Assessment of prescribing practices at the primary health care facilities in Botswana with an emphasis on antibiotics; findings and implications

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Abstract:
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 – December 2013 in 19 clinics were collected in a cross-sectional study. The WHO/INRUD 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 INN 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 (J01C) were most (45.1%) commonly prescribed 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 PHC facilities should be designed and implemented, including developing robust quality indicators.

What's known?
- There is considerable overuse of common antibiotics across countries particularly in primary health care centres, leading to increasing resistance rate.
- There are ongoing developments to improve the use of antibiotics across countries including WHO/ INRUD indicators as well as guidelines.

- However, there are concerns with the specificity of WHO/INRUD indicators to fully assess the quality of antibiotic prescribing in ambulatory care as well as adherence to ICD codes when prescribing.

What's new?

- There were high rates of INN prescribing in Botswana as well as high rates of 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 due to 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.

Key words: Inappropriate drug use, Primary Health Care, prescribing indicators, antibiotics prescribing, Botswana

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" [1]. 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 [2-8], the WHO in collaboration with the International Network for Rational Use of Drugs (INRUD) have developed core indicators for prescribing practices, patient care and facility specific factors [2,9,10]. These include the number of antibiotics per prescription without looking at issues of necessity or whether prescribing adheres to current guidelines [11]. The current World Health Organisation reference value for the average number of medicines per encounter is <2 [10,12,13], with a comprehensive review between 1990 and 2009 reporting the average number among 104 countries was 2.6 for the Africa region [14]. More recent reports indicate a 45.8% increase from 2.4 between 1995 – 2005 to 3.5 between 2006 and 2015 [10]. The percentage of medicines prescribed by the generic (International Non-proprietary Name; INN) name should be 100% (acceptable >80%) [2,9,13]. However, studies have reported lower rates for the African region at between 60% to 68% [5,12].

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 [4,15-19]. 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 [20-22], with most of the increase due to prescribing in URTIs which are typically viral in origin. Overall, approximately 50% of current antibiotic prescribing in outpatient departments is seen as inappropriate [23]. In Malaysia, as in Botswana, antibiotics are commonly and inappropriately prescribed by primary health care providers at Primary Health Care (PHC) facilities [24-27]. Most of these reports though are based on small-scale studies, which could be underestimation of the extent of antibiotic use in developing countries.

Following the Alma Ata Declaration in 1978 [28], Botswana developed a successful and comprehensive primary health care (PHC) system with treatment provided in accordance with the standards set out in the Ministry of Health guidelines [29]. However to date, few studies have been undertaken to assess prescribing practices in PHC facilities in Botswana [30-32]. We have previously reported that 52 different documents/guidelines existed at 18 PHC facilities in the Greater Gaborone area of Botswana, of which 50% focused on treatment and management of diseases, the remaining 50% were general information and policy related [33]. Except for the guidelines for treating STIs found at 86% of the facilities, the majority of PHC facilities (56%) did not have current guidelines and the Botswana Treatment Guide was only found at 50% of the clinics [33].

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 [9,10].

Methodology

This was a non-experimental cross-sectional descriptive study initially using the WHO/INRUD indicators [9] before looking more specifically at antibiotic prescribing. The study was carried out between November – 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.

Sample size and sampling procedures

The WHO [9] 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 was 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 realized. 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.

Quality of antibiotic prescribing

The quality of antibiotic prescribing practices were assessed as follows: (a) prescribing against WHO/ INRUD criteria [9,10,13]; (b) antibiotic prescribing against indicators developed and proposed by European organisations and (c) antibiotic prescribing against the Botswana Essential Drug List [34].

The following indicators have been proposed and used by European organisations to assess the quality of systemic antibiotic (J01) prescribing [35-37]:

- Utilisation of penicillin (J01C) as a % of total antibiotic use
- Utilisation of combination penicillin (e.g. co-amoxiclav) as a % of total amoxicillin use
- Utilisation of third- and fourth-generation cephalosporins versus 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 exists for these facilities in Botswana [37,38].

