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Prudent use and antimicrobial prescription practices in Ethiopian veterinary clinics located in different agroecological areas

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Abstract

Background Understanding antimicrobial prescribing (AMP) practices and their prudent use in livestock can support the implementation of stewardship programs in veterinary medicine. Empiric therapy using antimicrobials is widely practiced in resource-poor settings, including Ethiopia. This could significantly contribute to the global burden of antimicrobial resistance (AMR) and the potential accumulation of residues in food. This study assessed AMP practices in Ethiopian veterinary clinics located in different agroecological zones (AEZs) as well as adherence to antimicrobial stewardship principles (ASPs).

Methods Data were collected from case book records from four district veterinary clinics located in different AEZs in Ethiopia from 2015 to 2019. To identify factors associated with non-prudent AMP practices (i.e., the use of antimicrobials without therapeutic effects or benefits to the animal), data from registered clinical veterinary cases were selected using a systematic random sampling method. This led to the inclusion of approximately one-third of all records, including animal characteristics, disease symptoms and diagnosis, and details about the prescribed drugs. Descriptive statistics were used to report the proportions of drugs prescribed and adherence to the ASPs. The Chi-square test was used to establish an association between the drugs prescribed and the disease diagnoses and the districts. The factors associated with cases receiving antimicrobials and non-prudent AMP practices were also assessed using a multivariable logistic regression analysis.

Results In total, 12,438 clinical case records were considered. Approximately 97% of these cases received treatment without laboratory confirmation, and 15,243 drugs were prescribed. Among these prescriptions, 75% were for antimicrobials, with oxytetracycline (29%) and a combined formulation of penicillin-dihydrostreptomycin (19%) being the most often prescribed drugs. Overall, 19% of the cases were treated non-prudently with antimicrobials, with high incidences at Holeta (32%) and Sekoru (19%) ($p < 0.001$). Most cases, including viruses and other non-pathogens (100%), toxicants (97%), unknown causes (94%), fungi (70%), nutritional (64%), risk of bacterial infection (42%), and endo-ectoparasites (24%), were treated non-prudently. Cases receiving antimicrobials and non-prudent AMP were associated with Holeta and Sekoru study clinics, major clinical signs of bloat and loss of body condition, and illness

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due to viral infections ($p < 0.05$). Conversely, species of animals and cases diagnosed with multiple etiologic agents and respiratory diseases were negatively associated with prudent AMP practices ($p < 0.05$).

Conclusions Much of the prescription practice observed in this study did not adhere to the ASPs; there were significant discrepancies between the prescribed drugs and disease diagnoses. Prescribing antimicrobials for unrelated diagnoses may contribute to an increase in AMR. The study thus underlines the need for mechanisms to improve accurate disease diagnosis and prescriber adherence to prudent AMP in countries with limited resources.

Keywords Antimicrobials, District veterinary clinics, Empiric therapy, Ethiopia, Livestock diseases, Prudent prescribing practices, Stewardship principles

Introduction

Antimicrobials are extensively utilized in veterinary clinical practice to treat diseased animals and prevent suffering. Antimicrobial use (AMU) in food animal production sectors in low- and middle-income countries is increasing in conjunction with increased intensive production to fulfill the rapidly rising demand for animal-source foods [1].

Antimicrobials should be administered prudently to animals, with the aim of maximizing the intended benefit and minimizing side effects [2]. On the other hand, non-prudent use of antimicrobials (i.e., the use or misuse of antimicrobials without therapeutic effects or benefits to the animal) in both food-producing and companion animals promotes the emergence of antimicrobial resistance (AMR) in animal or human pathogens [3–5]. The non-prudent use of antimicrobials to maximize the productivity of food animals intended for human consumption may also increase the likelihood of detrimental effects on humans through the accumulation of drug residues in food [6]. In this paper, the term "non-prudent use" refers to prescribing antimicrobials without therapeutic value, i.e., inappropriate use of antimicrobials for diseases that have tentatively been diagnosed on the basis of etiologic agents– such as antibiotics for non-bacterial cases or withholding their use for bacterial infection, prescribing trypanocides for cases other than trypanosomiasis or withholding their use for trypanosomiasis, prescribing antibiotics for parasitic diseases, or prescribing two antibiotics with antagonistic activity.

The prudent use of antimicrobials can help to implement practical measures to improve animal health and welfare, while preventing or reducing the selection, emergence, and spread of AMR bacteria in both animals and humans [2]. Therefore, it is imperative that antimicrobials should be prescribed or administered only when the presence of a pathogen that causes disease is confirmed or suspected on the basis of the animal's clinical signs and previous experiences with disease incidence in the area. This assessment should be made on the basis of the patient's clinical history, physical examination, and if applicable and feasible, laboratory investigations [7]. Most antimicrobial therapy failures occur when a pathogenic microorganism is assumed, but the etiology is unknown. Clinically proven, effective antimicrobial combinations with distinct mechanisms of action could synergize for successful treatment [8].

In Ethiopia, both the public and private sectors are engaged in the provision of veterinary services. Veterinarians and para-veterinarians are expected to use the Standard Veterinary Treatment Guidelines (SVTG) to diagnose and treat diseases [9]. They should also use the Essential Veterinary Drug List (EVDL) to select appropriate drugs [10] and keep written records of cases encountered at clinics. The country has district veterinary clinics (types B and C), animal health posts (type D clinics at the village administration level), and livestock extension agents. There are also community animal health workers (CAHWs) with a limited level of training who assist with the delivery of animal health services in remote pastoral areas [11]. Despite several reforms and efforts to improve animal health care and access to veterinary pharmaceuticals, the quality of veterinary services in the public sector in Ethiopia remains substandard [11].

In response to the global threat posed by AMR to both human and animal health, Ethiopia has also established its third strategic plan (2021–2025) to prevent and contain AMR by adopting the One Health approach, with strategic objectives to optimize AMU in veterinary practice and agriculture [12]. However, misdiagnosis by animal health experts in the field is possible because of a lack of standard laboratory facilities and other rapid diagnostic aids. This is likely to result in non-prudent veterinary antimicrobial prescribing (AMP) practices, as previously reported from similar situations in central Ethiopia [13, 14]. However, studies that assess and compare veterinary AMP practices in district veterinary clinics located in different agroecological zones (AEZs) of Ethiopia are limited. It is expected that the incidence of livestock diseases, both in type and number, as well as the AMP patterns, may vary among different AEZs. In line with the country's aim of expanding animal health care services, identifying the factors that contribute to non-prudent AMP practices and assessing prescribers' adherence to the antimicrobial stewardship principles (ASPs) are important, but have not been well studied previously.

Our objective was to assess prudent veterinary AMP practices in accordance with ASP and World Health Organization (WHO) drug use indicators, as well as to compare the magnitude of the use of different antimicrobial classes commonly used for the treatment of livestock diseases in four district veterinary clinics located in different agroecology areas in central and western Ethiopia. This could reveal differences in AMP practices, which could help identify good practices and implement them widely. It could also help improve the quality of veterinary services and apply ASPs in resource-poor settings.

Materials and methods

Study setting

The study was conducted at B-type district veterinary clinics in central and western Ethiopia (Fig. 1) during 2018 and 2019. In Ethiopia, B-type clinics provide clinical services to all species of animals at the district level. It also has facilities for laboratory diagnosis and allows veterinarians to diagnose and prescribe drugs for use in animals. Hence, clinical data from B-type veterinary clinics can be used to assess the prudency of AMP practices. For this purpose, we selected three different agroecological areas on the basis of their altitudes (highland, mid-highland, and mid-lowland), geographical locations (central and western Ethiopia), and similarities in clinical settings (Table 1). The districts in the central highlands (Fiche and Holeta) represented cool humid mixed crop-livestock farming, the district in the western mid-highland (Sekoru) represented a hot−humid mixed crop−livestock farming and is located in the tsetse belt (trypanosomiasis endemic areas), while the district in the central mid-lowlands (Modjo) represented a semi-arid (dry) mixed crop−livestock farming system (Table 1). The distributions of livestock diseases and tsetse flies varied among study sites. Among livestock diseases that could affect AMP practices in the study areas, trypanosomiasis, febrile illness (generalized systemic infection), and respiratory diseases are mostly reported (see details in Table S1, Additional File 1).

