19.0%)                              |         |
| Divorced        | 33(3.0%)    | 25(75.8%)                          | 8(24.2%)                               |         |
| No information  | 34(3.1%)    | 25(73.5%)                          | 9(26.5%)                               |         |
| Educational level|             |                                    |                                        | 0.475   |
| None            | 69(6.3%)    | 52(75.3%)                          | 17(24.6%)                              |         |
| Primary         | 344(31.5%)  | 281(81.7%)                         | 63(18.3%)                              |         |
| Secondary       | 555(50.9%)  | 436(78.6%)                         | 119(21.4%)                             |         |
| University      | 114(10.4%)  | 86(75.4%)                          | 28(24.6%)                              |         |
| No information  | 9(0.8%)     | 8(88.9%)                           | 1(11.1%)                               |         |
| Monthly income (MT) |             |                                    |                                        | 0.271   |
| No income       | 287(26.3%)  | 217(75.6%)                         | 70(24.4%)                              |         |
| < 2500          | 241(22.1%)  | 203(84.2%)                         | 38(15.8%)                              |         |
| [2500–5000]     | 224(20.5%)  | 179(79.9%)                         | 45(20.1%)                              |         |
| [5001–10000]    | 183(16.8%)  | 143(78.1%)                         | 40(21.9%)                              |         |
| > 10000         | 117(10.7%)  | 91(77.8%)                          | 26(22.2%)                              |         |
| No information  | 39(3.6%)    | 30(76.9%)                          | 9(23.1%)                               |         |
| Neighborhood    |             |                                    |                                        | <0.001  |
| Central A       | 81(7.4%)    | 41(50.6%)                          | 40(49.4%)                              |         |
| Aeroporto B     | 176(16.1%)  | 136(77.3%)                         | 40(22.7%)                              |         |
| Polana Caniço A | 177(16.2%)  | 149(84.2%)                         | 28(15.8%)                              |         |
| Mahotas         | 334(30.6%)  | 274(82.0%)                         | 60(18.0%)                              |         |
| 25 de Junho A   | 323(29.6%)  | 263(81.4%)                         | 60(18.6%)                              |         |

https://doi.org/10.1371/journal.pone.0221452.t001
participants (94.8%) received instructions on how to use the antibiotics, but 28.7% (313/1091) did not complete the course of treatment. More than half (52.4%; 572/1091) had a poor knowledge about antibiotics and almost half (46.4%; 506/1091) had only a reasonable knowledge about use of antibiotics.

Bivariate analysis showed that frequency of use of non-prescribed antibiotics was higher in participants who obtained antibiotics for self-use (164/569; 28.8%) rather than for their children (35/290; 12.1%) or other household members (29/144; 20.1%). Most of the non-prescribed antibiotics were purchased in pharmacies (87.3%; 199/228), but use of non-prescribed antibiotics was more frequent among those who obtained from informal market (14/17; 82.6%) and home stores (12/18; 66.7%) as compared to pharmacies (199/810; 24.6%). Use of non-prescribed antibiotics was also associated with lack of instruction on how to use antibiotics (93.3%; 42/45), not completing the course (47.6%, 149/313) and poor knowledge about the use of antibiotics (33.7%).

