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National consumption of antimicrobials intended for use in animal livestock health: a retrospective data analysis of antimicrobial imports to Uganda from 2018 to 2020

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Abstract

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Background Antimicrobial use in animals is one of the major drivers for the emergence and spread of resistant microorganisms. Antimicrobial resistance (AMR) can spread from animals to humans and vice versa. However, there is scanty data on antimicrobial consumption in livestock in low and middle income countries especially Uganda. Monitoring antimicrobial consumption and use (AMCU) in the veterinary sector is important to identify areas of overuse and misuse and to design targeted interventions to reduce the need for unintentional exposure. This study aimed to quantify and characterize by pharmacological class the antimicrobials intended for use in animals in different livestock production systems imported annually in Uganda.

Methods We extracted data from the Uganda National Drug Authority (NDA) database on antimicrobials imported intended for veterinary use from 2018 to 2020. We analysed the guantities of the active pharmaceutical ingredient using the World Organization for Animal Health (WOAH) methodology and reported the consumption in kilograms and tonnes.

Results For our study period from 2018 to 2020; 210,419 kg, 150,032 kg and 142,069 kg of antimicrobials for animal use were imported into the country respectively with annual average importation of 167,507 kg (167.6 tons). Antibacterials accounted for 82% and antiprotozoals accounted for 18% of the total quantities over the three years. Oxytetracycline was the top most consumed antibacterial. The top five pharmacological classes were tetracyclines (22.5 tons, 44.8%), aminogylcosides + penicillin combination (15.3 tons, 29.7%), sulfonamides and trimethoprim (6.14 tons, 12.4%), macrolides (1.88 tons, 3.9%) and fluoroquinolones (1.676 tons, 3.5%). 97% (97%) of the antibacterials were from the WHO Veterinary Critically Important Antimicrobials, 57.1% were from the WHO Highly Important Antimicrobials group, 32.1% were from the Critically Important Antimicrobials group and 10.7% were from the

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Highest Priority group. The European Medicines Agency AMEG analysis revealed that 57.1% were from the lowest risk (D) category, 36.5% were from the intermediate risk (C) category and 6.5% were from the restricted use (B) category.

Conclusion This study provides baseline data on the national-level consumption of antimicrobials used in animal health in different livestock production systems in Uganda for future reference. Annual quantification and analysis of veterinary AMCU should continue to inform monitoring distribution and use in relationship to livestock population numbers and the burden of diseases. Antimicrobial stewardship and pharmacovigilance activities in the animal health sector should focus on raising awareness to adhering to national and international guidance for appropriate and prudent use of antimicrobial agents.

Keywords Antimicrobial resistance, Veterinary, Antimicrobial consumption, Antimicrobials, Livestock, One health, Surveillance, Uganda

Introduction

Antimicrobial resistance (AMR) is a serious and a growing threat to public health and sustainable development issue faced by mankind [1]. Recent comprehensive estimates of the global impact of AMR revealed an estimated 1.91 million deaths attributable to AMR and further forecasted 8.22 million deaths associated with AMR by 2050 [2] compared to previous estimates in 2019 of 4.95 million deaths associated with bacterial AMR [3]. The burden of AMR is more noticeable and high in low and middle income countries (LMICs) plunged with poverty and poor health care facilities estimated at 337,000 AMR associated deaths annually [4]. The escalating impact of AMR to public health has been attributed to global rise in overuse and misuse of antibiotics in both humans and livestock production [5]. The global consumption of antimicrobials in food-producing animals based on 2020-2030 data from 42 countries was estimated to be 99,502 tonnes in 2020 projected to increase by 8.0% to 107,472 tonnes by 2030 [6]. On the other hand, World Organisation for Animal Health (WOAH) recently published antimicrobial agents use in animals based on data analysed from 94 member states out of 152 normalised by estimated animal biomass to be 81,084 tonnes and adjusted to total amount of 88,827 tonnes [7]. This analysis reveals high levels of antimicrobial consumption in food producing animals that may require attention to country levels. According to WOAH 8th report, almost half of the antimicrobial agents were tetracyclines that remain the most used antimicrobial agent in animal health across the globe (35.6%) followed by penicillin (12.56%) [8]. The over usage of antibiotics in livestock production is believed to be driven by ever increasing demand of animal source proteins which in turn drives usage of antibiotics as growth promoters and for prophylactics to increase production [9–11].

Despite these estimates, the exact magnitude of the AMR problem worldwide and its overall impact on animal and human health especially in LMICs, on costs for the relevant sectors and in wider society remain largely based on estimates due to limited and incomplete data [2]. Hence monitoring of antimicrobial usage in different livestock systems especially in LMICs like Uganda is critical for both animal health as well as food safety for human consumption. The small percentages on antimicrobial consumption being reported in Africa is mainly due to lack of consistent reporting annually and hence difficult to make appropriate estimates. Whereas, World organisation for Animal Health has reported improvement in reporting antimicrobial agents data citing Europe and Africa, several gaps still exist.