Clinicians, technical assistants, laboratory analysts, and drug dispensers of animal health professionals with different educational levels (MVSc/DVM, BVSc, and Diploma) work in the study clinics. The study clinics contain physical facilities such as an open-air space with a crush for animal restraint (usually under the shed), a

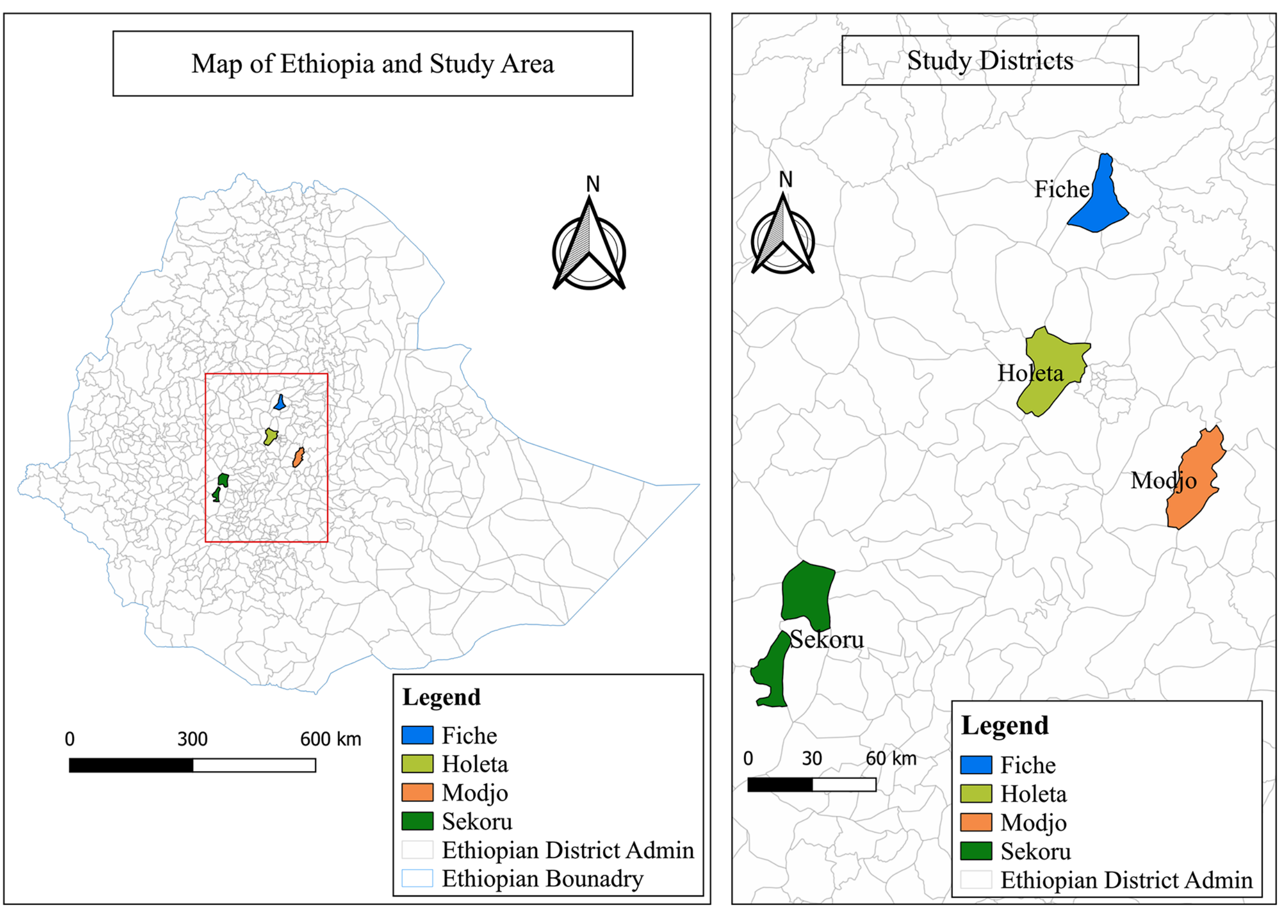

Fig. 1 Map of Ethiopia showing study districts

Table 1 Basic information on agroecology, animal health service features, and livestock producers' residence of the study areas

Study area	Distance from Addis Ababa	Location (coordinates)	Elevation (m)	Average Annual temperature	Average Annual rainfall (mm)	Peculiar features regarding animal health services	Residence of major livestock producers
Fiche	126 km North	Central highland (9°48′N 38°44′E)	2738	14.2 °C	1100	- Known for extensive dairy cow production and milk supply to the capital city. - Diseases of temperate regions, like RD and endoparasites are mostly reported while TSM is absent	Urban and peri-urban residents
Holeta	40 km West	Central highland (9°3′N 38°30′E)	2391	15.5 °C	1038	- Diseases of temperate regions, like RD and endoparasites are mostly reported.	Peri-urban and rural residents
Modjo	70 km Southeast	Central mid-lowland (dry/semi-arid) (8°35′N 39°10′E)	1779	19 °C	968	- High animal movement to export abattoirs found in the town. - Known for various contagious infectious diseases of livestock: pasteurellosis, PPR, and others. - The clinic has the highest caseload records throughout the year.	Urban and peri-urban residents
Sekoru	248 km Southwest	Western mid-highland (8°05′N 37°30′E)	1920 (Low around Ghibe river ~ 1160)	18.9 °C	1179	- The climatic conditions favor various livestock diseases, including blackleg and TSM. - Trypanocidal drugs are widely used in the district. - Farmers residing around the Ghibe area are practicing self-treating their animals against TSM.	Peri-urban and rural residents

RD, respiratory diseases; TSM, trypanosomiasis. **Sources:** [15–17] and https://www.weather-atlas.com/en/ethiopia-long-term-weather-forecast

laboratory room, a drug store, and offices for veterinary clinicians and dairy animal breeders. All healthcare services, including minor surgery (wound dressing, open castration, etc.) and major surgery (c-section, rumenotomy, etc.), are performed outside in the open air. The laboratory rooms were not fully functional in the three study clinics; however, parasite identification using microscopic examination (gastrointestinal helminths, blood parasites, and ectoparasites) was performed at the Modjo district veterinary clinic.

Study design and data sources

A mixed methods assessment was conducted as follows: ***First***, a 5-year retrospective analysis of medical records on AMP practices from district veterinary clinics was conducted (from January 01, 2015 to December 31, 2019). Data for this study were collected from registration casebooks at the four district veterinary clinics located in Fiche, Holeta, Modjo, and Sekoru. The clinics were selected at random from B-type clinics and easily accessible districts in three different agroecological areas in central and western Ethiopia. This study included all livestock (i.e., domesticated animals raised in an agricultural setting to produce labor and commodities: cattle, sheep, goats, equids, and chickens) of all ages and sex groups that visited the study clinics for the treatment of their illness and/or to receive prophylaxis/ metaphylaxis and treatment with drugs. A systematic random sampling method was used to select one-third of the cases recorded daily, with only those cases receiving treatment using drugs being selected. The initial case was selected from the first case listed and received treatment with drugs. After the first case was selected, every third case on the list was considered. However, if the next case was not eligible (i.e., it was not treated with drugs or the name of the drug was not written or readable), then the subsequent case was considered. Prescriptions containing the animal's characteristics, disease diagnosis, and drugs prescribed from more than 100,000 cases recorded for 5 years were used. Some of these cases were brought to clinics for nonclinical services, including vaccination, closed castration, pregnancy diagnosis, etc. However, our study aimed to assess the appropriateness of treatment and the AMP practices. Accordingly, we followed similar exclusion criteria suggested by previous studies conducted in Ethiopia [13, 14], where the studies excluded all randomly selected animal patients who were admitted to the clinics but did not receive any medicines. ***Second***, a group discussion with animal health professionals working in each study clinic was employed to gather detailed information about the availability and use of standard veterinary treatment guidelines (SVTG) and EVDL, the availability of antimicrobials, limiting factors and future directives on the use of various classes of antimicrobials.