| Table 2. Knowledge and practices regarding antibiotics by use of prescribed and non-prescribed antibiotics. |
|---------------------------------------------------------------|
| **Characteristics**                                           | **Total** | **Use of prescribed antibiotics** | **Use of non-prescribed antibiotics** |
|                                                              | n (%)     | n (%)                             | n (%)                                 |
| **Total purpose of the antibiotic purchased**                 |           |                                   |                                       |
| Self-use                                                      | 569(52.2%)| 405(71.2%)                        | 164(28.8%)                            |
| Child’s disease                                               | 290(26.6%)| 255(87.9%)                        | 35(12.1%)                             |
| Other household member’s disease                              | 144(13.2%)| 115(79.9%)                        | 29(20.1%)                             |
| No information                                                | 88(8.1%)  | 88(100%)                          | 0(0%)                                 |
| **Total source of antibiotic**                                |           |                                   |                                       |
| Pharmacy                                                      | 810(74.2%)| 611(75.4%)                        | 199(24.6%)                            |
| Informal market/Other                                         | 17(1.6%)  | 3(17.6%)                          | 14(82.6%)                             |
| Home store                                                    | 18(1.6%)  | 6(33.3%)                          | 12(66.7%)                             |
| No information                                                | 246(22.5%)| 243(98.8%)                        | 3(1.2%)                               |
| **Total received instructions for use of antibiotic?**       |           |                                   |                                       |
| Yes                                                           | 1034(94.8%)| 852(82.4%)                        | 182(17.6%)                            |
| No                                                            | 45(4.1%)  | 3(6.7%)                           | 42(93.3%)                             |
| Don’t remember                                                | 2(0.2%)   | 0(0.0%)                           | 2(100%)                               |
| No information                                                | 10(0.9%)  | 8(80.0%)                          | 2(20.0%)                              |
| **Total completed the course?**                              |           |                                   |                                       |
| Yes                                                           | 735(67.4%)| 663(90.2%)                        | 72(9.8%)                              |
| No                                                            | 313(28.7%)| 164(52.4%)                        | 149(47.6%)                            |
| Don’t remember                                                | 17(1.6%)  | 15(88.2%)                         | 2(11.8%)                              |
| No information                                                | 26(2.4%)  | 21(80.8%)                         | 5(19.2%)                              |
| **Total level of knowledge about antibiotics**                |           |                                   |                                       |
| Good                                                          | 327(30.0%)| 263(80.4%)                        | 64(19.6%)                             |
| Reasonable                                                    | 109(10.0%)| 77(70.6%)                         | 32(29.4%)                             |
| Poor                                                          | 572(52.4%)| 452(79.0%)                        | 120(21.0%)                            |
| No information                                                | 83(7.6%)  | 71(85.5%)                         | 12(14.5%)                             |
| **Total level of knowledge on the use of antibiotics**        |           |                                   |                                       |
| Good                                                          | 253(23.2%)| 208(82.2%)                        | 45(17.8%)                             |
| Reasonable                                                    | 506(46.4%)| 419(82.8%)                        | 87(17.2%)                             |
| Poor                                                          | 249(22.5%)| 165(66.3%)                        | 84(33.7%)                             |
| No information                                                | 83(7.6%)  | 71(85.5%)                         | 12(14.5%)                             |
Logistic regression analysis was performed to assess the variables independently associated with the use of non-prescribed antibiotics. Table 3 shows that the independently associated variables were as follows: male gender (p = 0.004, OR = 1.88 compared to reference group (female); living in the Central A neighborhood (p < 0.001, OR = 4.87), Aeroporto B neighborhood (p < 0.001, OR = 6.50) and 25 de Junho neighborhood (p < 0.001, OR = 3.43) compared to the reference neighborhood (Polana Cânico A); purchasing antibiotics from informal markets (p < 0.002, OR = 12.62) and from home stores (p = 0.026, OR = 4.54) compared to the reference group (pharmacy), not completing the course (p < 0.001, OR = 11.42) compared to the reference group (completing the course) and having poor knowledge on the use of antibiotics (p < 0.001, OR = 2.60) compared to the reference group (reasonable knowledge).

Factors associated with use of non-prescribed antibiotics

Logistic regression analysis was performed to assess the variables independently associated with the use of non-prescribed antibiotics. Table 3 shows that the independently associated variables were as follows: male gender (p = 0.004, OR = 1.88 compared to reference group (female); living in the Central A neighborhood (p < 0.001, OR = 4.87), Aeroporto B neighborhood (p < 0.001, OR = 6.50) and 25 de Junho neighborhood (p < 0.001, OR = 3.43) compared to the reference neighborhood (Polana Cânico A); purchasing antibiotics from informal markets (p < 0.002, OR = 12.62) and from home stores (p = 0.026, OR = 4.54) compared to the reference group (pharmacy), not completing the course (p < 0.001, OR = 11.42) compared to the reference group (completing the course) and having poor knowledge on the use of antibiotics (p < 0.001, OR = 2.60) compared to the reference group (reasonable knowledge).

Socio-demographic characteristics associated with poor level of knowledge of antibiotics

Because level of knowledge about antibiotics in this study was poor, we were interested in understanding the factors associated with poor level of knowledge about antibiotics. Table 4 shows that frequency of poor level of knowledge about antibiotics increased with increasing age. Poor level of knowledge was also higher in divorced participants, in those with a lower level of education, and lower monthly income.

Level of knowledge about antibiotics varied in different neighborhoods, with the worst knowledge observed in Polana Cânico.
Socio-demographic characteristics associated with poor level of knowledge about the use of antibiotics

Table 5 shows that there was a trend towards increased frequency of poor knowledge about use of antibiotics with increasing age. A poor level of knowledge was also more frequent in two groups: the widowed and illiterate. Marital status (p = 0.019), educational level (p < 0.001), monthly income (p < 0.001) and place of residence (p < 0.001) were associated with knowledge about use of antibiotics, but no specific trend was noted.

