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*Original Article*

# Surveillance of antibiotic use in the private sector in Namibia using sales and claims data

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## Abstract

Introduction: Antibiotics are among the most commonly used therapeutic agents for humans globally, and their use has been associated with the development of resistance. The objective of this study was to identify sources for quantifying antibiotic usage patterns and to assess such use in ambulatory patients in the private health sector of Namibia.

Methodology: A retrospective analysis of prescription claims data and sales data for the period 2008 to 2011 was conducted. Antibiotic use was expressed in the number of antibiotic-containing prescriptions and volume of units sold and then standardized using defined daily dose per 1,000 inhabitants per day.

Results: Antibiotic usage was highest in females (53%), in people 18–45 years of age (41%), and in Windhoek (34%). Overall, wholesale data showed higher antibiotic use than prescription claims data. However, both sources showed similar patterns of antibiotic use. Penicillins were the most used pharmacological group, with amoxicillin/clavulanic acid combination being the most used of the agents.

Conclusion: Antibiotic use in the private sector of Namibia is comparable to that of high-consuming European countries such as Italy. A trend observed in this study was the decrease in the use of narrow-spectrum antibiotics in favour of broad-spectrum and newer antibiotics. Since this was the first study to assess antibiotic use in the private sector of Namibia, it could serve as a starting point for continued monitoring of antibiotic use in the whole of Namibia in the context of the World Health Organization's Global Action Plan to contain antibiotic resistance.

**Key words:** antibiotics; antibiotic use; Namibia; private sector.

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## Introduction

Infectious diseases account for 15 million deaths per year globally, equivalent to a 43% global burden of disease [1]. Until recently, the management of these diseases has been made easier by antibiotics [2,3]. As a result, the use of these drugs has become so widespread that they have become the most widely prescribed agents globally [4] in both developed and developing countries [5-7], including Africa [8,9].

The biggest concern with the high use of antibiotics is the development of antibiotic resistance. High exposure to antibiotics is cited as the most important cause that can lead to resistance [10,11]. Numerous studies have elucidated the relationship between antibiotic use and resistance development [12,13].

Namibia has a dual healthcare system, with 82% of the population seeking healthcare in the public sector and 18% in the private sector. The majority of the health providers, particularly doctors (72%), are practicing in the private sector.

Antimicrobial surveillance is considered a cornerstone in promoting antimicrobial stewardship and the control of resistance development [14]. The World Health Organization (WHO)'s 2011 Policy Package and Global Action Plan to combat antimicrobial resistance [15,16] advocates for monitoring volumes and patterns of antibiotic use as part of the surveillance. No such surveillance has been carried out in the private health sector of Namibia.

The objective of this study was to identify and/or evaluate data sources for quantification of antibiotic usage patterns and to assess such use in ambulatory patients in the private health sector of Namibia.

## Methodology

### *Ethical clearance*

Ethical clearance for this study was obtained from the Research Ethics Committee (Human), Faculty of Health Sciences, North-West University (ethical clearance number NWU-00028-13-s1). Additionally, permission to use the data for the study was provided along with the data by the participating medical insurer, their medical fund administrator, and wholesaler.

*Study design*

This study was a retrospective drug utilization review in which data on antibiotic prescription claims and wholesale sales were collected and analyzed. Data collection occurred in December 2011 and covered a four-year period dating back to 1 January 2008. The prescription claims data were obtained from a medical aid fund that represented 55% of the Namibian population covered by medical aid. The wholesale data were obtained from one of the two leading wholesalers in the country. Only data related to antibiotics for systemic use (anatomical therapeutic classification [ACT] J01) were collected and analyzed.

The ACT/daily defined dose (DDD) methodology was used to evaluate the consumption of antibiotics. Each antibiotic in both databases was assigned a DDD obtained from the WHO ACT/DDD index of 2013 [17]. For wholesale data, the DDD was calculated as unit strength × pack size × quantity sold/ DDD assigned. The prescription claims and wholesale sales data were expressed as DDD/1,000 population/day using the following formula:

*DDD/1,000/day = (Total consumption in DDDs/Total population covered × Total days in the period of data collection) × 1,000.*

The population used for the prescription claims data was the population of people covered by the medical aid fund for each year. For the wholesale data, the population of the country that was estimated to be serviced by the wholesaler was used. The number of days used was 365.