Third, clinic-specific observations were made to document the drugs that were available in the study clinics.

Data collection

For each selected patient record the following data were retrieved: prescriptions containing the treatment date, animal characteristics (species, age, sex, breed, and clinical signs/ symptoms observed), name of tentatively diagnosed disease (empiric or physical clinical examination), confirmatory laboratory tests used [if performed]), prescribed drugs (type, name, naming [generic or brand], number of drugs prescribed, route of drug administration, and duration of treatment [if recorded]). Information about the availability and use of SVTG and the EVDL in the study clinic over the five years was also recorded. The class and specific drugs available in each study clinic were also recorded. Information regarding limiting factors and future directives on the availability of various classes of antimicrobials at each clinic was also documented.

Antimicrobial prescribing practices

To describe AMP, we employed the WHO prescribing indicators [18], as used previously in Ethiopia [13, 14]. Prescribing indicators with reference values for optimal AMP include the average number of drugs prescribed per encounter (<2), the percentage of drugs prescribed by generic name (100%) and those from the EVDL (100%), and the percentage of encounters with antibiotics (<30%), antimicrobials and other groups of drugs prescribed, which were adopted for veterinary medicine [13]. Prescription counts for each class of drugs were summarized using percentages of the total prescriptions.

The prudence of AMP practices was evaluated in accordance with prescribers' adherence to the ASP. Both SVTG [9] and the World Organization for Animal Health (WOAH) recommendations [2] to improve animal health and welfare while preventing or reducing the selection, emergence, and spread of antimicrobial-resistant bacteria in animals and humans, were used. In the present study, prudent AMP was defined as the use of appropriate antimicrobials for diseases that have been tentatively diagnosed on the basis of etiologic agents. As a result, the prescription of antimicrobials was defined as prudent if it met the following criteria:

a) Where antibiotics were used for bacterial and/or respiratory diseases, and where broad-spectrum antibiotics were used for cases of septicemia, gastroenteritis, contaminated wounds (high risk of infection), and retained fetal membranes (RFMs);
b) Trypanocidal agents were prescribed if the tentative diagnosis was trypanosomiasis, or if the case was suspected of infection with other hemoparasites (including babesiosis); and.
c) Combinations of antimicrobial(s) with anthelmintic(s) could be prescribed for bacterial or respiratory diseases or protozoal infections suspected with comorbidity of helminthiasis or a high burden of intestinal helminth parasites. Since the prevalence of parasites in apparently healthy animals was high (up to 75%) across the country [19–21], anthelmintics could be prescribed (prudent) with consideration of animal welfare in all cases as an adjunct therapy to control intestinal helminth infections.

In contrast, the prescription was considered inappropriate (non-prudent):

a) When antibiotics were prescribed for non-bacterial cases (viral, gastrointestinal parasites, and trypanosome infection) or antibiotic use was withheld when the infection is suspected to be bacterial;
b) When trypanocidal agent(s) were prescribed for tentatively diagnosed bacterial, viral, or parasitic cases and withholding their use when the tentatively diagnosed case was trypanosomiasis; and.
c) When two antibiotics with antagonistic activity, such as oxytetracycline–bacteriostatic with penicillin or penstrep–bactericidal agent, were prescribed, as well as the use of non-effective broad-spectrum antibiotics for cases requiring a long duration of therapy (e.g., brucellosis) or for inappropriate cases (e.g., oxytetracycline for strangles in equines).

Data management and analysis

All the registration casebook data were entered into a Microsoft Excel spreadsheet. On the basis of the recorded data, the following dummy variables were generated: (1) The type of diagnosis; a tentative/empirical diagnosis on the basis of signs and symptoms or laboratory-supported diagnosis where the diagnosis is supported by laboratory tests performed for each case (either parasitological, microbiological or not performed), was also generated. (2) Variables related to drug prescribing practices; number of drugs prescribed, drug naming, antimicrobials (list of drugs) prescribed (yes/no), anthelmintics (list of drugs) prescribed (yes/no), a combination of antimicrobials and anthelmintics prescribed (yes/no), and ectoparasiticides (list of drugs) prescribed (yes/no). Ivermectin was considered as both endo−ectoparasiticides. (3) Classification of antimicrobials by WOAH as veterinary critically important antimicrobials (VCIA) and by the WHO as critically important (CIA) and highly important antimicrobial (HIA) for human medicine. Prescriptions of combinations of antimicrobials from different classes (e.g., penicillin−streptomycin [penstrep], a fixed combination of natural penicillins and aminoglycosides) are counted as one prescription for each component ingredient. (4) Binary variables were created for AMP (yes/no) and the prudency of AMP practices for each case (prudent or non-prudent) using the criteria noted in the previous section. When antimicrobial(s) are prescribed for a case, this qualifies as a contributing factor to cases being treated with antimicrobials.

Data on patient demographic characteristics, the distribution of livestock diseases in the district clinics, drug prescribing practices, and adherence to the ASPs were analyzed descriptively as proportions and percentages. The Chi-square test was used to establish the statistical significance of the associations between the drugs prescribed and the etiologic-based diseases diagnosed, as well as with the districts.

A multivariable logistic regression analysis was carried out to assess the factors associated with cases being treated with antimicrobials and non-prudent AMP practices. The following variables were selected as potentially influenced the two variables of interest: year, season, study area, animal characteristics, major clinical symptoms recorded, etiologic-based disease diagnosed, and major livestock disease incidence. Before conducting the multivariable analyses, the presence of multicollinearity between independent variables was checked, and covariates with a variance inflation factor (vif) value >10 were excluded from the final model. Then, a univariable analysis was carried out for each of the independent variables to explore the unadjusted associations between the variables and outcomes, and variables with a significance level of $p \leq 0.05$ were included in the multivariable analysis, using Generalized Linear Model (GLM) with a logit link and a binomial distribution. The final regression model was generated using a forward stepwise selection GLM, including covariates with a p-value of <0.05.

The results of the multivariable logistic regression analyses are reported as adjusted odds ratios (OR_{adj}) together with their 95% corresponding confidence intervals (CI). Microsoft Excel 365 and Stata version 17 statistical software were used for all the analyses.

Results

Patient demographic characteristics

A total of 12,438 clinical case records were selected for this study and assessed. Cattle constituted the most commonly treated group of animals (62% of all patients reviewed), followed by sheep (23%), equines (9%), goats (5%), and chickens (2%). Except for chickens, adult (85%) and male (62%) animals were the most frequently recorded patients among all species of livestock that visited the veterinary clinics of the study districts. A large majority of the cases involved a single patient (94%) with similar clinical signs brought to clinics for treatment. A complete overview of the demographic characteristics of the patients at the study veterinary clinics is provided in Table S1, Additional File 1.

Etiologic-based livestock disease groupings recorded at four different veterinary clinics were assessed. Laboratory-supported diagnosis was uncommon, and cases were based on clinical signs, symptoms, and disease history. Among the 12,438 patient encounters, 97% of the cases were diagnosed solely by clinical examination, while 3% were confirmed for parasites via laboratory investigations. There were statistically significant differences in the incidence of generalized systemic infections, respiratory diseases, and trypanosomiasis among the study clinics ($p<0.05$). Bacterial infections were the most commonly reported cases in Modjo ($n=1{,}304$; 37%), whereas generalized systemic infections (i.e., diseases that were not specified as either caused by bacteria, viruses, or protozoa but with symptoms of febrile illness) accounted for more than half of all the cases recorded at Fiche. The majority of reports involving protozoal diseases were from Sekoru, which is in the tsetse belt area of western Ethiopia (67%), where almost all the cases were diagnosed as trypanosomiasis (99.7%). A high percentage of endoparasites and ectoparasites were recorded in central Ethiopia. Records indicating etiologic-based major livestock disease groupings at the study clinics are provided in Table S1, Additional File 1.

