Assessment of prescribing practices at the primary healthcare facilities in Botswana with an emphasis on antibiotics: Findings and implications

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Summary

Background and Aims: Inappropriate drug prescribing has increased especially in developing countries where systems for monitoring medicine use are not well developed. This increases the rate of antimicrobial resistance. The study aim was to assess the prescribing patterns among urban primary health facilities in Botswana to provide future guidance including developing future quality indicators.

Methods: Retrospective data from patients' records between January and December 2013 in 19 clinics were collected in a cross-sectional study. The WHO/International Network for Rational Use of Drugs indicators were used to assess prescribing patterns in the study clinics.

Results: Average number of drugs per prescription was 2.8; 78.6% of the prescribed antibiotics were by International Non-proprietary Name and 96.1% complied with the Botswana Essential Drugs List. Overall rate of antibiotic prescribing was high (42.7%) with 14.7%, 5.9% and 1.3% of prescriptions having two, three and four antibiotics, respectively. Systemic antibiotics (JO1C) accounted for 45.4% of prescribed antibiotics of which amoxicillin accounted for 28.4% and metronidazole 14.4% of all antibiotic prescriptions. There was low use of co-amoxiclav (0.3% of all antibiotic prescriptions). Third generation cephalosporins and macrolides accounted for 9.8% and 6.2% of antibiotic prescriptions respectively, with no prescribing of fluoroquinolones. The majority of indications (87%) for antibiotic prescriptions were according to ICD classification.

Conclusions: While most indications for antibiotic prescriptions were based on signs and symptoms according to ICD, antibiotic prescribing rates were high with some conditions not requiring antibiotics because they are viral infections. There is a need to further improve prescribing practices through induction and training of in-service prescribers. An effective management tool for monitoring antibiotic prescribing practices at Primary Health Care facilities should be designed and implemented, including developing robust quality indicators.
1 | INTRODUCTION

The World Health Organization (WHO) defines the rational use of medicines as “patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements for an adequate period of time, at the lowest cost to them and their community.” To address the irrational use of medicines, including inappropriate use of antibiotics leading to increasing rates of antimicrobial resistance (AMR) with its associated impact on morbidity, mortality and costs, the WHO in collaboration with the International Network for Rational Use of Drugs (INRUD) has developed core indicators for prescribing practices, patient care and facility-specific factors. These include the number of antibiotics per prescription without looking at issues of necessity or whether prescribing adheres to current guidelines. The current WHO reference value for the average number of medicines per encounter is <2 with a comprehensive review between 1990 and 2009 reporting the average number among 104 countries was 2.6 for the Africa region. More recent reports indicate a 45.8% increase from 2.4 between 1995 and 2005 to 3.5 between 2006 and 2015. The percentage of medicines prescribed by the generic (International Non-proprietary Name; INN) name should be 100% (acceptable >80%). However, studies have reported lower rates for the African region at between 60% and 68%.

Currently, there is a scarcity of data regarding the quality of antibiotic prescribing in developing countries. In these settings, it is common for antibiotics to be prescribed for typically self-limiting conditions such as acute upper respiratory tract infections (URTIs) that are predominantly viral in origin and for other infections which do not require antibiotics. This situation is worse in African countries. The comparative report of antibiotic prescribing rates in the Africa region between 1995-2005 and 2006-2015 shows during the later period high antibiotic prescribing rates (22%, 58% and 22%) in Ghana, Tanzania and Nigeria, respectively, with most of the increase because of the prescribing of medicines contained in the Botswana EDL. However, there were high rates of antibiotic prescribing as well as high rates of prescribing two or more antibiotics on the first encounter. This may be because of a high prevalence of gynaecological and sexually transmitted infections in presenting patients in Botswana. The majority of indications for antibiotic prescribing (87%) were in accordance with ICD-10 codes; however rates could be improved to enhance future quality of prescribing.

1.1 | Aims

The aim of this study was to assess current drug prescribing practices in PHC facilities in Gaborone and surrounding areas with a specific emphasis on antibiotic prescribing. The study results would be used to guide future corrective interventions. The interventions may include suggestions to develop new quality indicators, especially for antibiotic prescribing, in ambulatory care given the rather crude nature of current WHO/INRUD indicators.