*Data analysis*

The data were received from the suppliers in Microsoft Excel 2010 format. No other manipulation was done besides removing antimicrobials that were not antibiotics and also adding the ACT and DDD classifications.

Microsoft Excel and SAS Version 9.1.3 (SAS Institute, Cary, USA) were used for analysis. Descriptive statistics were used to understand frequencies and, in the claims data, to describe patient and provider variables. All statistical significances were considered with probabilities of $p < 0.05$. The practical significance of the results was computed when a p value was statistically significant ($p \leq 0.05$). The Chi-square test ($\chi^2$) was used to determine if an association existed between proportions of two or more groups (*e.g.*, age group, gender, dispenser, town, and generic indicator). Cramer's V statistic was used to test the practical significance of this association (with Cramer's V ≥ 0.5 defined as practical significance).

Results were presented in volume of antibiotic prescriptions dispensed, units of antibiotics sold, and DDD/1,000/day (DID) of antibiotics consumed.

## Results

In total, 1,129,053 antibiotic-containing prescription claims were made and 842,800 units of antibiotics were sold during the four-year study period with an overall increase in antibiotic use observed. The claims data showed a 25% increase in antibiotic prescriptions while the wholesale data showed a 57% increase in unit sales over the four years.

Wholesale data did not contain any demographic details (such as age and gender of patients) and demographic findings presented below were based on the analysis of the claims data only and are reported in prescription volumes.

*Age and gender distribution of patients*

More females (53%, n = 604,334) than males (47%, n = 524,869) received antibiotics over the four-year period under review ($p < 0.0001$; Cramer's V = 0.0424). This trend was observed also for most individual antibiotics with the exception of benzathine penicillin and procaine penicillin, which more males received (56%, n = 1,095; 57%, n = 222) than did females (44%, n = 897; 43%, n = 170) (Supplementary Table 1).

The highest number of consumers of antibiotics was in the age group ≥ 18 to ≤ 45 years (41%, n = 458,668), followed by the 45–65-year age group (28%, n = 319,581) ($p < 0.0001$; Cramer's V = 0.1025). The consumers who used antibiotics the least were those older than 65 years followed by teenagers (≥ 12 to ≤ 18 year olds). For individual antibiotics, similar trends as those in overall consumption trends by age were observed except with cefpodoxime, which was dispensed mainly to pediatric patients (age group 0 to ≤ 12 years; 66%, n = 22,582) (Supplementary Table 2).

*Antibiotic use by dispenser*

Fifty-four percent (n = 612,440) of antibiotic prescriptions was dispensed by pharmacists, and 46% (n = 516,750) by medical doctors ($p < 0.0001$; Cramer's V = 0.1093). Most of the injectable antibiotics were dispensed by doctors. There were no other significant differences between the two dispenser types. Seventy-seven percent (n = 857,817) of all antibiotic prescriptions were generic. The prevalence of generic dispensing was nearly the same between doctors and pharmacists ($p < 0.0001$; Cramer's V = 0.2154) (Supplementary Table 3).

*Antibiotic use by town*

Five towns in Namibia accounted for 60% of all consumption of antibiotics nationally. Windhoek, the capital, accounted for just over a third of all antibiotic consumption. With the exception of the top five towns listed below, there was no difference between rural and urban towns in terms of antibiotic consumption ($p < 0.0001$; Cramer's V = 0.1126). Table 1 below shows the top five towns that have the highest number of antibiotic consumers nationally.

Throughout all the towns, the trends in antibiotic choices were the same as the national trend presented below under pharmacological groups.

*Cost of antibiotics*

The total cost of antibiotics, as calculated from the prescription claims database per year, was R/N$58,964,678 (USD 7,279,589) in 2008. This increased to R/N$93,849,323 (USD 12,513,243) in 2011. For each study year, antibiotics accounted for 46% of the total cost of antibiotic-containing prescriptions. There was no data on total cost of all medication; therefore, antibiotic cost as a percentage of total medicine cost could not be calculated. The cost of the 10 most used antibiotics was calculated. These cumulatively accounted for 80% of the total antibiotic costs in each year (Supplementary Table 4).