### Table 4. Association between level of knowledge about antibiotics and socio-demographic characteristics.

| Characteristics | Knowledge about antibiotics | p-value |
|----------------|----------------------------|---------|
|                | Total | Good (32.4%) | Reasonable (10.8%) | Poor (56.7%) |
| Gender         |       |               |                    |               |
| Male           | 267(26.5%) | 99(31.7%) | 30(11.2%) | 138(51.7%) | 0.128 |
| Female         | 741(73.5%) | 228(30.8%) | 79(10.7%) | 434(58.6%) |
| Age (years)    |       |               |                    |               |
| 18–39          | 637(63.1%) | 226(35.5%) | 75(11.8%) | 336(52.7%) | 0.003 |
| 40–59          | 279(27.7%) | 79(28.3%) | 32(11.5%) | 168(60.2%) |
| ≥60            | 87(8.6%) | 21(24.1%) | 2(2.3%) | 64(73.6%) |
| No information | 5(0.5%) | 1(20.0%) | 0(0%) | 4(80.0%) |
| Marital status |       |               |                    |               |
| Single         | 307(30.5%) | 112(36.5%) | 42(13.7%) | 153(49.8%) | 0.001 |
| Married (officially) | 144(14.3%) | 62(43.1%) | 13(9.0%) | 69(47.9%) |
| Married (de facto) | 433(43.0%) | 121(27.9%) | 43(9.9%) | 269(62.1%) |
| Widowed        | 33(3.3%) | 10(30.3%) | 6(18.2%) | 17(51.5%) |
| Divorced       | 66(6.5%) | 16(24.2%) | 2(3.0%) | 48(72.7%) |
| No information | 25(2.5%) | 6(24.0%) | 3(12.0%) | 16(64.0%) |
| Educational level |       |               |                    |               |
| None           | 55(5.5%) | 5(9.1%) | 2(3.6%) | 48(87.3%) | <0,001 |
| Primary        | 310(30.8%) | 31(10.0%) | 27(8.7%) | 252(81.3%) |
| Secondary      | 526(52.2%) | 209(39.7%) | 69(13.1%) | 248(47.1%) |
| University     | 109(10.8%) | 79(72.5%) | 11(10.1%) | 19(17.4%) |
| No information | 8(0.8%) | 3(37.5%) | 0(0%) | 5(62.5%) |
| Monthly income (Meticais) |       |               |                    |               |
| No income      | 252(25.0%) | 80(31.7%) | 25(9.9%) | 147(58.3%) | <0,001 |
| <2500          | 235(23.3%) | 39(16.6%) | 18(7.7%) | 178(75.7%) |
| [2500–5000]    | 214(21.2%) | 54(25.2%) | 26(12.3%) | 134(62.7%) |
| [5001–10000]   | 166(16.5%) | 74(44.6%) | 16(9.6%) | 76(45.8%) |
| ≥10000         | 104(10.3%) | 70(67.3%) | 15(14.4%) | 19(18.3%) |
| No information | 37(3.7%) | 10(27.0%) | 9(24.3%) | 18(48.6%) |
| Neighborhood   |       |               |                    |               |
| Central A      | 80(7.9%) | 41(51.3%) | 8(10.0%) | 31(38.8%) | <0,001 |
| Aeroporto B    | 170(16.9%) | 40(23.5%) | 11(6.5%) | 119(70.0%) |
| P. Canico A    | 177(17.6%) | 26(14.7%) | 12(6.8%) | 139(78.5%) |
| Mahotas        | 330(32.7%) | 91(27.6%) | 37(11.2%) | 202(61.2%) |
| 25 de Junho    | 251(24.9%) | 129(51.4%) | 41(16.3%) | 81(32.3%) |

https://doi.org/10.1371/journal.pone.0221452.t004
Completeness of the antibiotic course was used as a proxy to assess practice in terms of use of antibiotics and Table 6 shows that the frequency of failure to complete the course was higher in younger and in single participants. Frequency of failure was heterogeneous across different income levels ($p = 0.000$) and in different neighbourhoods ($p < 0.001$) and no specific trend was noted.

**Socio-demographic characteristics associated with poor completeness of the antibiotic course**

Completeness of the antibiotic course was used as a proxy to assess practice in terms of use of antibiotics and Table 6 shows that the frequency of failure to complete the course was higher in younger and in single participants. Frequency of failure was heterogeneous across different income levels ($p = 0.000$) and in different neighbourhoods ($p < 0.001$) and no specific trend was noted.

**Reasons for use of non-prescribed antibiotics**

Fig 1 shows that the main reason for use of non-prescribed antibiotics was a perception by the participants that there was no need to attend a health facility (26.8%). Someone else’s advice

---

Table 5. Association between level of knowledge about the use of antibiotics and socio-demographic characteristics.