2 | METHODOLOGY

This was a non-experimental cross-sectional descriptive study initially using the WHO/INRUD indicators before looking more specifically at antibiotic prescribing. The study was carried out between November and December 2015, collecting retrospective data from patient records for the period between January and December 2013. The PHC facilities were from Gaborone District, Tlokweng (South East District) and Mogoditshane (Kweneng District). The facilities are representative of urban settings in Botswana where the majority of patients seek their treatment from.
2.1 Sample size and sampling procedures

The WHO recommends that there should be a minimum of 600 prescribing episodes included in a cross-sectional indicators survey, and where there are fewer than 20 facilities in a geographical or administrative region to be studied, all facilities should be included in the sample. The selected districts have a total of 20 PHC facilities; all were included in the study.

Data were collected by trained research assistants under the supervision of the principal researchers (YM and ES). Using patient’s records, we estimated to collect at least 30 prescriptions from each PHC. To achieve this, patient prescription records were listed according to the month in which they were prescribed and assigned random numbers. Records were then randomly selected until a sample size of 30 patient records was realised. We wanted to assess initial prescriptions only in this study. Consequently, all records that showed re-attendances were excluded from the study. The diagnoses on the patient’s records were used to determine the indication for antibiotic prescription without contact with the prescriber.

2.2 Quality of antibiotic prescribing

The quality of antibiotic prescribing practices was assessed as follows: (i) prescribing against WHO/INRUD criteria; (ii) antibiotic prescribing against indicators developed and proposed by European organisations and (iii) antibiotic prescribing against the Botswana Essential Drug List.

The following indicators have been proposed and used by European organisations to assess the quality of systemic antibiotic (J01) prescribing:

- Utilisation of penicillin (J01C) as a % of total antibiotic use.
- Utilisation of combination penicillin (eg, co-amoxiclav) as a % of total amoxicillin use.
- Utilisation of third- and fourth-generation cephalosporins vs first- and second- generation cephalosporins.
- Utilisation of fluoroquinolones (J01MA) as a % of total antibiotic use.

Prescribing rates at PHC facilities in Botswana were assessed against published rates among low and middle income European countries, including former Soviet Union Republics, as no baseline data currently exist for these facilities in Botswana.

The utilisation metric used is a prescription rather than internationally recognised metrics such as defined daily doses (DDDs) or DDDs per 1000 inhabitants per day (DIDs). This is because we wanted to assess antibiotic prescribing for the first indication, and we were evaluating antibiotic prescribing among providers at PHC facilities rather than the population as a whole.

2.3 Data processing and analysis

For the purpose of improving the quality of data and the rigour of research results, data management procedures and processes were in accordance with the methodology proposed by Vittinghoff et al. This included data preparation, cleaning, editing and creation of variables and identification of missing data. Since we were not testing any outcome variables against exposure interventions, and we were not assessing associations between the prescribers and prescribed drugs, only descriptive and inferential analysis frameworks were used to analyse prescribing information. Percentages, averages and frequencies were also used to describe the data.

2.4 Ethical considerations

The study received ethical clearance from the University of Botswana, Institutional Review Board (Ref. URB/IRB/1506) and a permit to carry out the study in the PHC facilities was obtained from the Ministry of Health and Wellness (Ref. PME.13/18/87). The District Health Management Team Coordinator granted access to the facilities vide letter Ref: GGDHMT/14/2/i dated 28 November 2014. The identity of the clinics was protected by keeping them anonymous and assigned coded numbers.

3 RESULTS

3.1 General

Data from 19 PHC facilities only were analysed. Data from one clinic were not collected because during data collection, the clinic staff were on vacation. Out of an estimated 570 prescriptions that were collected, 20 prescriptions were excluded from the final analysis because seven patients had come to the clinics for routine Antenatal Clinic, six were patients who had visited the clinics for counselling services and another seven visited the facilities for HIV testing. This report is therefore based on 550 prescriptions.