Drug prescribing practices

In the study clinics, 15,243 drug prescriptions were written for a total of 12,438 cases, comprising 12,294 (99%) single and 144 (1.2%) multiple diseases diagnosed (Table 2). The average number of drugs per encounter was 1.23 (15,243/12,438), with a maximum of three drugs, and 87% of them were prescribed by generic name. All prescribed drugs (100%) were available in the EVDL.

According to the drug prescribing pattern, the majority of the prescriptions (64%) were single drugs, while more than one-third were two drugs (35%). Multiple drug prescriptions were prominent in Holeta (39%) and Sekoru (33%) with statistically significant differences among the study districts ($p<0.05$) (Table 2). Furthermore, most prescriptions (68%) did not specify the duration of therapy, including all prescriptions at Fiche and Sekoru ($p<0.05$) (Table 2).

Antimicrobials (antibacterial and antiprotozoal agents) were the most commonly prescribed drugs (75%) in veterinary clinics. The prevalence of antimicrobial prescriptions was 97% in the Sekoru district veterinary clinic, followed by 77% in Holeta, 64% in Fiche, and 58% in Modjo veterinary clinics. Antibiotics (56%) and

Table 2 Multiple drugs prescription practices (total $N=15{,}243$) and duration of case therapy at study veterinary clinics

Number of drugs prescribed	Number of drug prescriptions at study clinics				
	Fiche	Holeta	Modjo	Sekoru	Total
One	2,358	1,770	3,148	2,418	9,694
Two*	68	1,105	349	1161	5,366
Three*	6	38	0	17	183
Total	2,432	2,913	3,497	3,596	15,243
Duration /Length of therapy					
Not specified	2432	1927	2335	3596	10,290
Specified	0	986	1162	0	2148

* Symbol indicating multiple drug prescriptions at each study clinic. Fixed combinations of penicillin-streptomycin injectable suspension, and intramammary infusion dosage forms of penicillin-cloxacillin are recorded as single prescriptions

trypanocides (20%) were the most commonly prescribed antimicrobials. Antibiotics were widely prescribed in central Ethiopia, with the highest proportion recorded in Holeta (76%), followed by Fiche (64%), whereas trypanocides were prescribed to two-thirds of cases from western Ethiopia (Sekoru). Oxytetracycline was the most prescribed antibiotic (29% of total prescriptions), followed by penstrep (19%) and sulfonamides (5%). Trypanocides accounted for 96% of all antiprotozoal drugs prescribed in the study areas. Combinations of two or more antimicrobials were also recorded. A summary of the veterinary drugs prescribed in the study clinics is presented in Table S2, Additional File 1.

Among the cases that received treatment with drugs, the proportion of cases treated with antimicrobials over time (between 2015 and 2019) in district veterinary clinics indicated that the trend of AMP slightly decreased by 3% (77% in 2015 and 74% in 2019). Antimicrobial prescription decreased over time by 9% in Modjo (62% in 2015 and 53% in 2019) and by 1% in Sekoru (97% in 2015 and 96% in 2019) but marginally increased in Fiche (63.7% and 64.5%) and Holeta (79% and 80%, in 2015 and 2019), with the lowest records in Fiche (63% in 2018) and Holeta (73.8% in 2017). The proportion of cases that received antibiotics decreased marginally by 1% over time (57% in 2015 and 56% in 2019), with the trend of penstrep prescriptions increasing marginally over time (18% in 2015 and 21% in 2019), whereas oxytetracycline prescriptions decreased (31% in 2015 and 28% in 2019). Similarly, prescriptions for trypanocides have decreased over time (22% in 2015 and 19% in 2019), with the lowest recorded in 2017 (18%). No significant changes in the prescription of trypanocides over time were recorded in Fiche (0%), Holeta (2%), or Modjo (0–1%), but the prescription rates decreased marginally by 1% (68% in 2015 and 67% in 2019) in Sekoru, with the lowest record in 2017 (65%).

In this study, all antimicrobials prescribed were classified as WOAH VCIA classes. However, these antimicrobials are also classified by the WHO as CIA (including aminoglycosides [dihydrostreptomycin and gentamicin] and natural penicillins) or HIA (including cloxacillin [beta-lactamase-resistant penicillins], sulfonamides and tetracyclines) for human medicine. All the prescribed antibiotics are categorized as VCIA (i.e., 50% of total active substances: tetracyclines 20%, natural penicillins 13%, aminoglycosides 13%, sulfonamides 3.6% and cloxacillin 0.2%), whereas 26% (aminoglycosides 13% and natural penicillins 13%) and 24% (tetracyclines 20%, sulfonamides 4% and cloxacillin 0.2%) of the prescriptions of the total active substances are categorized as CIA and HIA for human medicine, respectively. However, antimicrobials (e.g., third and fourth generation cephalosporins and fluoroquinolones), which are critically important for human medicine with the highest priority (CIHPA), were not used in this study.

Prudent prescription of antimicrobials

The associations of livestock characteristics and disease diagnoses with drug prescriptions were analyzed to establish prudent AMP practices in the study areas. Prudent AMP was assessed in relation to prescribers' adherence to the antimicrobial stewardship principles following the SVTG [9] and WOAH [2] recommendations (see details under the Materials and Methods section). However, identification of etiologic agents and antimicrobial susceptibility testing (AST) prior to antimicrobial prescription were not performed. As a result, veterinarians prescribed antimicrobials for diverse etiologic agents based on clinical signs and symptoms together with disease history, and they were administered without prior confirmatory diagnosis and AST.

Table 3 shows the associations between AMP practices and the etiologic-based diagnosis of livestock diseases in four district veterinary clinics in Ethiopia. Antibiotics were non-prudently prescribed for infections associated with unknown causes (90%), protozoal infections (15%), helminth infections (14%), ectoparasite infestations (7%), fungal infections (70%), and other mixed infections, according to the criteria we established to assess prudent AMP. Antibiotics were also non-prudently prescribed for almost all viral infections (99%) and toxicants (97%).

Table 3 Usage of major classes of drugs by broad etiological category of disease diagnoses at district veterinary clinics in Ethiopia (during 2015–2019) (*N* = 12,438 cases)

Etiologic based diagnosis	Number of cases	Percent of antimicrobial classes /anthelmintics prescribed								Category of AMP prudency (%)	
		Antibiotics		Trypanocides		Anthelmintic		Combination of AMs + AHs		Prudent	Non-prudent
		No	Yes	No	Yes	No	Yes	No	Yes		
Bacterial	2,671	3.4[$]	97	98	2.3[$]	84	16	84	16[*$]	96	4
Protozoal	2,620	86	15[$]	13[*$]	88[*$]	67	33	61	39[*$]	88	12
Unknown	2,228	10	90[$]	99	1.0[*$]	80	20	87	13[$]	93	8
Endoparasite	1,842	86	14[$]	99.6	0.4[$]	6[$]	94	91	9[$]	85	15
Ectoparasite	1,126	93	7[$]	98	1.8[$]	7	93[*$]	96	4.4[$]	92	8
Viral	929	1.4	99[$]	99	1.4[$]	93	7[*$]	93	7[*$]	0	100
Not mentioned	277	7	93	97	2.9	65	35	70	30	6	94
Other (risk of infection)	272	2[*$]	79	88	13[$]	78	22[*$]	87	13[$]	59	42
GI disorder	168	64	36[$]	99	0.6[$]	89	11	90	10[$]	79	21
Toxicants	93	3.2	97[$]	100	0.0	77	23	77	23	3.2	97
Endo-ectoparasites	66	73	27[$]	97	3.0[$]	6[$]	94	77	23[$]	73	27
Nutritional	47	62	38[$]	100	0.0	75	26	96	4[$]	36	64
Protozoal + endoparasite	29	66	35[$]	35	66[*$]	24[*$]	76	35[$]	66	79	21
Fungal	23	30	70[$]	100	0.0	100	0.0	100	0.0	30	70
Bacterial + endoparasite	17	0.0	77	100	0.0	18[$]	82	41[$]	59	77	24
Overall cases	12,438	44	56	80	20	61	40	82	18	81	19