| Characteristics               | Total       | Good (%) | Reasonable (%) | Poor (%) | $p$-value |
|------------------------------|-------------|----------|----------------|---------|-----------|
| Gender                       |             |          |                |         |           |
| Male                         | 267         | 65 (24.3%) | 139 (52.1%)   | 63 (24.6%) | 0.774     |
| Female                       | 741         | 188 (25.4%) | 367 (49.5%)   | 186 (25.1%) |           |
| Age (years)                  |             |          |                |         |           |
| 18–39                        | 637         | 187 (29.4%) | 296 (46.5%)   | 154 (24.2%) | 0.002     |
| 40–59                        | 279         | 47 (16.8%)  | 161 (57.7%)   | 71 (25.4%)  |           |
| >60                          | 87          | 17 (19.5%)  | 46 (52.9%)    | 24 (27.6%)  |           |
| No information               | 5           | 2 (40.0%)   | 3 (60.0%)     | 0         |           |
| Marital status               |             |          |                |         | 0.019     |
| Single                       | 307         | 91 (29.6%)  | 139 (45.3%)   | 77 (25.1%)  |           |
| Married (officially)         | 144         | 22 (15.3%)  | 87 (60.4%)    | 35 (24.3%)  |           |
| Married (de facto)           | 433         | 117 (27.0%) | 217 (50.1%)   | 99 (22.9%)  |           |
| Widower                      | 33          | 4 (12.1%)   | 16 (48.5%)    | 13 (39.4%)  |           |
| Divorced                     | 66          | 14 (21.2%)  | 36 (54.5%)    | 16 (24.2%)  |           |
| No information               | 25          | 5 (20.0%)   | 11 (44.0%)    | 9 (36.0%)   |           |
| Educational level            |             |          |                |         | <0.001    |
| None                         | 55          | 12 (21.8%)  | 21 (38.2%)    | 22 (40.0%)  |           |
| Primary                      | 310         | 97 (31.3%)  | 127 (41.0%)   | 86 (27.7%)  |           |
| Secondary                    | 526         | 132 (25.1%) | 282 (53.6%)   | 112 (21.3%) |           |
| University                   | 109         | 10 (9.2%)   | 72 (66.1%)    | 27 (24.8%)  |           |
| No information               | 8           | 2 (25.0%)   | 4 (50.0%)     | 2 (25.0%)   |           |
| Monthly income (Meticais)    |             |          |                |         | <0.001    |
| No income                    | 252         | 79 (31.3%)  | 112 (44.4%)   | 61 (24.2%)  |           |
| <2500                        | 235         | 71 (30.2%)  | 96 (40.9%)    | 68 (28.9%)  |           |
| [2500–5000]                  | 214         | 59 (27.6%)  | 104 (48.6%)   | 51 (23.8%)  |           |
| [5000–10000]                 | 166         | 31 (18.7%)  | 102 (61.4%)   | 33 (19.9%)  |           |
| ≥10000                       | 104         | 8 (7.7%)    | 70 (67.3%)    | 26 (25.0%)  |           |
| No information               | 37          | 5 (13.5%)   | 22 (59.5%)    | 10 (27.0%)  |           |
| Neighborhood                 |             |          |                |         | <0.001    |
| Central A                    | 80          | 9 (11.3%)   | 50 (62.5%)    | 21 (26.3%)  |           |
| Aeroporto B                  | 170         | 64 (37.6%)  | 59 (34.7%)    | 47 (27.6%)  |           |
| P. Canico A                  | 177         | 62 (35.0%)  | 76 (42.9%)    | 39 (22.0%)  |           |
| Mahotas                      | 330         | 86 (26.1%)  | 160 (48.5%)   | 84 (25.5%)  |           |
Table 6. Association between completeness of antibiotic course and socio-demographic characteristics.

| Characteristics | Completed the antibiotic course |
|-----------------|---------------------------------|
|                 | Total Yes | No | p-value |
| Total           | 1048(100%) | 735(70.1%) | 313 (29.9%) |
| Gender          |          |                |        |
| Male            | 280(26.7%) | 196(70.0%) | 84(30.0%) | 0.506 |
| Female          | 768(73.3%) | 539(70.2%) | 229(29.8%) |
| Age (years)     |          |                |        |
| 18–39           | 651(62.1%) | 432(65.6%) | 219(24.4%) | 0.002 |
| 40–59           | 283(27.0%) | 214(75.6%) | 69(22.4%) |
| >60             | 109(10.4%) | 86(78.9%) | 23(21.1%) |
| No information  | 5(0.5%)   | 3(60%) | 2(40%) |
| Marital status  |          |                |        |
| Single          | 317(30.2%) | 193(60.9%) | 124(39.1%) | <0.001 |
| Married (officially) | 158(15.1%) | 119(75.3%) | 39(24.7%) |
| Married (de facto) | 430(41.0%) | 313(72.8%) | 117(27.2%) |
| Widower         | 32(2.1%) | 23(71.9%) | 9(28.1%) |
| Divorced        | 78(7.4%) | 63(80.8%) | 15(19.2%) |
| No information  | 33(3.1%) | 24(72.7%) | 9(27.3%) |
| Educational level |          |                |        |
| None            | 65(6.2%) | 50(76.9%) | 15(23.1%) | 0.094 |
| Primary         | 334(31.9) | 246(73.7%) | 88(26.3%) |
| Secondary       | 531(50.7%) | 354(66.7) | 177(33.3%) |
| University      | 110(10.5%) | 77(70.0%) | 33(30.0%) |
| No information  | 8(0.8%) | 8(100%) | 0 |
| Monthly income  |          |                |        |
| No income       | 276(26.3%) | 182(68.4%) | 94(34.1%) | 0.005 |
| <2500           | 230(21.9%) | 174(75.7%) | 56(24.3%) |
| [2500–5000]     | 215(20.5%) | 147(68.4%) | 68(31.6%) |
| [5000–10000]    | 175(16.7%) | 115(65.7%) | 60(34.3%) |
| >10000          | 114(10.9%) | 93(81.6%) | 21(28.4%) |
| No information  | 38(3.6%) | 24(63.2%) | 14(26.8%) |
| Neighborhood    |          |                |        |
| Central A       | 75(7.2%) | 48(64%) | 27(36%) | <0.001 |
| Aeroporto B     | 168(16.0%) | 118(70.2%) | 50(29.8%) |
| P. Canico A     | 170(16.2%) | 139(81.8%) | 31(18.2%) |
| Mahotais        | 320(30.5%) | 191(59.70%) | 129(40.3%) |
| 25 Junho        | 315(30.1%) | 239(75.9%) | 76(24.1%) |