3.2 Prescribing practices against documented indicators

The total number of prescriptions analysed were 550 and the total number of medicines prescribed for all conditions were 1551, giving an average of 2.8 drugs per prescription. Of the total medicines prescribed, 1219 (78.6%) were prescribed using INN and 235 (42.7%) encounters contained at least one antibiotic prescription. 1490 (96.1%) were prescribed from the Botswana Essential Drug (EDL) (Table 1).

3.3 Prescriptions with antibiotics

Table 2 shows that 306 antibiotics were prescribed during 235 patient encounters, of which 17 were topical applications (13 Chloramphenicol ointments, 3 Tetracycline ointments and one gentamicin ointment prescription). Systemic antibiotics (J01) were the most commonly prescribed. The beta-lactam antibiotics (J01C) accounted for 45.4% of prescriptions, rising to 48.1% when only systemic antibiotics were considered. Amoxicillin was the most commonly prescribed antibiotic...
MASHALLA et al. (28.4%) followed by metronidazole (14.4%). Co-amoxiclav accounted for only 0.3% of all antibiotic prescriptions, while cotrimoxazole (sulfamethoxazole + trimethoprim) accounted for 9.2% of all antibiotic prescriptions. Third generation cephalosporin (ceftriaxone) and macrolides (erythromycin) accounted for 9.8% and 6.2% of antibiotic prescriptions, respectively. This increased to 10.4% and 6.6%, respectively when only J01 systemic antibiotics were considered. No fluoroquinolones (J01MA) were prescribed.

### 3.4 | Indications for antibiotic prescriptions

Table 3 shows 69 diagnoses for which antibiotic prescriptions were written. Most diagnoses were based on signs and symptoms whilst some were specific disease conditions including asthma, diabetes, bronchitis, tonsillitis, conjunctivitis and chicken pox. The majority of the antibiotic prescriptions (60) were compliant with the International Classification of Diseases (2017 ICD) while nine were not. The nine prescriptions were non-specific, unconventional and lacked crucial information such as sputum information on the amount, colour, odour and the presence of blood; "enlarged stomach" did not specify whether the enlargement was because of gas, solid mass, shifting or fluctuating; "local sepsis" did not contain information on location and nature of sepsis and for bacterial exudate the nature of the exudate (clear fluid, puss, odour) was not provided. Painful armpit lacked information on the nature of pain (throbbing, piercing, dull) and with or without induration.

Cough, vaginal discharge and sexually transmitted infections were most commonly indicated for antibiotic prescriptions in that order. For symptoms and signs involving the gastrointestinal system, diarrhoea was the commonest indication for antibiotic.

### 3.5 | Indications for more than one antibiotic per prescription

Out of the 235 encounters with antibiotic prescriptions, 45 (19.1%), 18 (7.7%) and 4 (1.7%) had two, three and four antibiotics per prescription, respectively. Doxycycline was the most common antibiotic combined as a second line drug followed by metronidazole and ceftriaxone, respectively (Table 4). The indications for combination of antibiotics were mostly sexually transmitted conditions including vaginal and urethral discharge and pelvic inflammatory diseases.

| Antibiotic                                      | ATC classification | Frequency (N) | Per cent |
|-------------------------------------------------|--------------------|---------------|----------|
| Beta-lactams (J01C)                             |                    |               |          |
| Amoxicillin                                     | J01CA04            | 87            | 28.4     |
| Ampicillin                                      | J01CA01            | 3             | 1.0      |
| Benzathine penicillin (Retapen)                 | J01CE08            | 13            | 4.2      |
| Cloxacillin                                     | J01CF02            | 21            | 6.9      |
| Co-amoxiclav                                    | J01CR02            | 1             | 0.3      |
| Crystalline penicillin                          | J01CE01            | 1             | 0.3      |
| Penicillin V                                    | J01CE02            | 13            | 4.2      |
| Total Beta-lactams                              |                    | 139           | 45.4     |
| Cotrimoxazole                                   | J01EE01            | 28            | 9.2      |
| Ceftriaxone                                     | J01DD54            | 30            | 9.8      |
| Chloramphenicol capsules                        | S01A01             | 3             | 1.0      |
| Chloramphenicol ointment                        | S01AA01            | 13            | 4.2      |
| Doxycycline                                     | J01AA02            | 23            | 7.5      |
| Erythromycin                                    | J01FA01            | 19            | 6.2      |
| Gentamicin                                      | J01GB03            | 2             | 0.7      |
| Metronidazole                                   | J01XD01            | 44            | 14.4     |
| Nitrofurantoin (nitrofuran derivative)          | J01X0              | 1             | 0.3      |
| Tetracycline ointment                           | S01AA              | 3             | 1.0      |
| Gentamicin ointment                             | S01AA              | 1             | 0.3      |
| Total                                           |                    | 306           | 100      |
**TABLE 3** Classification of the diseases, symptoms and signs indicated for antibiotics prescription at PHC facilities in Botswana by 2017 ICD10-CM/code

