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Antimicrobial Usage Surveillance Through Sales at Veterinary Drug Shops Intended for Livestock in Vietnam

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There is a pressing need to establish surveillance systems for antimicrobial use (AMU) intended for animal production particularly in many low- and middle-income countries. This is an extremely challenging task, notably due to the wide range of animal species, production types and antimicrobials available in the market. In Vietnam, farmers commonly buy antimicrobials from veterinary drug shops. Therefore, veterinary drug shops are a potential target for data collection on AMU. We collected antimicrobial sales data at veterinary drug shops and estimated the amount of AMU in different animal species by antimicrobial active ingredient (AAI) class using different measurement metrics. We compiled information on all antimicrobials licensed in Vietnam and used this information to develop a mobile application to capture sales of antimicrobials intended for use in poultry, pig, and ruminant. We provided tablets with this application to 60 veterinary drug shops in two provinces of the country (Bac Giang in the north, Dong Thap in the south; three districts and 30 shops per province) for data collection over 3 weeks. Total sales of antimicrobials were extrapolated to 1 year, and these amounts were related to three different denominator estimates in each province including standing animal body weight, animal biomass, and Population Correction Unit (PCU). A total of 3,960 transactions [2,577 (median 75.5 per shop) in Bac Giang; 1,383 (median 28.5 per shop) in Dong Thap] of 831 different antimicrobial-containing products were recorded in the 3-week period. Sales of 57 AAIs belonging to 17 classes were recorded. In the three Bac Giang districts, we estimated that 242.0 kg of AAI were hypothetically sold over 1 year. Of those, 202.2 kg (83.6%) were intended for poultry, 19.8 kg (8.1%) for pigs, and 20.0 kg (8.3%) for ruminants. In Dong Thap, an estimated 48.4 kg of antimicrobials were sold, including 28.9 kg (59.7%) for poultry, 16.0 kg (33.1%) for pigs, and 3.5 kg (7.2%) for ruminants. After standardized by different animal population denominators, AMU in Bac Giang amounted to 1129.2 mg/kg standing animal body weight, 480.2 mg/kg biomass, and 636.1 mg/kg PCU. In Dong Thap, AMU figures were 1211.0 mg/kg standing animal body weight, 595.8 mg/kg biomass and 818.5 mg/kg PCU. We discuss the observed differences between species, location and metrics, as well as the potential advantages and limitations (including potential sources of bias) of this methodology and its applicability at country level. Retail level data collection can effectively be integrated into AMU surveillance systems that help identify priority AMU management areas (species, regions, and antimicrobial classes), establish national benchmarks and reduction targets.

Keywords: antimicrobial use, antibacterial agents, pharmacists, veterinary drugs, animal, Vietnam, mobile applications, developing countries

INTRODUCTION

A recent study estimated that, in Vietnam (population 96.7 M in 2019), total annual antimicrobial use (AMU) amounts to 3,838 tons, of which 71.7% correspond to animal use (Carrique-Mas et al., 2020). The WHO Global Action Plan on antimicrobial resistance (AMR) (World Health Organization, 2015) identified surveillance of antimicrobial use (AMU) as a priority action. However, many low and middle-income (LMICs) countries lack adequate systems for AMU data collection due to limited resources and capacity and Vietnam is no exception. The World Organization for Animal Health (OIE) compiles and reports global data on AMU in animal production annually (International Organization of Animal Health, 2020). However, the OIE reports do not provide AMU data broken down by country, species, or production types, which would be necessary to identify priority areas for AMU management. In Vietnam, the majority of antimicrobials intended for use in medium and small-scale farms are directly or indirectly (i.e., through a veterinarian or an animal health worker) procured in licensed veterinary drug shops (Phu et al., 2019).