(7.7%), symptoms similar to a previous episode (6.2%), poor quality of care in health facilities (6.7%) and the inconvenience of a long waiting time (4.3%) were also mentioned as reasons for use of non-prescribed antibiotics.

**Discussion**

Mozambique and other countries in sub-Saharan Africa which are developing National Action Plans for combating AMR, are suffering from a paucity of data on knowledge, attitudes and practices regarding antibiotic use. In this study conducted in Maputo City, we found that use of non-prescribed antibiotics was reported by 20.9% of study participants, corroborating findings from other countries across the globe that shows that dispensing of antibiotics without
prescription is a serious problem, despite being prohibited [10, 18–21]. Frequency of use of non-prescribed antibiotics found in our study are similar to those from studies conducted in Egypt and Kosovo [22, 23], but lower than those from other studies in sub-Saharan Africa [10, 20, 24].

Men used non-prescribed antibiotics more frequently than women, a finding also reported from a study in Beirut [25]. The more frequent use of prescribed antibiotics by women may be due to more contact with the formal health services because of reproductive and child health needs.

We found that adults rely more on the clinician’s recommendation for use of antibiotics for their child than when using for their own health because our data showed that use non-prescribed antibiotics was higher when the purpose was for their own health, rather than for their child’s disease.

Most non-prescribed antibiotics were obtained from pharmacies. This practice is of concern and illegal. Mozambican law prohibits dispensing of antibiotics without prescription [13]. Similar findings have been reported in other countries in sub-Saharan Africa [19, 24]. This is different from developed countries, where most non-prescribed antibiotics are obtained from family, friends and home stores [10]. This practice indicates insufficient enforcement of current legislation and poor inspection of pharmacies, which is also seen in other countries where a significant number of pharmacists were unaware of local laws and legislation on prescription of antibiotics [12, 26].

As most of non-prescribed antibiotics were bought in pharmacies, public health interventions should target not only communities, but also pharmacies and pharmacists, as recommended by others [12, 24, 27]. These interventions should focus on education of pharmacists, combined with measures to enforce existing laws, such as frequent supervisions and inspections of all pharmacies [12]. Studies in Brazil, Mexico, Thailand and Vietnam have shown that implementation of measures for enforcement of existing laws led to a reduction in over consumption of antibiotics [28, 29].

Although the proportion of antibiotics obtained from informal markets and home stores was small, the use of non-prescribed antibiotics was more frequent in individuals who obtained antibiotics from these places. Efforts should therefore be made to also inspect informal markets [12].

Fig 1. Reasons for use of non-prescribed antibiotics in those who used non-prescribed antibiotics (n = 209). Frequency represents proportion of individuals.

https://doi.org/10.1371/journal.pone.0221452.g001
Use of non-prescribed antibiotics is known to be related to its incorrect use [30, 31] and data from this study showed an association between use of non-prescribed antibiotics and poor adherence to the full course of antibiotics. A similar finding was reported in Nigeria [24].

In terms of knowledge about antibiotics or their use, our data showed that more than half of the participants had a poor knowledge about antibiotics and frequency of use of non-prescribed antibiotics was significantly higher among those with poor knowledge on the use of antibiotics. Moreover, knowledge about antibiotics improved with increased educational level and monthly income. Similar results have been found in other countries [32]. Monthly income and educational level are a proxy of socio-economic status and people with higher income and education levels are likely to have better access not only to health care, but also to information [33, 34].

Although our data showed that majority of participants received instructions on the use of antibiotics, we strongly believe that instructions given to the participants were poor or inappropriate. We base this belief on the following reasons: i) a third of the participants did not complete the course, ii) more than half of the participants showed poor knowledge about antibiotics, iii) almost a quarter of the participants had poor knowledge about antibiotic use. These findings highlight the urgent need to regularly train and refresh pharmacists, along with abiding by the law and stopping the dispensing of non-prescription antibiotics.

The main reason for use/purchase of non-prescribed antibiotics was the perception that there was no need to go to a health facility. Prior experiences of poor quality of care and the inconvenience of long waiting times at health facilities were also mentioned by participants, although with less frequency. This is in agreement with findings from developing countries [35, 36], but contrasts with the reasons for self-use of antibiotics in developed countries, which are mostly related to someone else’s advice and previous experience [32, 37].