Therefore, it is important to examine and understand the magnitude of exposure to antimicrobials through periodic surveillance of their consumption and use. Unlike the global North, where comprehensive systems for monitoring antimicrobial use and its relationship with antimicrobial resistance (AMR) exist, similar systems are lacking in low- and middle-income countries (LMICs). However, antimicrobial consumption and use (AMC&U) surveillance is crucial for identifying problems and undertaking corrective action to optimize antimicrobial use, such as stewardship interventions and policy changes.

Methods and materials

Study design

We conducted a retrospective analysis study in which we analysed quantities of antimicrobials intended for use in animals imported into Uganda from 2018 to 2020. Data on antimicrobial agents were abstracted from Microsoft Excel spreadsheets accessed from the National Drug Authority (NDA) electronic management information system (NDAMIS).

Study setting

Uganda is a low-income country with a gross domestic product per capita of USD 940 [7]. The Uganda population has been growing since 1969 from 9.5 million to the current population of 45.9 million as per 2021 preliminary housing population census report [12]. The current population presents an addition of 11.3 million people with annual growth rate of 2.8% per annum since the last census in 2014 [12]. In 2018, the Uganda annual agricultural survey revealed that 80% of households were involved in agriculture, including crop growing and livestock farming, for both subsistence and commercial purposes [13]. At least 6.8 out of 10.8 million households in Uganda keep at least one livestock type. As per National Livestock Census of 2021, Uganda has a total of 14.5 million cattle (26.9% increase), 17.4% million goats (39.4% increase), 7.1 million pigs (122.5% increase), 4.4 million sheep (27.8% increase) and 57.8 million chickens (54.5% increase) with corresponding percentage increase from previous census of 2008 [14]. In monetary value, these animals are estimated to be equivalent to 8.02 trillion UGX (USD 2.2 billion) for cattle, 2.5 trillion UGX (USD 674 million) for chicken and 4.6 trillion UGX (USD 1.24 billion) for small ruminants and pigs as of 2018 Agriculture Survey report [13]. Agriculture contributes significantly (24.6%) to Uganda's GDP per capita (USD 607 per year), a sector that provides 71% employment with livestock sector contributing about 17% of the agriculture. Livestock alone contributes 4.3% to GDP [13]. In the financial year 2023/2024, agriculture sector contributed 24.7% to GDP registering the annual growth of 54.% [15]. The livestock sector is thus important to the livelihood of the Ugandan population for reasons including household income generation, gainful employment, cultural practices, societal expectations, food safety and food security [11, 16, 17].

Study procedure, variables and data sources

We obtained a database in MS Excel with 68,875 rows (number of products), each with 28 columns (variables or metadata about each product) extracted from NDA-MIS electronic resource planning systems from the NDA. The metadata of each product included the date of application for an import permit, unique application number, product trade name, generic name, registration number, manufacturer, country of origin, importing entity, strength or concentration, dosage form, pack size, quantity imported, unit cost and total cost. The process of separating antimicrobials intended for use in animal health from other products, data cleaning, and verification against product details from the NDA records of products granted marketing authorization in Uganda led to a final dataset with 2551 rows (Supplementary excel data sheets 1). Three research team members extracted the clean dataset into another data calculation tool that included additional variables required to analyse the data into aggregate quantities by kilograms and WHO and OIE Critically Important Antimicrobial classes. Completeness was checked by cross-checking the raw data with the marketing authorization number against the data provided. The data extraction and cleaning processes of the antimicrobial import data extracted from NDA records is summarised in a flow chart (Supplementary Fig. 1).

Calculation of the quantity of active ingredient

The authors identified each unique antimicrobial medicine product intended for animal use present in the database, organized the data accordingly and calculated the total quantity for each antimicrobial medicine product intended for animal use using the unit of measure that was stated in the NDA database. First, antimicrobial veterinary products were grouped by pack size. Then, the number of unit packs imported was multiplied by the pack size to obtain the total quantity of each antimicrobial veterinary product imported into the country per year. To determine the total quantity of active ingredients, the strength per unit dosage form was multiplied by the total number of units. The quantity of the antimicrobial agent (active ingredient) per pack was calculated. For combination antimicrobial veterinary products, quantities were determined for each active ingredient independently. The total sum of units for each antimicrobial veterinary medicine product within a month was multiplied by the pack size factor to obtain the total quantity in grams, milligrams, and millilitres. All strengths, including w/w, w/v, IU, and millilitres, were converted to milligrams and grams and then to kilograms and tonnes using conversion factors provided by OIE guidance [18]. New variables of the Anatomical Therapeutic Chemical Veterinary (ATCVet) code, total annual antimicrobial product imported, pharmacological class, European Medicines Agency's Antimicrobial Advice Adhoc Expert Group (EMA AMEG) classification [18], World Health Organization (WHO) Critically Important Antimicrobials (CIA) category [19], and World Organization of Animal Health (OIE) CIA category [20] were derived in the final dataset used for analysis.