*Antibiotic consumption expressed as DDD/1,000/day*

Both wholesale and claims data showed similar trends in antibiotic use. Overall antibiotic consumption from claims data was 28.2, 25.6, 25.3, and 29.2 DDD/1,000/day in 2008, 2009, 2010, and 2011, respectively. From wholesale data, antibiotic consumption showed increases from 19.0 to 22.11, 29.05, and 35.41 DDD/1,000/day in each of the years, respectively. These changes in consumption, however, were not statistically significant ($p = 0.988$). Table 2 shows overall antibiotic usage by antibiotic group over the four-year period by prescription claims and wholesale data.

Both sources showed penicillins to be the most used antibiotic class, accounting for 42% and 39% of all antibiotic use for claims and wholesale data, respectively. These were followed by cephalosporins, macrolides, tetracyclines, and quinolones. Claims data showed a decrease in the use of penicillins, while wholesale data showed an increase in sales of these antibiotics over the four-year period. All other antibiotic groups showed an increase in use in both claims and wholesale data with the exception of aminoglycosides, which showed a decrease on claims data and no change on wholesale data.

**Table 1.** Top five antibiotic-consuming towns.

| Town | Antibiotic consumption (n) (# of prescriptions) (N = 1,129,220) | Consumption % (N = 1,129,220) |
|---|---|---|
| Windhoek | 381,611 | 34.00 |
| Oshakati | 113,173 | 10.00 |
| Ondangwa | 80,047 | 7.09 |
| Rundu | 68,518 | 6.07 |
| Katima Mulilo | 38,190 | 3.38 |

DDD: daily defined dose.

**Table 2.** Antibiotic use by class over the four-year period expressed as DDD/1,000/day by prescription claims and wholesale data.

| Antibiotic group | ATC | Claims data | | Wholesale data | |
|---|---|---|---|---|---|
| | | DDD | % | DDD | % |
| Penicillin | J01C | 11.19 | 41.77 | 12.5 | 38.88 |
| Cephalosporins | J01D | 5.28 | 19.70 | 6.9 | 21.52 |
| Macrolides | J01F | 4.99 | 18.64 | 4.6 | 14.24 |
| Aminoglycosides | J01F | 0.08 | 0.29 | 0.1 | 0.16 |
| Tetracyclines | J01A | 1.99 | 7.43 | 4.3 | 13.30 |
| Quinolones | J01M | 2.68 | 10.00 | 3.5 | 10.84 |
| Chloramphenicol | J01B | 0.01 | 0.03 | 0.0 | 0.00 |
| Other beta-lactams | J01D | 0.49 | 1.83 | 0.0 | 0.12 |
| Other | J01X | 0.09 | 0.32 | 0.3 | 0.94 |
| **Total** | | **26.78** | **100.00** | **32.0** | **100** |

ATC: anatomic therapeutic classification; DDD: daily defined dose.

Substantial increase in usage was observed with the macrolides due to high increase in azithromycin use, from 0.278 DID in 2008 to 1.35 DID in 2011 (0.64 DID in 2008 to 1.45 DID in 2011 for wholesale data).

The top nine antibiotics based on sales volume and number of prescription claims are presented in Table 3.

In all the years under review, both sources of antibiotic consumption computations from wholesale and claims data showed amoxicillin/clavulanic acid combination as the most used antibiotic, accounting for about a third of all antibiotics used. This was followed by cefuroxime and clarithromycin from claims data computations. From consumption figure calculations using wholesale data, doxycycline was observed to supersede clarithromycin in quantities consumed per year (Table 3).

The macrolides azithromycin and clarithromycin showed substantial increases in use while the use of ciprofloxacin stayed constant throughout.