Altogether, data from this study suggest that additional studies should be conducted in the country in order to assess the effectiveness and impact of integrated interventions involving different approaches, as suggested by other authors [2, 38, 39]. Previous studies in other countries have demonstrated the importance of implementation of educational programs for pharmacists and at community level and measures to increase adherence to the existing laws and legislation on the use and dispensing of antibiotics [12, 24].

This study was based only on self-reporting information by participants, which represents a limitation due to recall bias.

Conclusions
This study expands the limited data regarding knowledge, attitudes and practices of communities regarding antibiotic use in sub-Saharan Africa and has shown for the first time that more than half of the participants had poor knowledge about antibiotics and 20.9% of participants reported they purchased non-prescribed antibiotics. This study also found that most non-prescribed antibiotics were purchased in pharmacies, despite this being legally prohibited. These findings provide evidence for the ongoing efforts in Mozambique to design interventions to reduce the use of non-prescribed antibiotics. We recommend multifaceted interventions, including reinforcement of current legislation and frequent inspections, combined with education of pharmacists and communities.

Supporting information
S1 Table. Calculation of the number of people to be enrolled from each Municipal District of Maputo City.
(DOCX)
S2 Table. Calculation of the number of people to be enrolled from each Municipal District of Maputo City after removal of Ka Tembe e Ka Nhaka Municipal Districts.

S1 File. Study questionnaire in Portuguese.

S2 File. Study questionnaire in English.

Acknowledgments

We would like to thank the Mozambique FELTP team, especially Mrs. Cynthia Sema, for their support. We also thank the enumerators/interviewers and the entire team from the Data Management Unit of the National Institute of Health.

Author Contributions

Conceptualization: Inocêncio Mate, Charlotte Elizabeth Come, Maria Patrícia Gonçalves, Julie Cliff, Eduardo Samo Gudo.

Formal analysis: Inocêncio Mate, Charlotte Elizabeth Come, Maria Patrícia Gonçalves, Julie Cliff, Eduardo Samo Gudo.

Funding acquisition: Inocêncio Mate, Eduardo Samo Gudo.

Investigation: Inocêncio Mate, Charlotte Elizabeth Come, Maria Patrícia Gonçalves, Eduardo Samo Gudo.

Methodology: Inocêncio Mate, Charlotte Elizabeth Come, Maria Patrícia Gonçalves, Julie Cliff, Eduardo Samo Gudo.

Project administration: Inocêncio Mate, Eduardo Samo Gudo.

Resources: Inocêncio Mate, Eduardo Samo Gudo.

Supervision: Eduardo Samo Gudo.

Writing – original draft: Inocêncio Mate, Charlotte Elizabeth Come, Maria Patrícia Gonçalves, Eduardo Samo Gudo.

Writing – review & editing: Inocêncio Mate, Maria Patrícia Gonçalves, Julie Cliff, Eduardo Samo Gudo.

References

1. WHO. Antimicrobial Resistance: Global Report on Surveillance 2014. Geneve, Switzerland: WHO, 2014.
2. WHO. Global Action Plan on AMR. Geneve, Switzerland: 2015.
3. O’Neill J. Antimicrobial Resistance:Tackling a crisis for the health and wealth of nations. UK: Wellcome Trust, 2014.
4. Tenover FC. Mechanisms of antimicrobial resistance in bacteria. Am J Infect Control. 2006; 34(5 Suppl 1):S3–10; discussion S64-73. https://doi.org/10.1016/j.ajic.2006.05.219 PMID: 16813980.
5. Goossens H, Ferech M, Vander Stichele R, Elseviers M, Group EP. Outpatient antibiotic use in Europe and association with resistance: a cross-national database study. Lancet. 2005; 365(9459):579–87. https://doi.org/10.1016/S0140-6736(05)17907-6 PMID: 15708101.
6. Jamhour A, El-Kheir A, Salameh P, Hanna PA, Mansour H. Antibiotic knowledge and self-medication practices in a developing country: A cross-sectional study. Am J Infect Control. 2017; 45(4):384–8. https://doi.org/10.1016/j.ajic.2016.11.026 PMID: 28087169.
7. Van Boeckel TP, Gandra S, Ashok A, Caudron Q, Grenfell BT, Levin SA, et al. Global antibiotic consumption 2000 to 2010: an analysis of national pharmaceutical sales data. Lancet Infect Dis. 2014; 14(8):742–50. https://doi.org/10.1016/S1473-3099(14)70780-7 PMID: 25022435.

8. Mshana SE, Matee M, Rwemyamur M. Antimicrobial resistance in human and animal pathogens in Zambia, Democratic Republic of Congo, Mozambique and Tanzania: an urgent need of a sustainable surveillance system. Ann Clin Microbiol Antimicrob. 2013; 12:28. https://doi.org/10.1186/1476-0711-12-28 PMID: 24119299; PubMed Central PMCID: PMC3852305.