Data analysis

The clean dataset was uploaded into IBM SPSS Statistics Software, version 23, for analysis. Summary statistics of total quantities of all antimicrobials per year, per pharmacological class and by the WHO CIA, OIE VIA and EMA AMEG classifications were run.

Results

A total of 42 antimicrobial products for veterinary use were imported into Uganda in 2018, 2019 and 2020, of which 32 were antibacterials and 10 antiprotozoals. Antibacterials made up the bulk (82%) of veterinary antimicrobials imported into Uganda, at an average of 167,507 kg (167.6 tons) per year. Antiprotozoals accounted for 18% of the total antimicrobials over the three years, with an average of 36,872 kg (38.9 tonnes) per year of active pharmaceutical ingredients per year. Over the three years, there was a steady decline in the total quantity of antibacterial agents imported into Uganda from an estimated 210,419 kg to 150,032 kg and 142,069 kg in 2018, 2019 and 2020, respectively. Table 1 gives a summary of the total quantities per class of antimicrobial agents imported during the study years.

Total quantities and proportions of different antimicrobial classes for use in livestock production systems classes imported into Uganda from 2018 to 2020

Oxytetracycline was the top-most consumed antibacterial agent, accounting for 43%, 45% and 40% of all antibacterial imports in 2018, 2019 and 2020, respectively, and averaging 71,519 kg per year. Diminazene was the most consumed antiprotozoal in all three years, averaging 29,190.95 per year. Table 2 summarizes the total annual quantities of antibacterial imports in kilograms, and Table 3 summarizes the antiprotozoal imports from 2018 to 2020.

Pharmacological class analysis of antibacterial import imports intended for use in animal health in Uganda from 2018 to 2020

Analysis by pharmacological class showed that tetracyclines were the top-most imported group, making up 93551.2 kg, 72765.8 kg and 58,604 kg (44.5%, 48.5% and 41.3%) of antibacterials from 2018 to 2020, respectively

Table 1	Summary of antimicrobial product imports intended for
use in ar	imal health in Uganda from 2018 to 2020

Characteristic	Quantity of Active Pharmaceutical Ingredi- ents Per Year				
	2018	2019	2020		
Total annual AMC quantity in Kgs	249,601.94 kg	177,676.95 kg	185,858.68 kg		
Total annual antibacte- rial consumption in Kgs	210,418.58 kg	150,032.48 kg	142,069 kg		
Total annual antipro- tozoal consumption in Kgs	39,183.35 kg	27644.47 kg	43789.56 kg		
Number of antimicro- bial products	41	38	37		
Number of antibacte- rial products	33	29	28		
Number of antiproto- zoal products	8	9	9		
Number of products with single antimicro- bial active ingredient	18	19	19		
Number of products with two antimicrobial active ingredients	22	17	16		
Number of products with three or more antimicrobial active ingredient	2	2	2		

as shown in Fig. 1. On average, this was followed by the aminoglycosides + penicillin combination (29.7%), sulfonamides and trimethoprim (12.4%), macrolides (3.9%) and fluoroquinolones (3.5%). Together, these five groups made up 98% of all antibacterials imported. Notably, there was a modest increase in the number of fluoroquinolones imported from 2%, 4.3% and 4.3% in 2018 to

Analysis by AMEG class: veterinary antibacterials imported in Uganda from 2018 to 2019

2020, respectively.

The European Medicines Agency AMEG categories consider the risk to public health from antimicrobial resistance (AMR) due to the use of antimicrobials in veterinary medicine. The majority of antibacterials were from Category D (lowest risk categories), with an average of 57.1%, followed by Category C (Caution, Intermediate risk), with an average of 36.5%, and Category B (Restricted use), with an average of 6.3% as per details in Table 4. Over the three years in our study, there were no antibiotics imported in category A (avoid). The proportions varied only slightly across the 3 years.

Analysis by OIE important veterinary antimicrobials: veterinary antibacterials imported in Uganda from 2018 to 2020

Only two categories from the OIE Antimicrobial Agents of Veterinary Importance list (May 2015) were imported from 2018 to 2020. These included the Veterinary Critically Important Antimicrobials (VCIA) (99.4, 96.4, 96.6%) and the Very Highly Important Antimicrobials (VHIA) 0.6%, 3.6% and 3.4%, respectively, for 2018 to 2020.