| Condition                                           | ICD-10-CM/code | Frequency |
|-----------------------------------------------------|----------------|-----------|
| **General symptoms and signs**                      |                |           |
| Fever                                               | R50            | 10        |
| Headache                                            | R51            | 8         |
| Dehydration                                         | E86.0          | 1         |
| **Symptoms and signs involving the circulatory and respiratory systems** | |           |
| Cough                                               | R05            | 37        |
| Acute tonsillitis                                   | J03            | 18        |
| Nasal congestion (common cold)                      | J00            | 7         |
| Pharyngitis                                         | J02            | 4         |
| Sputum (unspecified)                                | R09.3          | 3         |
| Swollen palate (acute laryngitis and tracheitis)    | J04            | 2         |
| Asthma                                              | J45.909        | 2         |
| Pleural thickening                                  | L85.9          | 2         |
| Upper respiratory infections                         | J06            | 2         |
| Aspiration pneumonia                                | J69.0          | 1         |
| Bronchitis                                          | J20.0          | 1         |
| **Symptoms and signs involving the digestive system and abdomen** | |           |
| Diarrhoea                                           | R19            | 15        |
| Abdominal and pelvic pain                           | R10            | 11        |
| Loss of appetite                                    | R63            | 6         |
| Nausea and vomiting                                 | R11            | 4         |
| Constipation                                        | K59.0          | 1         |
| Enteritis                                           | K52.9          | 1         |
| Heartburn (epigastric pain)                         | R12            | 1         |
| **Symptoms and signs involving the skin and subcutaneous tissues** | |           |
| Wound/sores                                         | T81.30         | 12        |
| Rash                                                | CM/21          | 9         |
| Boils and abscesses                                 | CM/22          | 8         |
| Skin condition unspecified                          | R23            | 7         |
| Herpes zoster                                       | B02            | 2         |
| Chickenpox                                          | B01            | 2         |
| Burn                                                | T30.0          | 2         |
| Allergic dermatitis (unspecified)                   | L23.89         | 2         |
| Acne                                                | CM/706         | 1         |
| Fibrobullar                                         | M72            | 1         |
| Viral warts (genital)                               | B07            | 1         |
| Implantation (sub-dermal contraceptive)             | V25.5          | 1         |
| Skin fungal infection (unspecified)                 | L08.9          | 1         |

(Continues)
4 | DISCUSSION

When treatments were assessed against crude WHO/INRUD indicators, there was evidence of good prescribing practices in Botswana. This is shown by the fact that 96% of medicines prescribed were in accordance with the Botswana EDL and 79% of prescribing was by INN name (Table 2). The high rate of prescribing in accordance with the Botswana EDL is comparable to 78% in the Western Pacific region but higher than rates of 27.7% and 48.9% reported in the Eastern Mediterranean and Southeast Asian regions, as well as 68% for Africa as a whole. Possible explanations for high INN prescribing in this study could be a result of frequent in-service training workshops for health workers in Botswana sponsored by the government, benchmarking with colleagues in the region, the establishment of a medical school whose trainees are exposed to patient care early in their training where prescribing is typically INN, and easy access to digital information. This mirrors successful campaigns in other countries.