The utilisation metric used is a prescription rather than internationally recognised metrics such as defined daily doses (DDDs) or DDDs per one thousand inhabitants per day (DIDs) [37-39]. 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.

Data processing and analysis

For the purpose of improving the quality of data and the rigor of research results, data management procedures and processes were in accordance with the methodology proposed by Vittinghoff *et al.* [40]. 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.

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 28th November 2014. The identity of the clinics were protected by keeping them anonymous and assigned coded numbers.

Results

General
Data from 19 PHC facilities only were analysed. Data from one clinic was 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.

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 International Non-proprietary Names (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).

Table 1: Prescribing practices against documented indicators

Prescription practices	**N**	**%**
Total number of prescriptions analysed	550	
Total number of drugs prescribed	1551	
Average drugs/prescription	2.8	
Total prescriptions with generic (INN) names	1219	78.6
Total antibiotic encounters	235	42.7
Medicines from EDL	1490	96.1

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 (28.4%) followed by metronidazole (14.4%). Co-amoxiclav accounted for only 0.3% of all antibiotic prescriptions, while cotrimoxazole (sulphamethoxazole + tromethropim) 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.

Table 2: Commonly prescribed antibiotics at PHC facilities in Botswana

Antibiotic	ATC classification	Frequency (N)	Per cent
Beta-lactams (J01C)			
Amoxicillin	J01CA04	87	28.4
Ampicillin	J01CA01	3	1.0
Benzathine Penicillin (Retarpen)	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)	J01XE	1	0.3
Tetracycline ointment	S01AA	3	1.0
Gentamicin ointment	SO1AA	1	0.3
Total		**306**	**100**

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, 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 due to 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.

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 & 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 & 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 & signs involving the digestive system & abdomen		
Diarrhoea	R19	15
Abdominal & pelvic pain	R10	11
Loss of appetite	R63	6
Nausea & vomiting	R11	4
Constipation	K59.0	1
Enteritis	K52.9	1
Heartburn (epigastric pain)	R12	1
Symptoms & signs involving the skin & subcutaneous tissues		
Wound/sores	T81.30	12
Rash	CM/21	9
Boils & 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
Endocrine, nutritional and metabolic disease		
Diabetes mellitus	E08	1
Symptoms & signs involving genitourinary system		
Vaginal discharge (unspecified)	N89.8	34
Sexually transmitted infections (Unspecified)	A64	25
Dysuria (Unspecified)	R30.0	6
Penile discharge (Unspecified)	R36.9	5
Pelvic Inflammatory Disease (PID)	N73.9	4
Vagina itching (Unspecified)	N89.4	3
Menstrual Disorder Syndrome	N92.6	3
Ovarian cyst	N83.2	3
Pregnancy masses	CM/09A	3

Orchitis	N45.2	2
Post Safe Male Circumcision (SMC)	Z41.2	2
Painful urinary bladder (unspecified)	N32.9	1
Diseases of the ear and mastoid process		
Otitis media	H60	7
Painful jaw		2
Disorders of soft tissues and chest		
Chest pain (unspecified)	R07.9	10
Backache	M54.9	2
Joint pain	M79.609	1
Diseases of the eye and adnexa		
Conjunctivitis	H10.0	5
Dacryocystitis (unspecified)	H04.309	1
Symptoms and signs involving breast		
Swollen breast (engorged)	N64.59	1
Dental and oral diseases		
Dental caries (Unspecified)	K02.9	3
Chronic Periodontitis	K05.3	2
Toothache (Unspecified)	K08.8	1
Traumatic disorders		
Injury (unspecified)	CM/929.9	14
Fractured index finger (unspecified)	S62.600A	1
Other unspecified symptoms and signs		
Altered discomfort		1
Swollen fore skin		1
Enlarged stomach		1
Swellings (unspecified)		4
Local sepsis		2
Bacterial exudate		1
Itchy eyes		8
Painful armpit		1
Muscle pain (unspecified)		1

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.

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.

Table 4: The pattern of antibiotic combinations and the indications at PHC facilities in Gaborone, South East and Kweneng districts, Botswana.