Analysis by world health organization critically important antimicrobials categories: veterinary antibacterials imported in Uganda from 2018 to 2020

The WHO list of critically important antimicrobials (2018) showed that the majority of imported veterinary antimicrobials belong to the Highly Important Antimicrobials group (average 57.1%), followed by the Critically Important Antimicrobials group (average 32.1%) and the Highest Priority Critically Important group (average 10.7%). Only a marginal proportion (0.1%) was from the Important Antimicrobials group. The distribution across the years is shown in Fig. 2 below.

Discussion

In this study, we report national-level aggregate values of annual quantities of antimicrobial imports intended for use in animal health in Uganda for three years from 2018 to 2020. The study was based on the retrospective analysis of import data from the National Drug Authority (NDA. We found antibacterials to constitute the majority

Table 2	Total annual quantity of antibacterial imports intended for	r use in animal h	ealth in kg from	2018 to 2020 in Uganda

No.	Antibacterial agent	ATC5	Quantity of Active Pharmaceutical Ingredients in kg Per Yea				n kg Per Yea	ar
			2018		2019		2020	
			kg	Propor- tion (%)	kg	Propor- tion (%)	kg	Pro- por- tion (%)
1	Oxytetracycline	QJ01AA06	89958.1	42.8	67230.2	44.8	57369.4	40.4
2	Penicillin G + Dihydrostreptomycin	QJ51RC22	54589.4	25.9	23501.1	15.7	22453.2	15.8
3	Penicillin G Procaine + Dihydrostreptomycin	QJ51CE59	16446.4	7.8	5823.2	3.9	20001.5	14.1
4	Sulfadimidine + Diaveridine	NA	11724.1	5.6	61.6	*	73.5	0.1
5	Sulfadimidine	QJ01EQ03	7228.0	3.4	7229.4	4.8	16205.0	11.4
5	Tylosin	QJ01FA90	5352.8	2.5	7313.4	4.9	4771.4	3.4
7	Sulfadiazine + Trimethoprim	QJ01EW10	4610.9	2.2	3785.6	2.5	2964.0	2.1
3	Neomycin + Procaine Penicillin G	QJ51RC23	4530.3	2.2	5501.8	3.7	-	-
9	Enrofloxacin	QJ01MA90	4116.5	2.0	6330.5	4.2	6042.8	4.3
10	Neomycin + Sulfaguanidine + Sulfadimi- dine + Sulfathiazole	NA	3999.6	1.9	3299.7	2.2	1237.4	0.9
11	Tetracycline	QJ01AA07	1505.0	0.7	3732.8	2.5	1050.0	0.7
12	Doxycycline	QJ01AA02	1356.3	0.6	1600.0	1.1	1.3	
13	Ampicillin + Colistin	QG51AG07	1007.5	0.5	5037.5	3.4	4554.9	3.2
4	Doxycycline + Tylosin		794.9	0.4	916.8	0.6	-	-
15	Erythromycin + Oxytetracycline + Streptomy- cin + Colistin	NA	713.3	0.3	1256.8	0.8	-	-
16	Doxycycline+Tetracycline	QJ01RA90	600.0	0.3	-	-	-	-
17	Erythromycin	QJ01FA01	472.2	0.2	770.6	0.5	125.3	0.1
8	Sulfamethoxazole+Trimethoprim	QJ01EW11	280.8	0.1	3129.5	2.1	3501.7	2.5
19	Sulfamonomethoxine + Trimethoprim	QJ01EW17	230.4	0.1	148.2	0.1	115.2	0.1
20	Gentamicin	QJ01GB03	181.9	0.1	366.5	0.2	217.9	0.2
22	Flumequine	QJ01MB07	120.0	0.1	50.0	*	-	-
23	Colistin	QA07AA10	104.9	*	57.5	*	-	-
24	Cefalexin + Kanamycin	QJ51RD01	86.0	*	32.5	*	32.6	*
25	Amoxicillin + Gentamicin	NA	76.0	*	-	-	-	-
26	Oxytetracycline + Colistin	QJ01AA56	55.0	*	44.0	*	40.1	*
27	Doxycycline + Neomycin	QA07AA51	52.0	*	301.4	0.2	24.0	*
29	Amoxicillin	QJ01CA04	39.4	*	0.8	*	114.0	0.1
30	Cloxacillin Benzathine	QJ01CF02	22.2	*	-	-	-	-
31	Ampicillin + Cloxacillin	QJ51RC20	13.8	*	-	-	-	-
32	Doxycycline + Sodium Sulfacetamide	NA	12.0	*	22.5	*	12.0	*
33	Colistin + Doxycycline	QA07AA98	4.3	*	-	-	-	-
34	Oxytetracycline + Neomycin	QJ01AA56	3.0	*	1541.2	1.0	462.6	0.3
35	Tylosin + Gentamicin	NA	-	-	429.7	0.3	210.3	0.1
36	Tiamulin	QJ01XQ01	-	-	214.0	0.1	200.0	0.1
37	Sulfaclozine	QP51AG04	-	-	98.0	0.1	3.9	*
38	Tilmicosin	QJ01FA91	-	-	3.0	*	-	-
39	Flumequine	QJ01MB07	-	-	-	-	100.0	0.1
	Total			100		100		100