## Discussion

This was the first study to assess antibiotic use in the Namibian private health sector. Depicting same trends as reported globally, the study showed increases in antibiotic consumption over the four-year period under study. The 25% increase observed in the consumption of the agents within the private health sector, however, is lower than the 36% global increase reported by Van Boeckel *et al.* [7]. Windhoek, among the towns and cities studied for their antibiotic consumption, had the largest associated antibiotic consumption figure. This finding was not surprising, the city being the capital of Namibia and having the majority of private healthcare services (63% of the doctors and 45% of pharmacies).

Higher consumption was observed in females than in males. This could be because females generally have a higher health-seeking tendency than males and because there are more female beneficiaries covered by medical aid than there are males [18].

The overall antibiotic consumption over the total study period in the Namibian private sector was 26.8 DDD/1,000/day. This figure is comparable to some European countries, as reported by the European Surveillance of Antimicrobial Consumption (ESAC) project in 2010. Namibia is comparable to Italy, Luxembourg, and France [19], and can be considered by the ESAC classification as a high antibiotic consumer. According to the ESAC classifications, countries with consumption figures of < 16.7 DID are considered low consumers, between 16.7 and 22.38 DID medium consumers, and > 22.38 DID high consumers [19].

This observed high and increasing antibiotic usage in the Namibian private sector is worrisome. While antibiotic use has increased by 25% over four years, there has not been a corresponding increase in the population that could explain the reason for the increase in use. This implies that the same population is having greater exposure to greater quantities of antibiotics, thus making for greater selective pressure favoring the development of resistance. It is important to understand what the factors contributing to this antibiotic use are in order to design targeted interventions to improve prudent use of the agents.

In addition to increased overall antibiotic use, our study uncovered significant trends in antibiotic usage patterns that have established within the private health sector an increased use of broad-spectrum antibiotics, which paralleled a decrease in use of narrow-spectrum antibiotics and an increased preference for newer antibiotics. Our data also showed that outpatient care within the sector was highly dependent on three classes of antibiotics, namely the penicillins, the cephalosporins, and the macrolides – and mainly on the broad-spectrum agents in these classes. These findings are not unique to Namibia; they have been reported by

**Table 3.** Top nine highest consumed antibiotics over a four-year period expressed as DDD/1,000/day (DID).

| **Antibiotic** | **Claims data** | | **Wholesale data** | |
|---|---|---|---|---|
| | **DID** | **%** | **DID** | **%** |
| Amoxicillin | 1.67 | 6.85 | 3.45 | 12.31 |
| Amoxicillin/clavulanic acid | 8.35 | 34.25 | 8.32 | 29.69 |
| Azithromycin | 1.63 | 6.69 | 1.51 | 5.39 |
| Cefpodoxime | 0.27 | 1.12 | 0.363 | 1.30 |
| Ceftriaxone | 0.04 | 0.16 | 0.14 | 0.50 |
| Cefuroxime | 5.94 | 24.35 | 6.23 | 22.23 |
| Ciprofloxacin | 1.55 | 6.36 | 2.45 | 8.74 |
| Clarithromycin | 3.2 | 13.13 | 1.51 | 5.39 |
| Doxycycline | 1.73 | 7.10 | 4.05 | 14.45 |
| **Total** | **24.38** | **100.00** | **28.02** | **100.00** |

DDD: daily defined dose.

others also. Lee *et al*. reported general increases in the use of broad-spectrum antibiotics in the United States [6], similar to findings of this study. Their study reported the USA as having an unprecedented high use of broad-spectrum antibiotics. Similar results were also reported in Malta [20], Israel [21], India [22], Italy [13], and in Europe and Eastern Europe [23,24]. South Africa, which has a very similar health system to Namibia, has also been reported as having an increased use of broad-spectrum antibiotics [7,25].

This high use of broad-spectrum and newer antibiotics is a cause for concern since increased use of broad-spectrum antibiotics has been associated with the development of cross-resistance to other agents in the same class, compromising the use of the antibiotic class as a whole [20,21,26]. In this era where there are few antibiotics in development, the greatest concern with the development of resistance is that it could lead to a situation where healthcare professionals will not have appropriate medications to effectively treat infections [27-30]. It is therefore of utmost importance that antibiotics are used prudently in order to ensure their long-term availability and effectiveness.