With ∼12,000 veterinary drug shops operating in the country (∼150–300 per province), they play a major role as gatekeepers of antimicrobials consumption in farming (Phu et al., 2019). These retail points are potential data source for a monitoring and surveillance of AMU in the country. Gathering data at the time of the transaction could potentially allow the calculation of each AAI amount for each target species. We developed a user-friendly mobile application "Antimicrobial Sales Recording Tool" (ASRT) to capture data on antimicrobials intended for use in poultry, pig, and ruminants at retail including amounts of AAIs sold, the target species and purpose (treatment or prevention), administration route (water, feed, injection). We collected sales data at the veterinary drug shops to determine its feasibility and estimated AMU in different species using different measurement metrics in two representative provinces in the north and the south of the country.

MATERIALS AND METHODS

We reviewed the list of all approved antimicrobial-containing products held by The Department of Animal Health - Ministry of Agriculture and Rural Development (Vietnam) (2019) and used this information to develop a mobile application to capture sales of antimicrobials intended for use in poultry, pig, and ruminant. We used the products' concentration (strength) data to calculate amounts of AAIs from antimicrobial-containing product sales.

Study Design

We haphazardly selected the provinces of Bac Giang and Dong Thap as representative of the north and south of the country. Bac Giang is one of the provinces with highest pig and poultry populations in Northern Vietnam and Dong Thap is a typical province of the Mekong Delta. Then we selected from each province the three districts with the highest number of veterinary drug shops. From each district, we randomly selected ∼10 veterinary drug shops (total 30 per province) to collect sales data. Selection of drug shops was conducted by the veterinary authorities (Sub-Departments of Animal Health of Bac Giang—SDAH-BG) and Dong Thap (SDAH-DT) and data collection were carried out from September to October 2020.

Development of the AAI Database and ASRT

A web-based database was developed to compile all antimicrobial AAI-containing products. The information gathered in the database contained: (1) Name and registration code of product; (2) Company; (3) Type of formulation (physical characteristics); (4) Product presentation (i.e., sachet, bottle); (5) Volume/weight of product; (6) Target species; (7) Names of Antimicrobial active ingredients (AAI/s) contained [based on the OIE list of antimicrobials (European Medicines Agency, 2021)]; and (8) Strength of AAI (expressed in mg of antimicrobial active ingredient per kg of product). The Antimicrobial Sales Recording Tool (ASRT) was made available in the Google play store (Antimicrobial Sales Recording Tool) and was installed on 60 Android tablets.

Field Data Collection

Owners of selected shops were provided with a tablet with the ASRT application installed and were asked to enter information on any AAI-containing products sold to terrestrial animals to customers presenting to their premises over 3 weeks. Daily follow-up of the respondents was done through telephone and messaging through a local social media application to provide participants with any technical support they may require. Further, weekly visits were made to the drug store owners to ensure that they entered and updated the information in the database.

Data Analyses: Crude and Adjusted Data

The average number of transactions per shop was computed for each district and province. Hypothetical annual antimicrobial sales in the three districts of each province were estimated based on the assumption that sales were constant throughout the year. The annual crude sales of AAI (mg) in each province (3 districts) were multiplied by the reciprocal of the fraction of shops sampled (i.e., 322/30 for Bac Giang and 157/30 for Dong Thap), and by 17.3 (52/3) since data collection was conducted over 3 weeks. The obtained amounts of AAI sold (mg) were related to three different population denominators: (i) standing bodyweight (kg) of the animal population (from census data), by multiplying the theoretical midlife weight of each species by the number of heads population of each species; (ii) weight of standing population combined with production (slaughter) data ("biomass," following OIE guidelines), and (iii) weight of the animal at the time of treatment (Population Correction Unit, PCU following ESVAC guidelines) (European Medicines Agency and European Surveillance of Veterinary Antimicrobial Consumption, 2020; International Organization of Animal Health, 2020). "Standing bodyweight," was calculated by multiplying the census population by the animals' mid-life weight which was taken as 50% of their weight at slaughter. The "biomass" estimate was calculated by adding up the standing bodyweight (breeders) plus the weight of slaughtered animals, obtained multiplying the number of slaughtered animals by the slaughter weight according to OIE (Góchez et al., 2019). The "PCU" estimate was obtained in a similar fashion to the biomass, except that the number of slaughtered animals by their weight at the time of treatment, as determined by ESVAC (European Surveillance of Veterinary Antimicrobial Consumption) (European Medicines Agency, 2021). Detailed calculations to obtain these figures are shown in **Supplementary Material 1**. AMU data were stratified by antimicrobial class and species group (poultry, pigs, ruminants, all). AAIs were classified based on the OIE list of antimicrobial agents; data on critically important AAIs as defined by International Organization of Animal Health (2019) and