ATC- Anatomical Therapeutic Chemical Classification Code

* Proportion antibacterial of < 0.1 of total annual antibacterial consumption

- Antibacterial agent not among those imported that year

NA- Antibacterial agent not assigned an ATC5 code in the 2021 index

(82%) of the antimicrobial imports, averaging 167,507 kg (167.6 tons) per year, and antiprotozoals made up the balance of 18%. Our results align with previous studies that reveal wide use of antibiotics in livestock for disease

treatment and growth promotion. For example, study by Mikecz et al., on antimicrobial use data in livestock in Uganda in 2020, revealed considerable use of antibiotics among livestock farmers not only for curative treatment

Table 3 Total annual quantity of	f antiprotozoal imports intended for use in animal	health in kg from 2018 to 2020 in	Uganda

Quantity of Active Pharmaceutical Ingredients in kg Per Year								
No.	Medicine Name	ATC5 Code	2018	%	2019	%	2020	%
1	Diminazene	QP51AX07	27,740.61	70.8	19,063.70	69.0	40768.55	93.1
2	Diminazene + Phenazone	QP51AX07	9,804.94	25.0	6,662.31	24.1	1193.55	2.7
3	Buparvaquone	QP51AX22	532.24	1.4	688.74	2.5	707.05	1.6
4	Parvaquone	QP51AX22	481.18	1.2	388.56	1.4	239.38	0.5
5	Isometamidium	QP51AX19	277.29	0.7	440.81	1.6	294	0.7
6	Amprolium + Sulfaquinoxaline	QJ01EQ16	119.22	0.3	91.53	0.3	278.01	0.6
7	Toltrazuril	QP51AJ01	83.8	0.2	203.83	0.7	150.25	0.3
8	Imidocarb	QP51AE01	144.07	0.4	80.98	0.3	155.77	0.4
9	Salinomycin	QP51AE01			24.00	0.1	3	0.0
		TOTAL	39,183.35	100	27,644.46	100	43,789.56	100

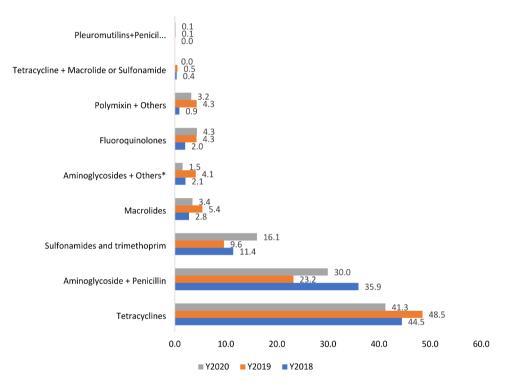


Fig. 1 Proportion (%) per pharmacological class of total consumption of veterinary antimicrobial imports from 2019 to 2020 in Uganda

	2018		2019		2020	
AMEG CLASS	Qty (kg)	%	Qty (kg)	%	Qty (kg)	%
B (Restrict)	6,121.49	2.9	12,776.22	8.5	10,737.87	7.6
C (Intermediate risk)	86,584.46	41.1	50,014.86	33.3	49,850.07	35.1
D (lowest risk)	117,712.62	55.9	87,241.40	58.1	81,481.18	57.4
Total	210418.58	100	150,032.48	100	142,069.12	100

(35%) but also for disease prevention and growth promotion [21]. In Africa and in particular Uganda, keeping livestock is important for production of animal source food contributing to households income as well as general economy, source of livelihood, employment and several social and cultural purposes [22]. Together with high burden of livestock diseases and increasing demand for animal source proteins, and trying to keep livestock healthy for increased production drives use of antibiotics. Globally, antibiotic use in livestock is still on the rise despite of the well-known consequences of antimicrobial resistance [6, 23, 24].Whereas we observed a decreasing trend in quantities imported from 2018 to 2020, this is probably due to mobility restrictions and unanticipated disruptions as a result of the COVID-19 pandemic [25]. Further analysis focused on the antibacterials, as