The observed situation in Namibia calls for immediate public health interventions. Measures such as the introduction of antibiotic prescribing guidelines, continuing professional development sessions on antibiotic usage data, and education on local sensitivity patterns should be considered. Namibia has national standard treatment guidelines. However, the guidelines are not enforced in the private sector. Local sensitivity data are also available but the health providers do not seem to be aware of these. Activities aimed at educating patients on antibiotics and their proper use should also be explored. In 2013, the Pharmaceutical Society addressed the issue of antimicrobial resistance during pharmacy week. Beyond this, there have not been dedicated national efforts to educate patients on antibiotics and their use.

In this study, two sources employing claims and wholesale data in estimating antibiotic usage in the private health sector were compared. Both sources showed similar trends in antibiotic usage, but computations using wholesale data showed higher consumption of antibiotics as compared to claims data, indicating an overestimation of consumption figures. This finding is consistent with what has been reported by other studies that employed similar comparative methodologies [23,31,32]. Medicine claims data is closest to consumption, as it is based on the actual scripts dispensed. Wholesale data includes stock that could be on the shelves, that expired at the pharmacies, and that broke or was not sold; some of these could account for the overestimation.

In our study, we found claims data more reliable and more informative in terms of patient and provider profiles. We would therefore recommend that future studies use claims data to quantify antibiotic usage. A main concern raised by other authors regarding claims data is that they do not cover over-the-counter antibiotic sales [31,32]. This should not be a major concern in Namibia, since by law, antibiotics are not sold without prescription. Using claims data can more accurately reflect antibiotic use because data used in calculations have been validated by the medical insurer and are also close to actual consumption data, *i.e.*, actual quantities dispensed to the patient. Wholesale data, in comparison, represent antibiotics sold to the dispenser and not necessarily what is sold to the patient.

This study had some limitations. First, the data were annual data, which did not allow for analysis to determine monthly trends and seasonal variations in antibiotic use. Second, data sources did not contain information on clinical indications for which the antibiotics were prescribed. This did not enable an evaluation of the appropriateness of the prescriptions to establish whether the observed high use of antibiotics in the private health sector was appropriate or not. Third, Namibia has a dual health system, which includes public and private health systems. The study was intended to determine antibiotic use in the private sector; therefore, the findings cannot be generalized to the entire country.

## Conclusions

Routine surveillance of antibiotic usage is an important step in antimicrobial stewardship. It generates valuable information for the formulation of policies on antibiotic use to improve appropriate prescribing and use of the agents to curb resistance development.

The study uncovered very high antibiotic use in the private sector of Namibia, particularly high use of broad-spectrum antibiotics. These findings are comparable with results of similar studies conducted in Europe and elsewhere on the African continent. The study also found claims data to be better than sales data in quantifying antibiotic use.

The findings of this study apply to a small fraction of the Namibian population accessing care in the private sector and do not provide a full picture of antibiotic consumption nationally. We recommend further studies that aim at estimating antibiotic usage patterns in both the public and private health sectors to reflect the national situation. We also recommend studies that similarly aim at investigating patterns of antibiotic resistance development and the effects of antibiotic use on such resistance development patterns. The results of such studies will provide baseline information required for the formulation of antibiotic usage policies to promote an appropriate use of the agents and a curbing of resistance development.

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## Annex – Supplementary Items