Antibiotics				**Diagnoses**	
Amoxicillin	Metronidazole			Cough	Chest pain
Amoxicillin	Gentamicin ear drops			Ear sores	
Amoxicillin	Metronidazole			Agsoris	Headache
Amoxicillin	Metronidazole	Retarpen		Pharyngitis	Swollen jaw
Amoxicillin	Cotrimoxazole			Post SMC	
Amoxicillin	Cotrimoxazole			Cough	Eye watering
Amoxicillin	Metronidazole			Abscess	
Amoxicillin	Ceftriaxone			PV discharge	
Amoxicillin	Metronidazole			Dental caries	
Augmentin	Doxycycline			Pelvic pain	Pleural thickening
Benzathine Penicillin	Doxycycline	Metronidazone	Ceftriaxone	PV discharge	
Benzathine Penicillin	Ceftriaxone			Gonococcal infection	
Benzathine Penicillin	Penicillin V			Tonsillitis	
Benzathine Penicillin	Amoxicillin			Sputum	
Benzathine Penicillin	Amoxicillin			NIL	
Benzathine Penicillin	Amoxicillin			Bacterial exudate	
Ceftriaxone	Metronidazole	Doxycycline		PV discharge	
Ceftriaxone	Doxycycline	Metronidazole		PV discharge	
Ceftriaxone	Doxycycline	Metronidazole		PV discharge	
Ceftriaxone	Doxycycline	Metronidazole		Penile rash	
Ceftriaxone	Metronidazole			Abdominal pain	
Ceftriaxone	Doxycycline			Urethral discharge	
Ceftriaxone	Doxycycline	Metronidazole		Pelvic pain	PV discharge
Ceftriaxone	Doxycycline	Metronidazole		PV discharge	
Ceftriaxone	Doxycycline	Metronidazole		STI discharge	
Ceftriaxone	Erythromycin			PV discharge	Gynaecological pelvis
Ceftriaxone	Doxycycline	Metronidazole		PV discharge	VRT
Ceftriaxone	Cotrimoxazole	Metronidazole	Doxycycline	PV discharge	
Ceftriaxone	Metronidazole	Erythromycin		Pregnant masses	
Ceftriaxone	Erythromycin	Metronidazole	Cotrimoxazole	PV discharge	Dysuria
Ceftriaxone	Doxycycline			Urethral discharge	
Cloxacillin	Bactrim			Abscess	
Cotrimoxazole	Ceftriaxone	Doxycycline	Metronidazole	PID	
Doxycycline	Ceftriaxone			Orchitis	
Doxycycline	Metronidazole			STI contact	

Doxycycline	Metronidazole			STI contact	
Doxycycline	Ceftriaxone	Metronidazole		PV discharge	
Gentamicin	Chloramphenicol			Dacryocystitis	Chest pain
Metronidazole	Ceftriaxone	Erythromycin		PV discharge	
Metronidazole	Ceftriaxone	Doxycycline		PV discharge	
Metronidazole	Cotrimoxazole			Abscess	Scapular wound & cold
Metronidazole	Doxycycline	Ceftriaxone		Pelvic pain	Ovarian cyst
Metronidazole	Doxycycline			MDS	PV discharge
Metronidazole	Erythromycin			Genital warts	Cough
Penicillin V	Cotrimoxazole			Tonsillitis	
Frequency	**45**	**18**	**4**		

NB: MDS = Menstrual Disorder Syndrome; PID = Pelvic Inflammatory Disease; SMC = Safe Male Circumcision; Cold = common cold.

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 [34] compares favourably with WHO recommendations of 100% [10,12,13,41] as well as rates of 55% to 80% reported for the Africa, Europe, Americas and South East Asia regions [2,10,42]. The high prescribing rate from the EDL could be attributed to easy accessibility of the Botswana Treatment Guidelines at PHC facilities [33], the routine availability of medicines incorporated into the Botswana EDL in PHCs, and the limited influence of pharmaceutical companies unlike other countries [2,21,43-46].