Key: Groups involving multiple diagnoses with less than 10 cases (total N = 23) are not shown

[$] indicates a non-prudent prescription

[*$] indicates the possible use of the drug class depending on the animal situation (requires further assessment and clinician's decision)

The value without superscript indicates prudent prescription

Unknown means for cases recorded as systemic infection

AMs + AHs, prescribed both antimicrobials and anthelmintics together for the same animal; AMP, antimicrobial prescribing. Anthelmintics prescribing practices assigned for ectoparasites in this study are due to the use of ivermectin as both anthelmintics and ectoparasiticides

Similarly, antiprotozoals were prescribed non-prudently to treat diseases caused by bacteria (2.4%), ectoparasites (1.8%), viruses (1.4%), and endoparasites (0.4%), and prophylactic use was practiced for cases at risk of bacterial infection (13%) (Table 3). In this study, a combination of antimicrobials and anthelmintics was also prescribed for parasitic cases (Table 3).

The results of the Chi-square test revealed statistically significant differences in the prudent AMP between district veterinary clinics ($p < 0.001$), with Holeta (32%) having the highest level of non-prudent prescribing, followed by Sekoru (19%), Modjo (16%), and Fiche (12%).

Antimicrobial prescribing (AMP) practices were also evaluated in relation to different livestock species that visited the veterinary clinics. Differences could be observed in AMP practices among diverse animal species (see details in Figure S1A–D, Figure S2A–D, Figure S3A–C, and Figure S4A–C, Additional File 2).

Antimicrobials were widely prescribed to manage cattle diseases (76%). An evaluation of the appropriateness of AMP practices in cattle showed that antibiotics were administered non-prudently to almost all viral infections, with the majority of them receiving oxytetracycline (70%). Antimicrobial combinations, either of two antibiotics or antibiotics with trypanocides, were mostly prescribed for babesiosis (16%), mastitis (13%), colibacillosis (9%), trypanosomiasis (4%), foot and mouth disease (FMD), respiratory diseases and pneumonia (each 3%). Two antibiotics were also non-prudently prescribed for the same case: wound (oxytetracycline with penstrep), colibacillosis (oxytetracycline with sulfonamides), and mastitis (penstrep with penicillin-cloxacillin and oxytetracycline with penicillin-cloxacillin). Antimicrobials were also prescribed non-prudently to treat non-infectious diseases such as closed castration, ectoparasites, and endoparasites. However, prophylactic antibiotic use for retained fetal membranes (RFMs) and wounds (mechanical injury), as well as the use of oxytetracycline instead of penicillin for cases suspected of being caused by gram-positive bacteria, are considered prudent. Detailed information about AMP in cattle at the study clinics is provided in Figure S1A-D, Additional File 2.

Antimicrobials were also extensively and non-prudently prescribed to treat 79% of small ruminant (sheep and goats) cases, primarily for viral and parasitic diseases, poisoning (95%), and non-surgical cases of closed castration (88%). Compared with cattle, small ruminants received a higher proportion (71%) of antibiotics to treat viral infections (100% – orf and PPR, and 99% - pox) and generalized infections (94%). Surprisingly, a high percentage of male sheep (rams) brought to veterinary clinics for castration received antibiotics (81%). However, a low level of antiprotozoal agents was prescribed for small ruminants (8%) (see detailed information in Figure S2A-D, Additional File 2).

Antibiotics are the most widely prescribed drugs to manage chicken diseases (98%), with oxytetracycline (52%) and sulfonamides (44%) being the most frequently prescribed drugs for bacterial, viral, and protozoal infections. Oxytetracycline was used to treat all cases of fowl cholera (100%), Newcastle disease (NCD, 94%), and respiratory diseases (78%), whereas coccidiosis was usually treated with sulfa drugs (50%) and oxytetracycline (29%), as well as their combinations with amprolium. The current study found that non-prudent use of oxytetracycline was recorded to manage all viral infections associated with NCD (100%). Combination antimicrobials were also being prescribed non-prudently to treat coccidiosis and NCD. Details of antimicrobial prescribing practices in poultry are provided in Figure S3A–C, Additional File 2.

The anthelmintics (60%) of ivermectin (53%) were more commonly prescribed in equines than were the antimicrobials (48%). Compared with other species of animals, a high proportion of penstrep was prescribed in equines in our study (36%). African horse sickness (AHS) cases received a high percentage of non-prudent prescriptions (100%), followed by epizootic lymphangitis (EL, 43%), colic (24%), and lungworm (12%) cases. A summary indicating antimicrobial and anthelmintic prescribing practices in equines at the study clinics is provided in Figure S4A–C, Additional File 2.

Influencing factors of antimicrobial prescribing

The results of the multivariable logistic regression model are provided in Table 4. The analysis revealed that animals treated at the study clinics of Holeta and Sekoru had higher odds of being treated with antimicrobials than those treated at Fiche. The analysis also revealed that animals brought to clinics with major clinical signs such as depression and diarrhea; infection with bacteria, viruses, trypanosomes; and cases diagnosed with multiple etiologic agents and respiratory diseases were more likely to be (had higher odds of being) treated with antimicrobials ($p<0.05$). For instance, cases infected with viruses were approximately 221.3 times more likely to demonstrate receiving antimicrobial agents than cases that were not infected ($p<0.001$). AMP, on the other hand, decreased significantly for cases recorded from the Modjo veterinary clinic and female patients, who were presented with symptoms of bloat and loss of body condition and who were treated for endoparasites and ectoparasites ($p<0.05$) (Table 4).

Factors that contribute to non-prudent AMP practices were also assessed. The multivariable analysis result showed that in adult patients in the Modjo study clinic, infections with bacteria, *Trypanosoma* spp., endoparasites, and ectoparasite infestations were found to receive prudent therapy with antimicrobials ($p<0.05$). However, in cases recorded from Holeta and Sekoru, symptoms of depression, infection with viruses and multiple etiologies, and respiratory diseases were negatively associated with prudent AMP practices ($p<0.05$) (Table 4).

The results of discussions that were held with animal health professionals at each study clinic, revealed that limited budgets to purchase medicine in combination with increasing drug prices made some drugs unaffordable, particularly penstrep. In contrast, oxytetracycline is the cheapest and most widely available antibiotic on the local market for veterinary use. In addition, the list of medicines provided by the regional government procurement system was also quite limited. Finally, there was a poor level of awareness among prescribers about the availability of alternative and narrow-spectrum antimicrobials/antibiotics.

At Sekoru, two trypanocides were used concurrently, and the dose was increased twofold (doubling dose) because treating trypanosomiasis with a single drug and at the recommended dose did not improve the prognosis of sick animals. This is a result of continuous and long-term drug use (isometamidium, homidium, and diminazene aceturate) in the area. Clinicians are concerned about the development of resistance caused by causative agents. CAHWs in the area, particularly in the Ghibe valley, were administering trypanocides and using acaricides to control animal trypanosomiasis.

Discussion

Antimicrobial prescribing practices in district veterinary clinics in different agroecological areas of Ethiopia have not been widely studied. To the best of our knowledge, this is the first study to compare the prudency of AMP practices at three separate AEZs with variations in disease incidence and tsetse fly distribution. Our current study analyzed factors that influence AMP in four district veterinary clinics located in different AEZs with limited resources from 2015 to 2019. Assessing AMP practices is essential for developing a surveillance strategy capable of limiting the inappropriate use of antimicrobials. It is also an integral part of good antimicrobial stewardship to maximize therapeutic effects and reduce the risk of AMR.

The case book data of the current study did not provide sufficient detailed information to assess some criteria listed in the recommendations for prudent AMP.