**Supplementary Table 1.** Antibiotic use by gender.

| Number of antibiotic prescriptions by gender | | | | |
|---|---|---|---|---|
| **Antibiotics** | **Gender** | | | |
| **Frequency** | **F** | **M** | **N** | **Total** |
| Amikacin | 91 | 122 | 0 | 213 |
| Amoxicillin/clavulanic acid | 127,412 | 112,688 | 7 | 240,107 |
| Amoxicillin | 29,892 | 21,441 | 1 | 51,334 |
| Amoxicillin/flucloxacillin | 8,824 | 9,058 | 0 | 17,882 |
| Ampicillin | 439 | 430 | 0 | 869 |
| Ampicillin/cloxacillin | 4,638 | 5,064 | 0 | 9,702 |
| Azithromycin | 46,107 | 35,855 | 1 | 81,963 |
| Benzathine penicillin | 897 | 1095 | 0 | 1,992 |
| Benzyl penicillin | 191 | 180 | 0 | 371 |
| Cefaclor | 1,463 | 1,258 | 0 | 2,721 |
| Cefadroxil | 2,180 | 1,598 | 0 | 3,778 |
| Cefazolin | 14 | 5 | 0 | 19 |
| Cefepime | 3 | 1 | 0 | 4 |
| Cefotaxime | 32 | 47 | 0 | 79 |
| Cefoxitin | 19 | 34 | 0 | 53 |
| Cefpirome | 401 | 315 | 0 | 716 |
| Cefpodoxime | 17,669 | 16,617 | 3 | 34,289 |
| Cefprozil | 2,322 | 2,216 | 0 | 4,538 |
| Ceftazidime | 3 | 0 | 0 | 3 |
| Ceftriaxone | 32,015 | 29,418 | 0 | 61,433 |
| Cefuroxime | 96,257 | 77,468 | 5 | 173,730 |
| Cephalexin | 2,023 | 1,937 | 0 | 3,960 |
| Cephradine | 16 | 18 | 0 | 34 |
| Chloramphenicol | 346 | 244 | 0 | 590 |
| Ciprofloxacin | 56,141 | 45,858 | 0 | 101,999 |
| Clarithromycin | 40,347 | 34,078 | 0 | 74,425 |
| Clindamycin | 3,742 | 3,206 | 0 | 6,948 |
| Cloxacillin | 3,911 | 4,087 | 0 | 7,998 |
| Doxycycline | 19,614 | 16,655 | 0 | 36,269 |
| Ertapenem | 37 | 8 | 0 | 45 |
| Erythromycin | 10,910 | 9,275 | 0 | 20,185 |
| Flucloxacillin | 49 | 70 | 0 | 119 |
| Gemifloxacin | 4,948 | 4,655 | 0 | 9,603 |
| Gentamicin | 3,789 | 3,687 | 0 | 7,476 |
| Levofloxacin | 8,543 | 5,646 | 0 | 14,189 |
| Linezolid | 2 | 3 | 0 | 5 |
| Lomefloxacin | 294 | 218 | 0 | 512 |
| Loracarbef | 6,910 | 6,452 | 0 | 13,362 |
| Lymecycline | 45 | 38 | 0 | 83 |
| Meropenem | 21 | 18 | 0 | 39 |
| Minocycline | 627 | 410 | 0 | 1,037 |
| Moxifloxacin | 6,516 | 5,826 | 0 | 12,342 |
| Norfloxacin | 4,814 | 3,156 | 0 | 7,970 |
| Ofloxacin | 4,082 | 3,694 | 0 | 7,776 |
| Oxytetracycline | 169 | 136 | 0 | 305 |
| Penicillin | 1,225 | 809 | 0 | 2,034 |
| Piperacillin | 4 | 10 | 0 | 14 |
| Procaine penicillin | 170 | 222 | 0 | 392 |
| Roxithromycin | 592 | 444 | 0 | 1,036 |
| Streptomycin | 125 | 92 | 0 | 217 |
| Telithromycin | 3,945 | 3,247 | 0 | 7,192 |
| Trimethoprim | 49,508 | 55,760 | 0 | 105,268 |
| **TOTAL (N)** | **604,334** | **524,869** | **17** | **1,129,220** |
| **PERCENT (%)** | **53.52** | **46.48** | **0** | **100** |

$p < 0.0001$; Cramer’s V = 0.205.