TABLE 1 | Summary information of 3,778 products containing antimicrobial active ingredients (AAIs) intended for terrestrial food animal production for which complete information could be collected.

Item	No. products (*n* = 3,778)	%	Poultry (*n* = 2,746)	%	Pigs (*n* = 3,150)	%	Ruminants (*n* = 2,841)	%
Source								
Imported	864	22.9	558	20.3	660	21.0	548	19.3
Domestic	2,914	77.1	2,188	79.7	2,490	79.0	2,293	80.7
Formulation								
Powder	1,891	50.1	1,741	63.4	1,525	48.4	1,292	45.5
Liquid	1,887	49.9	1,005	36.6	1,625	51.6	1,549	54.5
Route of administration								
Oral (water or feed)	2,307	61.1	2,127	77.5	1,804	57.3	1,459	51.4
Injectable	1,427	37.8	583	21.2	1,304	41.4	1,340	47.1
Oral/Injectable	35	0.9	33	1.2	33	1.0	33	1.2
Spray	9	0.2	3	0.1	9	0.3	9	0.3
No, of AAIs and WHO CIA category†								
One AAI	2,250	59.6	1,558	56.8	1,859	59.0	1,609	56.7
"Highest priority"	1,086	28.7	753	27.4	863	27.4	790	27.8
"High priority"	342	9.0	233	8.5	304	9.6	287	10.1
Other ("Highly important", "Important")	822	21.7	572	20.8	692	22.0	532	18.7
Two AAIs	1,517	40.1	1,151	41.9	1,282	40.7	1,248	43.9
At least one "Highest priority"	815	21.6	665	24.2	686	21.8	657	23.1
At least one "High priority"	288	7.6	198	7.2	242	7.7	247	8.7
Other ("Highly important", "Important")	414	11.0	320	11.6	354	11.2	319	11.2
Three AAIs	9	0.2	3	0.1	7	0.2	7	0.2
At least one "Highest priority"	1	0.0	1	0.0	0	0.0	0	0.0
At least one "High priority"	3	0.1	1	0.0	2	0.1	2	0.1
Other ("Highly important", "Important")	5	0.1	1	0.0	5	0.2	5	0.2
Four AAIs	2	0.1	2	0.1	2	0.1	2	0.1
At least one "Highest priority"	1	0.0	1	0.0	1	0.0	1	0.0
Other ("Highly important")	1	0.0	1	0.0	1	0.0	1	0.0

Products intended for eye treatment (i.e., eye drops) and companion animal-only products were excluded.
†Based on the World Health Organization (2019).

World Health Organization (2019) were highlighted. All analyses were carried out using R (version 3.6.3) (R Core Team, 2021) and the "*dplyr*" (Wickham et al., 2021), "*tidyverse*" (Wickham et al., 2019), and "*ggplot2*" packages (Wickham, 2009). The Mann-Whitney *U*-test (Wilcoxon rank-sum test) was used to test the association of the number of transactions between the districts within each province, and between species groups within each province when they did not have a normal distribution.

Ethics

Ethical approval for this project was obtained from OxTREC (Oxford Tropical Research Ethics Committee) (Ref. No. 551-20).