Table 4 Multivariable logistic regression models exploring factors associated with cases being treated with antimicrobials and prudent antimicrobial prescribing practices

Final generalized linear models	Factors associated with cases being treated with antimicrobials				Factors associated with prudent AMP practices			
	Coeff.	OR_{adj}	95% CI	p-value	Coeff.	OR_{adj}	95% CI	p-value
Location of study clinic								
Fiche	Ref.				Ref.			
Holeta	1.45	4.27	3.14–5.79	0.000	-0.94	0.39	0.30–0.50	0.000
Modjo	-0.87	0.42	0.29–0.61	0.000	1.32	3.73	2.66–5.24	0.000
Sekoru	2.80	16.48	10.76–25.23	0.000	-2.15	0.12	0.08–0.16	0.000
Animal characteristics								
Age								
Young	Ref.							
Adult	-0.19	0.83	0.61–1.12	0.230	0.39	1.49	1.19–1.87	0.001
Both	-0.23	0.79	0.13–4.95	0.805	1.52	4.56	0.36–57.51	0.241
Sex					*			
Male	Ref.							
Female	-0.41	0.65	0.54–0.81	0.000				
Both	-0.59	0.56	0.21–1.47	0.235				
Major clinical symptoms recorded								
Bloat (yes)	-1.87	0.15	0.09–0.26	0.000	0.21	1.23	0.78–1.97	0.375
Depression (yes)	0.69	1.98	1.43–2.76	0.000	-0.32	0.73	0.58–0.91	0.005
Diarrhea (yes)	0.96	2.62	1.87–3.68	0.000	*			
Loss of body condition (yes)	-0.38	0.68	0.54–0.86	0.001	0.07	1.08	0.89–1.29	0.440
Etiologic-based major disease diagnosed								
Bacterial (yes)	2.95	19.02	12.53–28.87	0.000	4.25	77.13	48.1-102.3	0.000
Viral (yes)	5.39	221.3	68.24–717.8	0.000	-7.37	0.00	0.0-0.003	0.000
Trypanosoma (yes)	0.84	22.32	1.34–4.03	0.003	4.15	63.14	45.8–87.1	0.000
Endoparasite (yes)	-3.28	0.04	0.03–0.05	0.000	1.65	5.19	4.13–6.51	0.000
Ectoparasite (yes)	-3.77	0.02	0.02–0.03	0.000	2.44	11.47	8.73–15.06	0.000
Multiple disease diagnosis (yes)	3.07	21.44	10.57–43.49	0.000	-2.39	0.09	0.05–0.16	0.000
Respiratory disease (yes)	2.12	8.32	5.45–12.69	0.000	-1.06	0.35	0.24–0.50	0.000

CI, Confidence interval; Coeff., Coefficient; OR_{adj}, adjusted Odds Ratio; Ref., Referent category

* Indicates not considered in the final model (as the univariable logistic regression analysis showed the variables were not significantly associated with prudent AMP practices, $p > 0.05$)

Values with p-value < 0.05 indicate a significant difference from the reference category

Factors that were not significantly associated with either of the two dependent variables were excluded from the table

For example, it was difficult to determine whether a correct diagnosis was made prior to antimicrobial therapy because laboratory diagnoses were uncommon for all cases of bacterial, fungal, protozoal, and viral infections, as well as for most helminth parasite cases. As a result, the diagnosis was established on the basis of the patient's common clinical signs and symptoms. In this study, it was also difficult to determine whether the patient received the correct treatment based on the recorded common clinical symptoms. The duration of therapy was also not recorded in the majority of cases. Consequently, the present AMP practices would be compared with study clinics, patient demographics, etiologic agents of tentatively diagnosed diseases, adopted WHO drug use indicators, and prescriber adherence to selected aspects of prudent use.

The findings of our study revealed that varying proportions of antimicrobials were prescribed at district veterinary clinics located in different AEZs. The odds of animals being treated with antimicrobials at Sekoru and Holeta study clinics were significantly higher than those animals treated at Fiche, indicating that antimicrobials were extensively prescribed at Sekoru and Holeta. The high percentage of encounters receiving antibiotics (56%) without an appropriate diagnosis at the four studied clinics with inadequate laboratory facilities deviates from the WOAH recommendation on the responsible and prudent use of antimicrobials in veterinary medicine [2]. This finding is also inconsistent with those of previous studies from Ethiopia [14] (39%) and Bhutan [22] (31%), but it is comparable to that reported by [13] from Ethiopia (54%). The high proportion of antibiotic prescriptions in these veterinary settings may be attributed to a lack of antibiotic alternatives at district clinics, prescribers' strong belief in the therapeutic efficacy and prophylactic effects of antibiotics, and prescribers' lack of awareness about the risks associated with extensive antibiotic use in the livestock sector. This could also be attributed to variations in the prevalence of livestock diseases owing to diversified climatic conditions that favor the occurrence of pathogens [23].

Our findings indicate that antimicrobials are heavily overprescribed in Ethiopian district veterinary clinics. The percentage of antimicrobials prescribed at the study clinics (79%) was significantly greater than that reported in an earlier study [13] (67%). Similarly, the average proportion of drugs prescribed per encounter in this study (1.23) is not in line with the findings reported from the Rift Valley areas of Ethiopia (1.6) [14], but it is in line with the study reported from Central Ethiopia (1.23) [13]. This discrepancy could be attributed to the absence of diverse classes of veterinary drugs at district veterinary clinics, as observed in this study.

The widespread use of antimicrobials in veterinary care may select for resistant bacteria to grow and spread in human, animal, and environmental reservoirs [24]. The extensive antibiotic prescriptions coupled with incorrect diagnoses observed in the present study could have resulted in a significant amount of antimicrobial contamination of the environment via excretions (urine and feces), as suggested by [25]. As a result, there could be a significant level of antibiotic-resistant bacteria in the study areas, as supported by an earlier study showing the association between AMU on animal farms and the AMR *Escherichia coli* [26]. This is further justified by the findings of a systematic review and meta-analysis conducted in Ethiopia [27], which revealed a high pooled prevalence of bacterial resistance against widely used veterinary antimicrobials in food animals (16–42%). A high level of pooled estimates of bacterial resistance was reported from live animals, with *E. coli* being resistant to tetracycline (79%) and streptomycin (31%) and *Salmonella* spp. being resistant to penicillin (78%), tetracycline (44%), and streptomycin (49%). Similarly, *E. coli* isolated from environmental sample sources demonstrated resistance to ampicillin (97%) and tetracycline (21%), whereas *Salmonella* spp. demonstrated resistance to tetracycline (65%) and sulfamethoxazole-trimethoprim (33%) [27]. The high estimate of AMR prevalence reported in several sample sources in Ethiopia could indicate a possible link between widespread antibiotic use on livestock and resistance, as supported by other studies elsewhere [23, 28, 29].

Our findings also revealed that the proportion of cases receiving oxytetracycline prescriptions has decreased over time, although the drug is inexpensive, widely accessible, and most commonly prescribed for livestock in Ethiopia. This could be due to an increase in prescriber awareness of the emergence of high levels of resistance to oxytetracycline or an increase in the availability of other antibiotics, such as penstrep and sulfa drugs, at district veterinary clinics. A decrease in the number of cases reaching government clinics due to an increase in private veterinary practices or self-treatments by farmers could also contribute to the decrease in the proportion of trends in oxytetracycline prescription. However, the extensive use of oxytetracycline to treat various livestock diseases, particularly in ruminants, in the current study is similar to that reported in food animals in Ethiopia [13, 14] but different from that reported in other countries [30–32]. These disparities could be explained by the fact that oxytetracycline is one of the most affordable antimicrobials in Ethiopia, as evidenced by the group discussion at the study clinics. Similarly, our study revealed high use of penicillin–dihydrostreptomycin fixed combination (penstrep) in equines, which is consistent with reports from the United States [30] and Italy [33]. However, the use of other antibiotic classes, such as other aminoglycosides, macrolides, and fluoroquinolones in food animals and horses in other countries [33, 34], indicates a lack of narrow-spectrum antibiotics in Ethiopian district veterinary clinics.