9. Hart CA, Kariuki S. Antimicrobial resistance in developing countries. BMJ. 1998; 317(759):647–50. https://doi.org/10.1136/bmj.317.7519.647 PMID: 9727995; PubMed Central PMCID: PMC1113834.

10. Morgan DJ, Okeke IN, Laxminarayan R, Perencevich EN, Weisenberg S, World Health Organization. Non-prescription antimicrobial use worldwide: a systematic review. Lancet Infect Dis. 2011; 11(9):692–701. https://doi.org/10.1016/S1473-3099(11)70054-8 PMID: 21659004; PubMed Central PMCID: PMC3543997.

11. Okeke IN, Laxminarayan R, Bhutta ZA, Duse AG, Jenkins P, O'Brien TF, et al. Antibacterial resistance in developing countries. Part I: recent trends and current status. Lancet Infect Dis. 2005; 5(8):481–93. https://doi.org/10.1016/S1473-3099(05)70189-4 PMID: 16048717.

12. Leung E, Weil DE, Raviglione M, Nakatani H, World Health Organization World Health Day. Antimicrobial Resistance Technical Working G. The WHO policy package to combat antibiotic resistance. Bull World Health Organ. 2011; 89(5):390–2. https://doi.org/10.2471/BLT.11.088435 PMID: 21556308; PubMed Central PMCID: PMC3089396.

13. MISAU. Lei do Medicamento. Maputo, Moçambique: MISAU, 2017 September 8th, 2017. Report No.: Contract No.: 141.

14. Farmácia M-CtDeTe. Formulário Nacional de Medicamentos. Maputo, Moçambique: MISAU, 2007.

15. Mandomando I, Sigauque B, Morais L, Espasa M, Valles X, Sacralia J, et al. Antimicrobial drug resistance trends of bacteremia isolates in a rural hospital in southern Mozambique. Am J Trop Med Hyg. 2010; 83(1):152–7. https://doi.org/10.4269/ajtmh.2010.09-0578 PMID: 20595494; PubMed Central PMCID: PMC2912592.

16. Mandomando I, Espasa M, Valles X, Sacralia J, Sigauque B, Ruiz J, et al. Antimicrobial resistance of Vibrio cholerae O1 serotype Ogawa isolated in Manhica District Hospital, southern Mozambique. J Antimicrob Chemother. 2007; 60(3):662–4. https://doi.org/10.1093/jac/dkm257 PMID: 17626024.

17. van der Meeren BT, Chhaganlal KD, Pfeiffer A, Gomez E, Ferro JJ, Hilbink M, et al. Extremely high prevalence of multi-resistance among uropathogens from hospitalised children in Beira, Mozambique. S Afr Med J. 2013; 103(6):382–6. https://doi.org/10.7196/samj.5941 PMID: 23725956.

18. Al-Faham Z, Haboub G, Takriti F. The sale of antibiotics without prescription in pharmacies in Damascus, Syria. J Infect Dev Ctries. 2011; 5(5):396–9. PMID: 21628818.

19. Kalungia AC, Burger J, Godman B, Costa JO, Simuwelu C. Non-prescription sale and dispensing of antibiotics in community pharmacies in Zambia. Expert Rev Anti Infect Ther. 2016; 14(12):1215–23. https://doi.org/10.1080/14787210.2016.1227702 PMID: 27548601.

20. Ekwuchi U, Chinawa JM, Osuorah CD, Odetunde OI, Olu HA, Agwu S. The use of unprescribed antibiotics in management of upper respiratory tract infection in children in Enugu, South East Nigeria. J Trop Pediatr. 2014; 60(3):249–52. https://doi.org/10.1093/tropej/fmt111 PMID: 24436341.

21. Ekwuchi U, Chinawa JM, Obi I, Olu HA, Agwu S. Use and/or misuse of antibiotics in management of diarrhoea among children in Enugu, Southeast Nigeria. J Trop Pediatr. 2013; 59(4):314–6. https://doi.org/10.1093/tropej/fmt016 PMID: 23619599.

22. Sabry NA, Farid SF, Dawoud DM. Antibiotic dispensing in Egyptian community pharmacies: an observational study. Res Social Adm Pharm. 2014; 10(1):168–84. https://doi.org/10.1016/j.sapharm.2013.03.004 PMID: 23665078.

23. Zajmi D, Berisha M, Begoli I, Hoxha R, Mehmeti R, Mulliqi-Osmani G, et al. Public knowledge, attitudes and practices regarding antibiotic use in Kosovo. Pharm Pract (Granada). 2017; 15(1):827. https://doi.org/10.1093/ tropej/fmt016 PMID: 23665078.

24. Esimone CO, Nwonu CS, Udogaranya OP. Utilization of antimicrobial agents with and without prescription by out-patients in selected pharmacies in South-eastern Nigeria. Pharm World Sci. 2007; 29(6):655–60. https://doi.org/10.1016/S1478-7210(07)70125-5 PMID: 17464572.