RESULTS

Description of AAI-Containing Products

Of the 7,484 antimicrobial-containing products reviewed, information about their content was available for 3,778 (50.5%) of them. Detailed information of the AAIs content of these products is presented in **Supplementary Material 2** and are further summarized in **Table 1**. In our study shops, 831 products containing 57 different AAIs belonging to 17 antibiotic classes were identified (**Supplementary Material 2**). Of these, 406 contained one AAI (48.9%), 421 contained 2 AAIs (50.7%) and 4 contained 3 AAIs (0.4%). In Bac Giang, 607 different antibiotic-containing products were sold, including 438 for poultry, 198 for pigs and 127 for ruminants. In Dong Thap, 329 products were sold in total, including 226 for poultry, 141 for pigs, and 53 for ruminants.

Number of Transactions of AAIs

A total of 3,960 transactions of AAI-containing products were registered over the 3-week study period (2,577 and 1,383 in Bac Giang and Dong Thap shops, respectively). In Bac Giang, the overall median number of transactions of AAI-containing products per shop over the 3-week period was 76 [Interquartile range (IQR) 45–119]. Transactions intended for poultry were the most common (44 [IQR 33–62]) follow by pigs (5 [IQR 1–25]) and ruminants (5 [IQR 2–13]). In Dong Thap, the overall median number of transactions was 29 [IQR 20–54] (21 [IQR 13–36] for poultry, 6 [IQR 4–14] for pigs, and 0 [IQR 0–3] for ruminants) (**Figure 1**). The number of transactions was significantly greater in Bac Giang than in Dong Thap study shops [Wilcoxon rank sum test (W) 696.5; $p < 0.001$]. Between provinces, there were