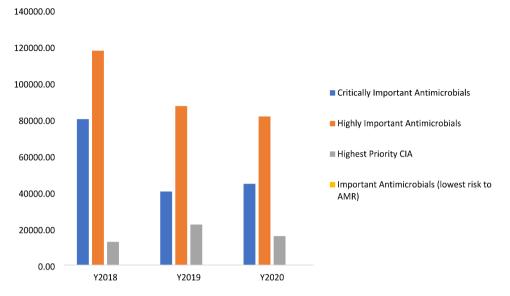


Fig. 2 Quantity (kg) of imported veterinary antibacterials in Uganda from 2018 to 2020 classified by the WHO as critically important antimicrobials for human use

antimicrobial resistance and its dire consequences seem to disproportionately affect the antibacterials, especially when considering the crossover of resistant pathogens from animals to humans and vice versa. Of the antibacterials, oxytetracycline made up over 40% of imports each year, followed by penicillin G+dihydrostreptomycin, penicillin G procaine + dihydrostreptomycin, sulfadimidine + diaveridine, sulfadimidine and tylosin. Consequently, the pharmacological analysis revealed the top five classes including tetracyclines, aminogylcosides + penicillin combinations, sulfonamides and trimethoprim, macrolides and fluoroquinolones as most imported antibiotics for use in animals. There are only two categories in the OIE Antimicrobial Agents of Veterinary Importance List: 97% in the Veterinary Critically Important Antimicrobials (VCIA) and 3% in the Veterinary Highly Important Antimicrobials (VHIA). Considering the WHO list of critically important antimicrobials for human use, just over half (57%) were in the highly important group, followed by nearly one-third (32%) in the critically important antimicrobial group. The EMA classifies antimicrobials based on their risk of transmitting resistance to the human sector following use in the veterinary and animal sectors. Our study revealed that there were no Category A (Avoid) drugs, the majority were lowest risk (Category D), approximately one-third were intermediate risk (Category C) and a small proportion (6%) were restricted use class (Category) B. The findings of this study clearly agrees with most recent reports of antimicrobial consumption in food producing animals that reported tetracyclines and penicillin's as the most used antibiotics as well as classifications of antimicrobial agents intended for use in animals by WHO, WOAH (VCIA, VHIA), EMA [6, 7, 23].

To the best of our knowledge, our study is the first to conduct a systematic quantification of total annual antimicrobial imports intended for use in animal health in Uganda and their analysis by antibacterial agent, pharmacological class, EMA AMEG categorization, OIE CIA categorization and WHO CIA classification. Aggregate data of antimicrobial quantities in a geographical location or defined population is considered to be a fairly good proxy of the consumption patterns or use by that population as per recent WOAH reports of antimicrobial consumption [8]. Our data therefore represent nationwide consumption of antimicrobial in animals over the three year study period.

Our study reports an average of 167,507 kg (167.6 tonnes) of antimicrobials imported per year intended for use in animals especially food producing animals. By comparison, a recent study on antimicrobial consumption in food producing animals based on import data between 2019 and 2021in Rwanda, reported total importation of 32,297.4 kg with annual mean of 11,763.8 kg [26]. The reported consumption trends based on import data in Rwanda in much lower compared to Uganda mainly because the livestock population in Rwanda is much smaller compared to Uganda as reflected by the data on the adjusted antibiotics per animal biomass of 20.1 mg/kg, 24.3 mg/kg and 30.3 mg/kg for 2019, 2020 and 2021 respectively [26]. However, the data from Tanzania for the reported period from 2010 to 2017 shows a higher consumption level compared to Uganda that reported 12,147,491.5 kg with mean annual consumption of 1,518,436.4 kg [27]. This could be attributed to the size of the animal population and differences in the ways import data is captured. On the other hand, Kenya reported the mean antimicrobial consumption