25. Cheaito L, Azizi S, Saleh N, Salameh P. Assessment of self-medication in population buying antibiotics in pharmacies: a pilot study from Beirut and its suburbs. Int J Public Health. 2014; 59(2):319–27. https:// doi.org/10.1007/s00038-013-0493-y PMID: 23942698.

26. Hadi MA, Karami NA, Al-Mualid AS, Al-Otabi A, Al-Subahi E, Bamomen A, et al. Community pharmacists’ knowledge, attitude, and practices towards dispensing antibiotics without prescription (DAwP): a cross-sectional survey in Makkah Province, Saudi Arabia. Int J Infect Dis. 2016; 47:95–100. https://doi.org/10.1016/j.ijid.2016.06.003 PMID: 27343987.
27. Roca I, Akova M, Baquero F, Carlet J, Cavaleri M, Coenen S, et al. The global threat of antimicrobial resistance: science for intervention. New Microbes New Infect. 2015; 6:22–9. https://doi.org/10.1016/j.nmmni.2015.02.007 PMID: 26029375; PubMed Central PMCID: PMC4463399.

28. Santa-Ana-Tellez Y, Mantel-Teuwen AK, Dreser A, Leufkens HG, Wirtz VJ. Impact of over-the-counter restrictions on antibiotic consumption in Brazil and Mexico. PLoS One. 2013; 8(10):e75550. https://doi.org/10.1371/journal.pone.0075550 PMID: 24146761; PubMed Central PMCID: PMC3797702.

29. Chalker J, Ratnawijitrasin S, Chuc NT, Petzold M, Tomson G. Effectiveness of a multi-component intervention on dispensing practices at private pharmacies in Vietnam and Thailand—a randomized controlled trial. Soc Sci Med. 2005; 60(1):131–41. https://doi.org/10.1016/j.socscimed.2004.04.019 PMID: 15482873.

30. Awad AI, Eltayeb IB. Self-medication practices with antibiotics and antimalarials among Sudanese undergraduate university students. Ann Pharmacother. 2007; 41(7):1249–55. https://doi.org/10.1345/aph.1k068 PMID: 17565044.

31. Pan H, Cui B, Zhang D, Farrar J, Law F, Ba-Thein W. Prior knowledge, older age, and higher allowance are risk factors for self-medication with antibiotics among university students in southern China. PLoS One. 2012; 7(7):e13134. https://doi.org/10.1371/journal.pone.0041314 PMID: 22911779; PubMed Central PMCID: PMC3401104.

32. Shehadeh M, Sulaiman G, Darwish RM, Wazayf M, Zaru L, Aljafari S. Knowledge, attitudes and behavior regarding antibiotics use and misuse among adults in the community of Jordan: A pilot study. Saudi Pharm J. 2012; 20(2):125–33. https://doi.org/10.1016/j.jsps.2011.11.005 PMID: 23960783; PubMed Central PMCID: PMC3744980.

33. Baskaradoss JK. Relationship between oral health literacy and oral health status. BMC Oral Health. 2018; 18(1):172. https://doi.org/10.1186/s12903-018-0640-1 PMID: 30355347.

34. Zajacova A, Lawrence EM. The Relationship Between Education and Health: Reducing Disparities Through a Contextual Approach. Annu Rev Public Health. 2018; 39:273–89. https://doi.org/10.1146/annurev-publhealth-031816-044628 PMID: 29328865; PubMed Central PMCID: PMC5880718.

35. Saha S, Hossain MT. Evaluation of medicines dispensing pattern of private pharmacies in Rajshahi, Bangladesh. BMC Health Serv Res. 2017; 17(1):136. https://doi.org/10.1186/s12913-017-2072-z PMID: 28193274; PubMed Central PMCID: PMC5307842.

36. Babatunde OA, Fadare JO, Ojo OJ, Durowade KA, Atoyebi PO, et al. Self-medication among health workers in a tertiary institution in South-West Nigeria. Pan Afr Med J. 2016; 24:312. https://doi.org/10.11604/pamj.2016.24.312.8146 PMID: 26154667; PubMed Central PMCID: PMC5267862.

37. Napolitano F, Izzo MT, Di Giuseppe G, Angelillo IF. Public knowledge, attitudes, and experience regarding the use of antibiotics in Italy. PLoS One. 2013; 8(12):e84177. https://doi.org/10.1371/journal.pone.0084177 PMID: 24376793; PubMed Central PMCID: PMC3871866.

38. Arnold SR, Straus SE. Interventions to improve antibiotic prescribing practices in ambulatory care. Cochrane Database Syst Rev. 2005;(4):CD003539. https://doi.org/10.1002/14651858.CD003539.pub2 PMID: 16235325.

39. Al-Tawfiq JA, Alawami AH. A multifaceted approach to decrease inappropriate antibiotic use in a pediatric outpatient clinic. Ann Thorac Med. 2017; 12(1):51–4. https://doi.org/10.4103/1817-1737.197779 PMID: 28197223; PubMed Central PMCID: PMC594174.