**Supplementary Table 2.** Antibiotic use by age group.

| **Antibiotic** | **Age group (n = # of prescriptions)** | | | | | |
|---|---|---|---|---|---|---|
| **Frequency** | **< 12** | **≥ 12 to ≤ 18** | **≥ 18 to ≤ 45** | **≥ 45 to ≤ 65** | **> 65** | **Total** |
| Amikacin | 0 | 3 | 125 | 77 | 8 | 213 |
| Amoxicillin/clavulanic acid | 78,700 | 20,722 | 84,832 | 52,182 | 3,628 | 240,064 |
| Amoxicillin | 12,408 | 4,451 | 21,487 | 12,109 | 840 | 51,295 |
| Amoxicillin/flucloxacillin | 4,083 | 1,754 | 7,455 | 4,310 | 279 | 17,881 |
| Ampicillin | 217 | 59 | 307 | 268 | 18 | 869 |
| Ampicillin/cloxacillin | 2,405 | 895 | 3,881 | 2,413 | 106 | 9,700 |
| Azithromycin | 16,067 | 4,891 | 37,616 | 21,784 | 1,596 | 81,954 |
| Benzathine penicillin | 141 | 112 | 1,010 | 708 | 21 | 1,992 |
| Benzyl penicillin | 129 | 20 | 124 | 97 | 1 | 371 |
| Cefaclor | 1,683 | 188 | 405 | 416 | 29 | 2,721 |
| Cefadroxil | 894 | 277 | 1,502 | 1,064 | 41 | 3,778 |
| Cefazolin | 0 | 1 | 11 | 6 | 1 | 19 |
| Cefepime | 0 | 0 | 3 | 1 | 0 | 4 |
| Cefotaxime | 2 | 2 | 31 | 37 | 7 | 79 |
| Cefoxitin | 2 | 2 | 30 | 19 | 0 | 53 |
| Cefpirome | 5 | 42 | 451 | 218 | 0 | 716 |
| Cefpodoxime | 22,582 | 3,649 | 5,163 | 2,704 | 181 | 34,279 |
| Cefprozil | 3,298 | 463 | 488 | 273 | 16 | 4,538 |
| Ceftazidime | 0 | 0 | 0 | 2 | 1 | 3 |
| Ceftriaxone | 8,354 | 2,756 | 28,673 | 20,422 | 1,221 | 61,426 |
| Cefuroxime | 46,806 | 14,504 | 65,281 | 43,417 | 3,692 | 173,700 |
| Cephalexin | 3,412 | 185 | 276 | 80 | 7 | 3,960 |
| Cephradine | 0 | 5 | 18 | 11 | 0 | 34 |
| Chloramphenicol | 21 | 39 | 255 | 235 | 40 | 590 |
| Ciprofloxacin | 897 | 2,636 | 56,210 | 38,329 | 3,927 | 101,999 |
| Clarithromycin | 16,504 | 5,114 | 29,893 | 21,504 | 1,407 | 74,422 |
| Clindamycin | 106 | 436 | 3,322 | 2,649 | 435 | 6,948 |
| Cloxacillin | 485 | 732 | 3,807 | 2,819 | 155 | 7,998 |
| Doxycycline | 266 | 1,799 | 21,136 | 12,339 | 728 | 36,268 |
| Ertapenem | 0 | 0 | 14 | 28 | 3 | 45 |
| Erythromycin | 8,522 | 2,300 | 5,599 | 3,401 | 348 | 20,170 |
| Flucloxacillin | 11 | 5 | 56 | 43 | 4 | 119 |
| Gemifloxacin | 13 | 119 | 4,736 | 4,261 | 474 | 9,603 |
| Gentamicin | 1,691 | 442 | 2,809 | 2,262 | 272 | 7,476 |
| Levofloxacin | 65 | 203 | 7,654 | 5,657 | 610 | 14,189 |
| Linezolid | 0 | 0 | 2 | 3 | 0 | 5 |
| Lomefloxacin | 1 | 7 | 259 | 219 | 26 | 512 |
| Loracarbef | 6,805 | 1,315 | 3,135 | 2,017 | 90 | 13,362 |
| Lymecycline | 0 | 21 | 38 | 20 | 4 | 83 |
| Meropenem | 0 | 1 | 20 | 13 | 5 | 39 |
| Minocycline | 8 | 91 | 699 | 225 | 14 | 1,037 |
| Moxifloxacin | 133 | 232 | 5,308 | 5,699 | 970 | 12,342 |
| Norfloxacin | 40 | 154 | 4,275 | 3,045 | 456 | 7,970 |
| Ofloxacin | 22 | 105 | 4,176 | 3,241 | 232 | 7,776 |
| Oxytetracycline | 1 | 46 | 168 | 83 | 7 | 305 |
| Penicillin | 376 | 491 | 724 | 419 | 24 | 2,034 |
| Piperacillin | 0 | 0 | 4 | 6 | 4 | 14 |
| Procaine penicillin | 118 | 42 | 154 | 74 | 4 | 392 |
| Roxithromycin | 7 | 45 | 481 | 464 | 39 | 1,036 |
| Streptomycin | 0 | 18 | 116 | 80 | 3 | 217 |
| Telithromycin | 20 | 202 | 3,649 | 3,085 | 236 | 7,192 |
| Trimethoprim | 15,024 | 3,612 | 40,800 | 44,743 | 1,082 | 105,261 |
| **TOTAL (N)** | **252,324** | **75,188** | **458,668** | **319,581** | **23,292** | **1,129,053** |
| **PERCENT (%)** | **22** | **7** | **41** | **28** | **2** | **100** |