Consistent access, widespread use, and underdosing of trypanocidal drugs in livestock without guidance may also contribute to the emergence of trypanosome resistance [35, 36]. Our findings indicate that a greater proportion of cases were treated with trypanocidal drugs in Ethiopia's western tsetse belt areas (Sekoru). The current study also revealed that CAHWs practice self-administration of trypanocides to manage animal trypanosomiasis in remote Ghibe Valley areas. This finding is consistent with a recent study [11], which revealed that CAHWs with a limited level of training assist in the provision of animal health services in remote and marginal areas of Ethiopia. Our previous research also confirmed that farmers in the tsetse belt areas of western Ethiopia practice self-administration of antimicrobials on their farms [37]. Moreover, a study reported that poor-quality trypanocidal agents circulate in the current study area [38]. All of these factors could lead to a high level of trypanocidal drug resistance among trypanosome species in the study area, as described previously [39–41].

Previous studies, including a recent meta-analysis, revealed that high resistance was reported in the tsetse belt areas of Ethiopia and other African countries [35, 42, 43]. In order to combat resistance and improve therapeutic efficacy, veterinary clinicians in the current study area are practicing concurrent administration of two trypanocidal drugs and increasing (doubling) drug doses. Although drug resistance to all available major trypanocides is cross-reactive [42], the problem of resistance may be solved by concurrent administration of two drugs, as supported by [36, 44]. Although doubling the dose of diminazene slightly improved the therapeutic efficacy against *T. congolense*-resistant strains [45], a meta-analysis revealed that increasing the dosage and duration of treatment did not improve the prognosis of affected animals with resistant strains [42]. However, switching to non-commonly used trypanocides (e.g., pentamidine) improved patient prognosis [46]. As a result, the high level of trypanocide prescribing practices in the current study area may increase selective drug pressure on trypanosomes, as supported by [47]. This contributes to the development of multidrug cross-resistance to the available trypanocides, justifying the need for the availability of new trypanocides and the implementation of ASPs in the Ethiopian livestock sector. However, the decrease in the proportion of cases receiving trypanocides over time in the current study could be related to changes in the veterinary service delivery system, which could be related to increased private practices by both veterinary professionals and CAHWs [11], or self-treatment by farmers [37], or a decrease in the incidence of protozoal disease over time, resulting in a decrease in the number of cases reaching government clinics. The decrease in protozoal disease incidence over time is consistent with the introduction of new strategies in Ethiopia to control and reduce the burden of animal trypanosomiasis using integrated insect control and trypanocides [48, 49].

The antimicrobials prescribed in this study were categorized as WOAH (OIE) VCIA [50]; the most commonly used classes were tetracyclines, sulfonamides, penicillins, and aminoglycosides (dihydrostreptomycin) in combination with natural penicillin (penstrep). Except for dihydrostreptomycin, all of these drugs are classified as category D, indicating that they are used as primary treatments in animals and should be administered with caution only when they are medically needed [51]. Alternative therapies are available for humans, and this category has a lower risk of AMR [52]. However, antimicrobials such as aminoglycosides, aminopenicillins, and natural penicillins are categorized as CIA by the WHO, and sulfonamides and tetracyclines are HIA for human medicine [52]. Tetracyclines, HIA for human medicine and the most frequently prescribed antimicrobial class in this study, were used at higher proportions than the WHO CIA. Uncontrolled animal use of CIA and HIA for human medicine may pose public health risks because of AMR and antibiotic residues. The non-prudent use of VCIA in animals may also promote AMR in bacteria and have a negative impact on animal health and welfare, as well as human and environmental health.

Antimicrobial stewardship programs employ an accurate diagnosis with appropriate treatment selection approaches to maintain antimicrobial efficacy while minimizing the emergence of AMR [53–55]. As a result, evidence-based prescription, which uses bacterial culture and antimicrobial susceptibility testing (AST), is the primary driver of antimicrobial prescription in developed countries [56–58]. To rationalize the empirical use of antimicrobials in veterinary clinical practice to address the AMR threat, it is recommended to conduct bacterial culture followed by AST of isolates [59, 60]. However, in the current study, there was poor compliance with prescription guidelines, with no respect for the prescription recommended by [2, 61]. Laboratory confirmation of bacterial infections was also uncommon, and AST prior to antimicrobial prescribing was not practiced at all. As a result, veterinarians are prescribing broad-spectrum antimicrobials for diverse etiologic agents on the basis of clinical signs and symptoms and disease history, and administering them without a prior confirmatory diagnosis and AST. However, the use of broad-spectrum antibiotics in this study may be associated with the lack of diagnostic facilities to identify the pathogens, while an unknown bacterial infection is suspected, or with prophylactic use for viral infections to prevent secondary bacterial infections. On top of this, drug prescribing practices using the generic name in our current study (81%) are inconsistent with previous studies conducted in Ethiopia [13, 14]. Moreover, the duration of therapy is a crucial determinant in the selection of antimicrobials to treat infections in livestock. Despite the fact that the majority of prescriptions in this study (Table 2) did not specify the duration of therapy, the long-acting formulation (20%) of oxytetracycline is frequently prescribed in all study clinics. This is because most animal owners opt for a single parenteral injection as opposed to multiple doses administered over the course of three or more consecutive days. *Stat order* reduces the frequency of medication administration and enhances animal owners' adherence to therapy. This could be due to the patient's inability to reach distant veterinary clinics or the animal owner's work overload from other activities. However, further in-depth studies are needed to determine the effects of high-dose *stat order* long-acting oxytetracycline on AMR and animal welfare.

The prudent use guidelines that assist veterinarians in selecting and prescribing antimicrobials to animals helps improve AMP practices [24, 62–64]. In this study, approximately 19% of the prescriptions did not conform to prudent AMU guidelines. The results of the present study's multivariable analysis revealed a significant association between the non-prudent use of antimicrobials in the treatment or control of livestock diseases at the Holeta and Sekoru study clinics. Our findings indicate that the non-prudent use of antimicrobials in livestock is highly linked to variations in endemic disease distribution in study areas where antimicrobials are widely prescribed to treat or control endemic diseases, such as trypanosomiasis, respiratory diseases, and viral infections, as well as multiple disease diagnoses. This could also be related to the lack of diagnostic facilities at the study clinics to identify the causative agents of tentatively diagnosed diseases, whereas an attempt was made to diagnose parasite cases at the Modjo clinic.

When antimicrobial(s) are prescribed for a case, this qualifies as a contributing factor to a high rate of AMP practices. Our current study revealed that the major clinical symptoms of depression and diarrhea recorded at veterinary clinics are strongly associated with cases being treated with antimicrobials, whereas depression is also associated with the non-prudent use of antimicrobials (Table 4). This suggests that a disease diagnosis using major clinical symptoms (syndromes) alone may assist veterinarians in prescribing antimicrobials, but it could also lead to inappropriate antimicrobial selection. This study also revealed that respiratory diseases, as well as infection with viruses and multiple etiologic agents, were strongly associated with non-prudent AMP, with a significant proportion of cases being treated with antimicrobials (Table 4). This is due to the fact that all cases suspected of being caused by a viral infection are not supposed to be treated with antibiotics.

The use of empirical antimicrobial combinations is justified, but it is limited to medical conditions characterized by polymicrobial infections [65]. However, it is unnecessary to use empirical combinations without an appropriate diagnosis [66]. In our study, the records revealed that patients received antimicrobial combinations without a laboratory diagnosis. An empirical combination of two antimicrobials that contradict one another, namely, oxytetracycline (bacteriostatic) and pen-strep (bactericidal), was used. These findings suggest that prescribers have a limited understanding of judicious antimicrobial selection.