The high rate of INN prescribing in this study 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 [41] as well as 68% for Africa as a whole [10]. 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 such as the UK with its high rate of INN prescribing [47,48]. In order to attain WHO recommendation [9,10], we believe INN prescribing training should be intensified through regular training of in-service practitioners.

In this study, 42.7% of the encounters contained an antibiotic prescription, higher than < 30% recommended by WHO [10,12,13]. This is marginally higher than 39% and 34% for the Americas and European regions, but lower than 53% for the Eastern Mediterranean region [41] and Africa as a whole (47%) [10]. This rate is also higher than 27% in a previous study in Botswana [31], and higher than 30% for Acute Respiratory Infections in children under 5 years old previously reported in Botswana [32]. The high use of antibiotics could be due to a high burden of gynaecological and sexually transmitted infections (Table 3). There is also high prevalence (pandemic) of HIV in Botswana [49]. 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. We found that most of the indications for antibiotic prescriptions were based on signs and symptoms, rather than specific diagnoses, and were compliant with ICD (Table 3). However, nine conditions did not match the ICD which could either result from failure of patients to express themselves during history taking, poor history taking or the inability of prescribers to apply ICD codes when arriving at differential and definitive diagnoses.

Adoption of ICD 10 codes for primary care diagnoses would go a long way towards creating a common language for classifying undifferentiated conditions that are seen in primary health care settings.

There are concerns that some diagnoses such as a common cold, diarrhoea, painful legs, constipation, and unclassified muscular pains, do not warrant antibiotics (Table 3). In addition, four prescriptions each containing antibiotics had no established diagnosis. The situation in this study is however better than reported in Nigeria where over 50% of the patient's folders reviewed had no established diagnosis [50]. The factors that contribute to over prescribing of antibiotics include inadequate in-service training, socio-cultural factors and patient demand [16,18,27,51]. Most health facilities in Botswana and elsewhere are characterised by inadequate skilled human resources. These lower level healthcare workers are overwhelmed by the large number of patients seeking care and some pressurising on prescribers to prescribe injections and antibiotics [52-54]. The establishment of the Medical School in 2009 is a dedicated effort by the Government of Botswana to improve the number and quality of health care providers in the country. Assessment of factors influencing antibiotic prescribing practices was outside the scope of this study but will be explored further in future research.

The high use of beta-lactamase antibiotics compares favourably with former Soviet Union Republics and Turkey with rates of 37.5% to 65.6% of total J01 antibiotics [37]. 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 [55-57]. With rising concerns on the development of *C.difficile* resistance [58,59], the low utilisation of cephalosporins in this study (Table 2) is also encouraging and compares favourably with rates of 0.5% to 12.2% among former Soviet Union Republics and Turkey [37]. Similarly, the lack of fluoroquinolone prescribing is encouraging, helped by the lack of inclusion of the drugs in the Botswana EDL [34].

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 [60]. Adherence is a complex phenomenon and typically far from optimal across countries [19,61-63]. For instance, 46% of antibiotic prescriptions in a recent study were not indicated by the guidelines [64]. However, higher adherence rates were recently seen in Namibia (62%), although below national target rates of 95% [11]. Guideline adherence is influenced by several factors including the level of training of PHC personnel, available resources at health care 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 [65]. Effective monitoring can enhance adherence rates [66]. Care though must be taken in communicating appropriate guidelines, especially if there are differences between different policies and guidelines as recently seen in Namibia [67].

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 ICD 10 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 with similar populations.

Limitations
The study was carried out in an urban area of Botswana and did not include rural areas. However, as mentioned, this is where the majority of patients are currently treated in Botswana, although we recognise there could be differences in the characteristics of the respective patient populations. In addition, the results are from a retrospective collection of data, and information on the characteristics of practitioners was not collected. However, we believe our findings will already give guidance to key stakeholders on ways to improve antibiotic prescribing in Botswana. We also believe our on-going research to develop pertinent quality indicators across all locations, including both urban and rural PHCs, will be of interest to other African countries and wider.

Acknowledgements and conflicts of interest
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Competing interest
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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