$p < 0.0001$; Cramer's V = 0.0424.

**Supplementary Table 3.** Antibiotics by dispenser and generic indicator.

| Antibiotic use by dispenser | | |
|---|---|---|
| **Dispenser** | **Frequency** | **Percent** |
| Doctor | 516,780 | 45% |
| Pharmacist | 612,440 | 54% |
| Total | 1,129,220 | 100% |

| Antibiotics dispensed as generic by dispenser | | | |
|---|---|---|---|
| **Frequency** | **Antibiotic prescription a generic** | | |
| **Dispenser** | **N** | **Y** | **Total** |
| Doctor | 117,043 | 392,972 | 510,015 |
| Pharmacist | 140,384 | 466,845 | 607,229 |
| **Total (N)** | **257,427** | **859,817** | **1,117,244** |
| **Percent (%)** | **23.05** | **76.96** | **100** |

$p < 0.0001$; Cramer's V = 0.1093.

**Supplementary Table 4.** Top 10 antibiotics and their associated cost.

| **Total AB cost per year** | **2008 (Total = R26,941,120)** | | **2009 (Total = R33,423,266)** | | **2010 (Total = R36,651,164)** | | **2011 (Total = R43,711,348)** | |
|---|---|---|---|---|---|---|---|---|
| Antibiotic | Cost per antibiotic | % total AB cost | Cost per antibiotic | % total AB cost | Cost per antibiotic | % total AB cost | Cost per antibiotic | % total AB cost |
| Amoxicillin/clavulanic acid | R6,386,213 | 23.70 | 6,920,556 | 20.71 | R7,144,060 | 19.49 | R9,210,120 | 21.07 |
| Amoxicillin | R252,666 | 0.94 | R269,922 | 0.81 | R277,172 | 0.76 | R268,151 | 0.61 |
| Azithromycin | R1,658,627 | 6.16 | R2,854,055 | 8.54 | R3,478,219 | 9.49 | R4,496,379 | 10.29 |
| Cefpodoxime | R1,306,707 | 4.85 | R1,101,067 | 3.29 | R1,262,629 | 3.44 | R1,250,311 | 2.86 |
| Ceftriaxone | R1,043,787 | 3.87 | R1,663,353 | 4.98 | R1,607,022 | 4.38 | R1,861,870 | 4.26 |
| Cefuroxime | R5,728,547 | 21.26 | R7,803,031 | 23.35 | R8,928,472 | 24.36 | R11,816,865 | 27.03 |
| Ciprofloxacin | R1,200,562 | 4.46 | R1,613,330 | 4.83 | R1,934,721 | 5.28 | R2,115,987 | 4.84 |
| Clarithromycin | R2,301,450 | 8.54 | R2,469,922 | 7.39 | R3,216,891 | 8.78 | R3,119,778 | 7.14 |
| Doxycycline | R708,616 | 2.63 | R840,303 | 2.51 | R686,809 | 1.87 | R550,878 | 1.26 |
| Trimethoprim/sulfa | R979,800 | 3.64 | R924,622 | 2.77 | R744,401 | 2.03 | R800,654 | 1.83 |
| **TOTAL** | **R21,566,975** | **80.05** | **R26,460,162** | **79.17** | **R29,280,396** | **79.89** | **R35,490,993** | **81.19** |