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In this study, 42.7% of the encounters contained an antibiotic prescription, higher than <30% recommended by WHO. This is marginally higher than 39% and 34% for the Americas and European regions, but lower than 53% for the Eastern Mediterranean region and Africa as a whole (47%). This rate is also higher than 27% in a previous study in Botswana, and higher than 30% for Acute Respiratory Infections in children under 5 years old previously reported in Botswana. The high use of antibiotics could be because of a high burden of gynaecological and sexually transmitted infections (Table 3). There is also high prevalence (pandemic) of HIV in Botswana. However, these patients are normally treated in specialist clinics, although in some cases, opportunistic infections may be treated in PHCs. The extent of multiple antibiotic prescribing is a concern, but again may reflect the high prevalence of gynaecological and sexually transmitted infections in our study with up to three antibiotics recommended in the Botswana guidelines for these patients (Table 4). This will be a future area of research.

Regarding the quality of antibiotic prescribing, it is generally accepted as good clinical practice that antibiotics should be prescribed for specific diagnosis. The high rate of INN prescribing in this study is comparable to the high prescribing rate from the EDL could be attributed to easy accessibility of the Botswana Treatment Guidelines at PHC facilities, the routine availability of medicines incorporated into the Botswana EDL in PHCs, and the limited influence of pharmaceutical companies unlike other countries.

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The high use of beta-lactamase antibiotics compares favourably with former Soviet Union Republics and Turkey with rates of 37.5%-65.6% of total J01 antibiotics. The low use of co-amoxiclav is also encouraging as there are concerns that high utilisation increases side effects and resistance as well as costs. With rising concerns on the development of Clostridium difficile resistance, the low utilisation of cephalosporins in this study (Table 2) is also encouraging and compares favourably with rates of 0.5%-12.2% among former Soviet Union Republics and Turkey. Similarly, the lack of fluoroquinolone prescribing is encouraging attributed to the non-inclusion of these medicines in the Botswana EDL.

In our future research, we will aim to explore adherence to treatment guidelines alongside establishing quality indicators for antibiotic prescribing among providers in both urban and rural PHC facilities in Botswana, which will assist prescribers with improving their quality of care. Adherence is a complex phenomenon and typically far from optimal across countries. For instance, 46% of antibiotic prescriptions in a recent study were not indicated by the guidelines. However, higher adherence rates were recently seen in Namibia (62%), although below national target rates of 95%. Guideline adherence is influenced by several factors including the level of training.
of PHC personnel, available resources at healthcare facilities, workload, staff motivation, staff experience and the availability of managerial tools for monitoring prescribing patterns. Physicians may also misinterpret patient expectations, influencing adherence rates. Effective monitoring can enhance adherence rates. Care though must be taken in communicating appropriate guidelines, especially if there are differences between different policies and guidelines as recently seen in Namibia.