of 14,594+/-1457 kg per year based on five year data between 1995 and 1999 which is lower than that of Uganda [28]. The data available for Kenya is not recent and may not reflect a true scenario of the current importations of antimicrobials. Whereas we note variations in the data available on the estimated antimicrobials consumptions in food producing animals based on import data, the data remains valuable and a proxy for estimation of antimicrobial consumptions. In our estimate calculations based on import data, we could not assign consumption use per species and hence our data was not normalised by the use of an estimated animal biomass indicator that vary in size and composition overtime. However, Uganda is among the 44 WAOH African member states that participated in 152 out of 182 (84%) member states in 2021 that submitted antimicrobial data (sales and import data) to ANIMUSE system established by WOAH. Based on that data, WOAH, estimated total amount of antimicrobial agents intended for use in animals to be 81,084 tonnes adjusted to be as high as 88,927 tonnes annually [8]. WOAH further estimated antimicrobial agents used per kilogram of animal biomass based on data from 96 member states to be 122 to116 milligrams (normalised to be 109.7 mg/kg) representing 65% of the global animal biomass [8]. The report reveals a decrease in animal biomass in America (-9%), Europe (-6%), Asia and Pacific (-0.7) and a dramatic increase in Africa (+197%) [8]. It was emphasised however, that the remarkable increase in Africa does not affect animal biomass indicator as it only represents 10% of the biomass and only 2% of the antimicrobial data analysed among 81 member states in 2021. The percentage representation from Uganda is even smaller to the total biomass and antimicrobial usage probably due to incomplete and inconsistences in data collection and submission. The antimicrobial import data is captured at customs based on approved import permits and customer invoices through the National Drug Authority (NDA) integrated Regulatory Information Management System (NDA iRIMS) that was established in 2018 and still undergoing improvements- NDA Portal. Based on the data available from NDA iRIMS, the majority of the veterinary medical products in Uganda are imported from Kenya, China, and Europe by licensed entities, then distributed to wholesalers, retailers (drug shops and pharmacies) and finally to the end-users, who include both domestic farmers and commercial livestock farmers. Currently, the distribution data by whole sellers and sales by retailers are not being collected and hence not available in the NDA iRIMS presenting challenges for estimating antimicrobial consumption at species and region level. As per the 2021 record from the NDA veterinary updates bulletin, Uganda has 421 registered veterinary medicines as well as 1,141 veterinary drug shops and 84 pharmacies distributed across all regions, with the majority being in the southwestern, western and central regions that are supervised [29, 30]. In addition Ministry of Agriculture, Animal Industry and Fisheries (MAAIF) published in 2020 Uganda's Essential Veterinary Medicines List(EVML) [31]. The successes of NDA in establishing the iRIMS supported by strong regulatory and pharmacovigilance system [32, 33] is likely to drive enforcement of reporting antimicrobial sales among whole sellers and retailers in nearby future. A system for capturing and reporting antimicrobial sales data needs to be adopted and aligned with established guidelines by WOAH, a limitation of our dataset collected between 2019 and 2021. The existing gaps in Uganda for capturing and reporting antimicrobial data shares similar situation with other African countries leading to limited published literature to allow comparison between locations with a similar economic and agricultural profiles. Previous studies in Rwanda, Tanzania, and Kenya have all reported different quantities mainly in kgs for annual antimicrobial consumption data based on import data capturing different reporting periods [26-28] some lower and others higher compared to our current report for Uganda. This calls for harmonisation of data capture systems to allow uniform reporting as recommended by World Organisation for Animal Health [34].

The majority of the antimicrobial agents reported in our study were from the WOAH critically important antimicrobials for veterinary use. Oxytetracycline as an active pharmaceutical ingredient and tetracyclines as a group made up over 45% of total imports per annum. Our data agrees with previous reports in Rwanda, Tanzania and Kenya that all reported tetracyclines as most highly imported antibacterial agent [26-28]. This is further similar to other reports from elsewhere by Timor, where tetracyclines (35.5%), penicillins (23.7%), and macrolides (15.9%) [24], and Cameroon, where tetracyclines (31.71%), sulfonamides (23.84%), quinolones (11.11%) and β -lactams (10.17%) were the most commonly imported classes of antimicrobials [34]. In contrast, the 2020 ESVAC report collected data from 31 European countries, where penicillins were the most commonly used group at 31.1%, followed by tetracyclines at 26.7%. The percentages for sulfonamides and trimethoprim were similar, at 11.4% IN ESVAC and 12.3% in Uganda [35]. The differences could be explained by the variations in treatment protocols or accessibility for the different regions, driven by the commercial market importers and distributors of the drugs.

One of the major concerns of AMR is the cross-linkages and spread of resistance between humans, animals and the environment [36]. A recent report by the ECDC, EMA and EFSA demonstrated significant linkages between the emergence of antimicrobial-resistant organisms and their use in humans and animals [26]. In comparison, consumption reports in humans show high usage of the antibiotics to which high resistance is reported and conversely low usage in those to which organisms exhibit low resistance, indicating a direct relationship between use and observed AMR patterns [37].

A third of the AMC in our study was from the WHO CIA, and 10.7% was from the highest priority CIA group, which includes classes such as the 3rd, 4th, and 5th generation cephalosporins, glycopeptides, macrolides and ketolides, polymixins and quinolones. In our study, the most common macrolide used was tylosin, and enrofloxacin was the most common fluoroquinolone. This indicates the need for stewardship programs targeting these classes need to be instituted at the user-end level. Much as polymyxins were not highly used, the fact that they appear, especially in fixed-dose combinations with other antibiotics, they are on the WHO Reserve list of AWaRe classifications, and many countries in the developed world are moving away from using them in food-producing animals [38, 39]. Regulatory measures to ensure that further marketing authorizations to products containing polymixins and cephalosporins intended for veterinary medical and growth promotion purposes need to be instituted. This will ensure that polymyxin is reserved as a last-resort antibiotic when there is resistance to other first- and second-line agents.