The absence of SVTG in most clinics ($n=3$ out of 4) and the absence of EVDL observed in the study clinics during data collection may exacerbate the problems associated with the overuse/misuse of limited classes of antimicrobials. Furthermore, no animals were weighed during physical clinical examinations in any of the study clinics, and antimicrobials were administered on the basis of simple body weight estimates. This could lead to inaccurate dosing, which could result in drug misuse (overuse or underuse) and contribute to the AMR problem [67].

The findings of the present study provide evidence of a large proportion of AMP, combined with bad diagnosis–treatment connectivity, in livestock in resource-poor settings. The non-prudent use of antimicrobials may be a key barrier to national and global efforts to curb AMR. Therefore, the findings of this study emphasize the importance of accurate disease diagnosis and appropriate antimicrobial selection for the proper implementation of antimicrobial stewardship programs in veterinary medicine.

Conclusions

This study provides information about the factors contributing to AMP practices and the non-prudent use of antimicrobials in Ethiopian veterinary clinics with poor diagnostic facilities. The empirical treatment of diseases is commonly practiced with limited classes of broad-spectrum antibiotics and trypanocides. Approximately one-fifth of the prescriptions do not conform to prudent AMU guidelines. AMP and non-prudent use of antimicrobials in veterinary clinics are linked to the study clinics, endemic livestock diseases, and major clinical signs. Diseases caused by viruses and multiple etiologic agents and clinical signs of depression are highly associated with cases being treated with antimicrobials and non-prudent AMP. Infections with bacteria and trypanosomes and clinical signs of diarrhea are also associated with AMP. The non-prudent use of antimicrobials in livestock could also be associated with the absence of appropriate diagnostic tools and guidelines that assist veterinarians in selecting antimicrobials. These findings emphasize the importance of improving prudent AMP practices in livestock to curb AMR. As a result, the study highlighted the need for diverse classes of veterinary antimicrobials, tools for improving prescriber adherence to prudent AMP, and the implementation of ASPs in veterinary medicine in resource-limited countries.

Abbreviations

AHS	African horse sickness
AEZs	Agroecological zones
AMP	Antimicrobial prescribing
AMR	Antimicrobial resistance
AMU	Antimicrobial use
ASP	Antimicrobial stewardship principles
AST	Antimicrobial susceptibility testing
CAHWs	Community animal health workers
CBPP	Contagious bovine pleuropneumonia
CIA	Critically important antimicrobials for human medicine
EVDL	Essential veterinary drug list of Ethiopia
FMD	Foot and mouth disease
HIA	Highly important antimicrobials for human medicine
LSD	Lumpy skin disease
NCD	Newcastle disease
WHO	World Health Organization
WOAH	World Organization for Animal Health
VCIA	Veterinary critically important antimicrobials

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12917-024-04380-6.

Supplementary Material 1: Table S1: Demographic characteristics of the patient and major diseases encountered at the study veterinary clinics (N = 12,438). [a] indicates there were statistically significant differences in disease incidence at the study clinics (p < 0.05) when compared with Fiche whereas [b] denotes not statistically significant (p = 0.05). Not specified* means the case was recorded as either systemic infection or septicemia which might also be caused by infection with bacteria, viruses, fungi, protozoans, or other febrile symptom-causing diseases. Fiche, Holeta, and Modjo are representative of different agroecological zones of central Ethiopia whereas Sekoru is from tsetse belt areas of western Ethiopia. Table S2: Summary of veterinary drugs prescribed in the district veterinary clinics located in different agroecological areas of Ethiopia (2015-2019) (N = 12438 cases). AMs, antimicrobials (i.e., antibacterials or antibiotics and antiprotozoals); AHs, anthelmintics. Trypanocides* include isometamidium chloride, diminazene aceturate, homidium, and non-specified agents. Ectoparasiticides** also include ivermectin. Penstrep, fixed combinations of penicillin G and dihydrostreptomycin. Others$ include atropine sulfate, diclofenac, dexamethasone, calcium borogluconate, furosemide, ichthammol, iodine tincture topical application, ketoconazole, and magnesium hydroxide.

Supplementary Material 2: Figure S1: Antimicrobial and antiparasitic prescribing practices for cattle in government veterinary clinics in Ethiopia between January 2015 and December 2019 (N = 7685 cases). (A) Proportion of overall cases received major class of drugs; (B) Proportion of overall cases received specific antimicrobials and antiparasitic agents; (C) Proportion of major cattle diseases treated with each antimicrobial and anthelmintics as single or in combinations; and (D) Proportion of major cattle diseases received correct treatment using either antimicrobial or/and anthelmintic as single or in combinations. ABZ, albendazole; DA, Diminazene aceturate; D+, disease; FMD, Foot and mouth disease; Gen., Generalized; IVM, ivermectin; ISM, isometamidium; LSD, Lumpy skin disease; Multivit, Multivitamin; OXYTC, oxytetracycline; Pen-Cloxacillin, fixed combination of penicillin-cloxacillin intramammary infusion; RFM, Retained fetal membrane; Trypanocides_NS, the name of trypanocides were not specified. Figure S2: Antimicrobials and antiparasitic agents prescribing practices for small ruminants in government veterinary clinics in Ethiopia between January 2015 and December 2019 (N = 3385 cases). (A) Proportion of overall cases received major class of drugs; (B) Proportion of overall cases received specific antimicrobials and antiparasitic agents; (C) Proportion of major small ruminant diseases treated with each antimicrobial and anthelmintics as single or in combinations; and (D) Proportion of major small ruminant diseases received correct treatment using either antimicrobials or/and anthelmintics as single or in combinations. * Ivermectin was considered as an ectoparasiticides; Antibiotics_NS, the name of antibiotic were not specified; D+, disease; Pen-Cloxa, fixed combination of penicillin-cloxacillin intramammary infusion; PPR, Peste des petites ruminants; Trypanocides_NS, the name of trypanocides were not specified. Figure S3: Antimicrobials prescribing practices for poultry (N = 253) at district government veterinary clinics in Ethiopia between January 2015 and December 2019. (A) Proportion of overall chicken cases received antimicrobials and anthelmintics; (B) Percentage of major chicken diseases treated with each antimicrobial as single or in combination; and (C) Proportion of major chicken diseases received correct treatment using either antimicrobials or/and anthelmintics as single or in combinations. Antibiotics include oxytetracycline (OXYT), sulfonamides (Sulfa), tetracycline and penstrep; AMs+AHs, prescribing both antimicrobials and anthelmintics at a time; D+, diseases; inf. Infection; Newcastle, Newcastle disease. Figure S4: Antimicrobials and anthelmintics prescribing practices for equine at district government veterinary clinics in Ethiopia between January 2015 and December 2019. (A) Proportion of overall equine cases (N = 1115) received antimicrobials and anthelmintics; (B) Proportion of major equine diseases treated with antimicrobials; and (C) Proportion of major equine diseases received correct treatment using either antimicrobials or/and anthelmintics as single or in combinations. Antibiotics_NS, the name of antibiotics were not specified; AHS, African horse sickness; AMs & AH, prescribing both antimicrobials and anthelmintic at a time; DA, Diminazene aceturate; EL, epizootic lymphangitis; inf., infection; GI, gastrointestinal; OXYT, oxytetracycline; UL, ulcerative lymphangitis.

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Author contributions
T.B.T. Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. F.R. Funding acquisition, Methodology, Project administration, Resources, Writing – review & editing. N.F. Investigation. C.R. and T.J.B. Conceptualization, Writing – review & editing. K.A., H.H., and J.A.S. Conceptualization, Formal Analysis, Methodology, Supervision, Writing – review & editing. All authors approved the final manuscript.

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Data availability
The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
This study was performed in line with the principles of the Declaration of Helsinki [68]. The institutions (district livestock health bureau) authorized us to access patient data from the clinics. Prescribers' confidentiality was protected by using a unique code. The study received ethical approval from the Addis Ababa University College of Veterinary Medicine and Agriculture Institutional Board of Research Ethics Committee (Ref. No: VM/ERC/01/06/10/2018) and data were collected after getting permission from the district veterinary clinics. Written informed consent was also obtained by signing a form by professionals who participated in group discussions.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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