| Antibiotics                  | Diagnoses          |
|------------------------------|--------------------|
| Amoxicillin Metronidazole    | Cough              |
| Amoxicillin Gentamicin ear drops | Ear sores       |
| Amoxicillin Metronidazole    | Cough              |
| Amoxicillin Metronidazole Retarpen | Pharyngitis     |
| Amoxicillin Cotrimoxazole    | Post SMC           |
| Amoxicillin Cotrimoxazole    | Cough              |
| Amoxicillin Metronidazole    | Abscess            |
| Amoxicillin Ceftriazone      | PV discharge       |
| Amoxicillin Metronidazole    | Dental caries      |
| Augmentin Doxycycline        | Pelvic pain        |
| Benzathine Penicillin Doxycycline Metronidazole Ceftriazone | PV discharge Pleural thickening |
| Benzathine Penicillin Ceftriazone | Gonococcal infection |
| Benzathine Penicillin V      | Tonsilitis         |
| Benzathine Penicillin Amoxicillin | Sputum         |
| Benzathine Penicillin Amoxicillin | NIL              |
| Benzathine Penicillin Amoxicillin | Bacterial exudate |
| Ceftriazone Metronidazole Doxycycline | PV discharge   |
| Ceftriazone Doxycycline Metronidazole | PV discharge   |
| Ceftriazone Doxycycline Metronidazole | PV discharge   |
| Ceftriazone Doxycycline Metronidazole | Penile rash     |
| Ceftriazone Metronidazole    | Abdominal pain     |
| Ceftriazone Doxycycline      | Urethral discharge |
| Ceftriazone Doxycycline Metronidazole | Pelvic pain PV discharge |
| Ceftriazone Doxycycline Metronidazole | PV discharge   |
| Ceftriazone Doxycycline Metronidazole | STI discharge   |
| Ceftriazone Erythromycin     | PV discharge Gynaecological pelvis |
| Ceftriazone Doxycycline Metronidazole | PV discharge VRT |
| Ceftriazone Cotrimoxazole Metronidazole Doxycycline | PV discharge   |
| Ceftriazone Metronidazole Erythromycin | Pregnant masses  |
| Ceftriazone Erythromycin Metronidazole Cotrimoxazole | PV discharge Dysuria |
| Ceftriazone Doxycycline      | Urethral discharge |
| Cloxacillin Bactrim          | Abscess            |
| Cotrimoxazole Ceftriazone Doxycycline Metronidazole | PID              |
| Doxycycline Ceftriazone      | Orchitis           |
| Doxycycline Metronidazole    | STI contact        |
| Doxycycline Metronidazole    | STI contact        |
| Doxycycline Ceftriazone Metronidazole | PV discharge   |
| Gentamicin Chloramphenicol   | Dacryocystitis Chest pain |
| Metronidazole Ceftriazone Erythromycin | PV discharge   |
| Metronidazole Ceftriazone Doxycycline | PV discharge   |

Continues
Based on our findings, we recommended that in order to improve prescribing at PHC facilities in Botswana, it is essential that prescribers be provided with in-service training on the use of current national treatment guidelines, classification of diseases, INN prescribing, as well as proper history taking and recording of diagnoses. In addition, Botswana should consider adopting ICD10 for primary care to aid easier classification of undifferentiated conditions that present in PHC facilities. Pharmacists should also play a key role in promoting rational prescribing practices by conducting drug utilisation reviews and using the findings to stimulate dialogue among practitioners to enhance the future rational use of medicines at PHC facilities.

The Ministry of Health and Wellness, as the major stakeholder responsible for policy formulation and guidance, should seek to design a harmonised managerial tool that will contain pertinent quality indicators for monitoring antibiotic prescribing practices at all PHC facilities. This includes targets for adherence to National Treatment Guidelines as well as classes of antibiotics prescribed, building on European and other guidance. Any quality indicators developed must reflect current conditions in ambulatory care as seen by the high prevalence of gynaecological and sexually transmitted infections in Botswana, which is not universal especially among European populations. This will help address concerns with current WHO/INRUD criteria. Similarly, multi-sector antimicrobial initiatives and programmes should be developed and implemented across all locations to improve future antibiotic prescribing through monitoring antimicrobial usage as well as developing and implementing strategic interventions aimed at optimising antimicrobial use and reducing AMR. This may help to improve antibiotic prescribing in the future in Botswana and reduce AMR rates. Hopefully any quality indicators developed will also be of interest to other African countries and wider.

ACKNOWLEDGEMENTS

This study was funded by the University of Botswana Office of Research and Development and the authors wish to acknowledge the Ministry of Health, Botswana for granting permission to carry out the study and to the staff and patients in the PHC facilities. We would also like to thank Dr Amanj Baker Kurdi for his helpful comments regarding potential statistical analyses.

DISCLOSURE

The authors declare no competing interests with this study.

AUTHOR CONTRIBUTIONS

YM, VS, AM, ES and MC designed the study and were involved in the collection and analysis. YH, AM and BG produced the initial draft manuscript. All authors critiqued successive drafts of the manuscript before submission and re-submission.

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How to cite this article: Mashalla Y, Setlhare V, Massele A, et al. Assessment of prescribing practices at the primary healthcare facilities in Botswana with an emphasis on antibiotics: Findings and implications. *Int J Clin Pract.* 2017;71:e13042. https://doi.org/10.1111/ijcp.13042