The EMA AMEG classification seeks to further guide rationalizing the appropriate use of antimicrobials in animals to prevent AMR that could reduce the availability of alternatives for use in human medicines in the face of resistant infections. Approximately 97% of the products were from the class D (low risk) and C (intermediate risk) categories [35, 40]. Positively, only a small proportion was from the restricted use (B) category, and none were from the A category, which contains antibiotics that should not be used at all in animals, such as carbapenems, 3rd -5th generation cephalosporins and antipseudomonal penicillins. This status should be maintained by instituting managerial, regulatory and educational activities at both national and subnational levels.

There were some limitations for our study that could have influenced the results. The use of import data at the national level was based on the assumption that the data entered are accurate and complete and that all drugs that come into the country by the different routes are captured. Any locally manufactured animal products were also not included in this study. Analysis by standardized animal biomass metrics, such as mg per population correction unit (mg/PCU) and mg/kg of final flock weight, could not be performed, as the data on animal populations to assess actual exposure in Uganda were not available at the time. Our aggregate data could also not differentiate the species in which the antimicrobials were used or determine which proportions were used for growth promotion and medical purposes. These gaps can be explored in further studies on AMC and AMU in Uganda.

We have identified priorities for targeted antimicrobial stewardship programmes in veterinary medical practice and farming for food-producing animals, aimed at reducing the use of macrolides, fluoroquinolones and polymixins. In addition, we identified actions that different stakeholders in the AMR fight could take, such as restricting market authorizations for HP CIA and AMEG A and B classes. Furthermore, cognizant that the AMC surveillance systems in Uganda are still in their early stages, our work provides baseline results onto which further work on AMC in animal health can be built and complements the efforts of similar activities ongoing in the human sector.

Conclusions

This comprehensive analysis of annual antimicrobial imports for animal health in Uganda between 2018 and 2020 showed antibacterials constituted 82% of imports, averaging 167,507 kg annually. Oxytetracycline was the top most consumed antibacterial and top five pharmacological classes captured were tetracyclines, aminogylcosides + penicillin combination, sulfonamides and trimethoprim, macrolides and fluoroquinolones. 97% of the antibacterials were from the WHO Veterinary Critically Important Antimicrobials. Hence, our study provides a snapshot view of the quantified antimicrobial agents imported and intended for use in animal health, identified gaps in data collection and reporting of sales data, all of which will support national efforts of establishing comprehensive system for monitoring of antimicrobial consumption and antimicrobial resistance in animal industry. We recommend annual quantification of the antimicrobials imported into the country for animal use following the guidelines established by World Organisation for Animal Health and routinely upload sales and import data into ANIMUSE system.

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

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Author contributions

FEK & LM designed and conceptualized the study. FEK, JSN and LM developed and refined the study tools. FEK, JSN and LM contributed to data collection. JSN led the data cleaning, processing and analysis and interpretation. FEK, JSN, JN, BS, JK and LM contributed to data analysis and interpretation. FEK wrote the first paper draft. FEK, JSN, JN, BS, JK and LM revised the first draft. FEK, JSN, JS, JN, BS, EK, JK, NA, HBN, DKN and LM reviewed and contributed to writing the final draft paper. All the authors have read and approved the final manuscript.

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Data availability

on AMC&U are scanty in LMICs, fragmented in time and space, and from small research studies, and Uganda is no different. In this study, we aimed to narrow the knowledge gap by analysing abstracted import data of antimicrobials intended for use in veterinary medicine from 2018 to 2020 based on an electronic database provided by the National Drug Authority (NDA), the drug regulatory agency in Uganda, quantify volumes by antimicrobial class and categorize by the World Health Organization (WHO) and World Organization for Animal Health (WOAH) Critically Important Antimicrobials (CIA Classification, and the European Medicines Agency AMEG classification.

Data availability

Datasets and materials can be provided on request, with redaction of personal identifiers of persons and entities involved in the importation of medicines imports.

Declarations

Ethics approval and consent to participate

This study was reviewed and approved by the Makerere University School of Health Sciences Research and Ethics Committee, reference number MAKSHSREC-2019-099. It was then cleared and registered by the Uganda National Council for Science and Technology (UNCST), reference number HS538ES. Further research administrative clearance to access and use import data was obtained from the National Drug Authority in consultation with the Uganda Ministry of Agriculture, Animal Industry and Fisheries (MAAIF). All methods in the study were carried out according to relevant guidelines and regulations as established by the UNCST and as per international standards. We confirm that the study only used import data for antimicrobials and there were no animals or human subjects involved.

Consent for publication

Not Applicable.

Competing interests

The authors declare no competing interests.

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