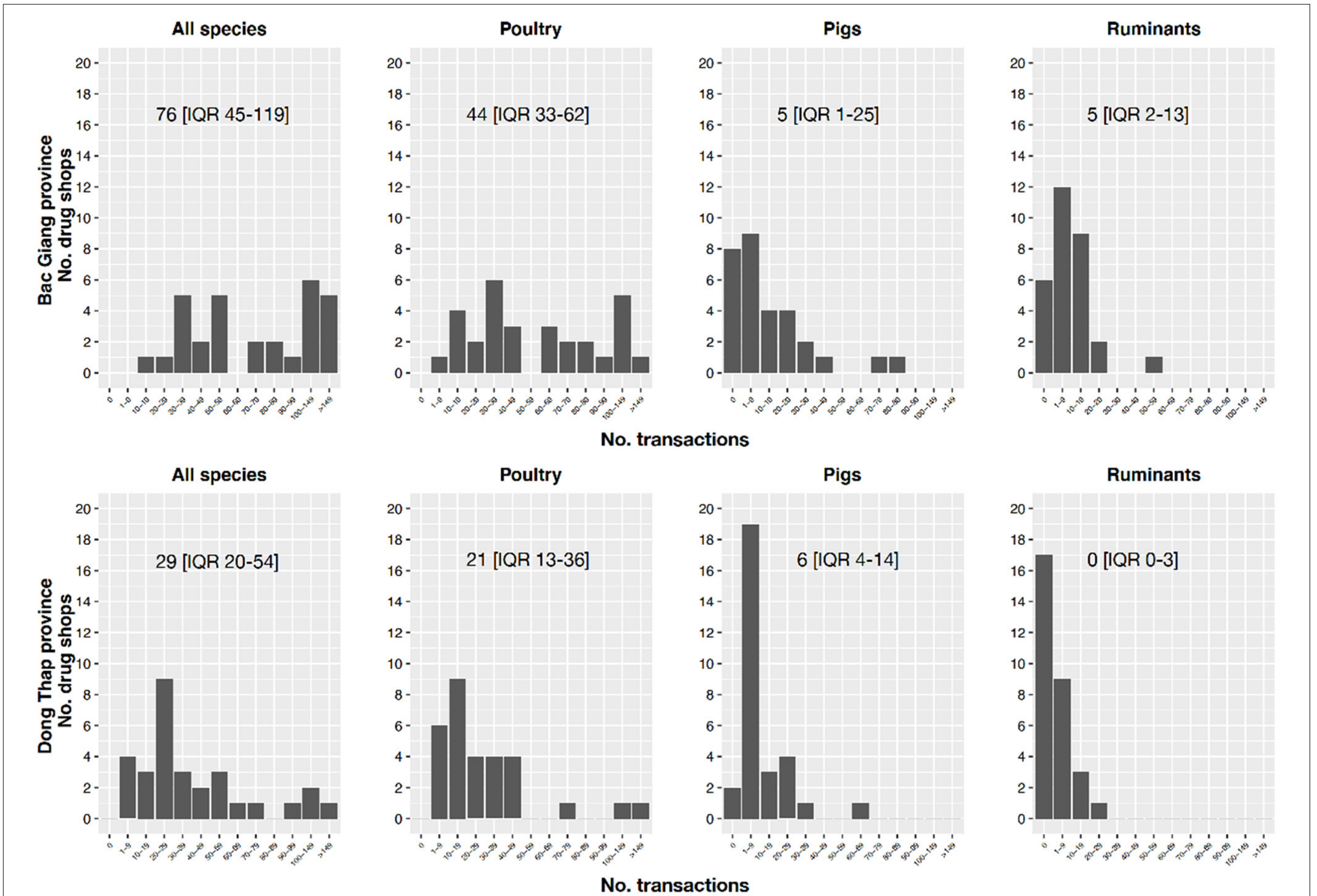

FIGURE 1 | The frequency of transactions in vet drug shop by province and species group during the 3-week survey period.

TABLE 2 | Total antimicrobial sales in the 3-week observation period in study districts.

Antimicrobial class	CIA level	Bac Giang (3 districts combined)				Dong Thap (3 districts combined)			
		All species	Poultry	Pigs	Ruminants	All species	Poultry	Pigs	Ruminants
		kg AAI (%) (mean ± SD)	kg AAI (%) (mean ± SD)	kg AAI (%) (mean ± SD)	kg AAI (%) (mean ± SD)	kg AAI (%) (mean ± SD)	kg AAI (%) (mean ± SD)	kg AAI (%) (mean ± SD)	kg AAI (%) (mean ± SD)
Macrolides	Highest priority	17.9 (7.4%) (0.60 ± 0.92)	16.8 (8.3%) (0.56 ± 0.93)	0.6 (3.2%) (0.02 ± 0.03)	0.5 (2.1%) (0.01 ± 0.03)	4.1 (8.4%) (0.14 ± 0.34)	1.7 (5.9%) (0.06 ± 0.08)	1.6 (9.7%) (0.05 ± 0.20)	0.8 (23.0%) (0.03 ± 0.11)
Quinolones		8.7 (3.6%) (0.29 ± 0.46)	8.0 (3.9%) (0.27 ± 0.46)	0.5 (2.6%) (0.02 ± 0.03)	0.2 (0.8%) (0.01 ± 0.01)	1.8 (3.7%) (0.06 ± 0.09)	1.3 (4.6%) (0.04 ± 0.06)	0.4 (2.1%) (0.01 ± 0.04)	0.1 (4.1%) (0.01 ± 0.02)
Polymyxins		8.5 (3.5%) (0.28 ± 0.27)	6.7 (3.3%) (0.22 ± 0.26)	0.9 (4.6%) (0.03 ± 0.05)	0.9 (4.5%) (0.03 ± 0.09)	2.2 (4.5%) (0.07 ± 0.15)	1.2 (3.9%) (0.04 ± 0.11)	0.9 (5.5%) (0.03 ± 0.06)	0.1 (4.1%) (0.00 ± 0.01)
Cephalosporins 3 and 4 generation		1.6 (0.7%) (0.05 ± 0.13)	0.5 (0.3%) (0.02 ± 0.05)	0.3 (1.3%) (0.01 ± 0.02)	0.8 (4.0%) (0.03 ± 0.11)	0.1 (0.2%) (0.00 ± 0.00)	0.1 (0.3%) (0.00 ± 0.01)	0	0
Penicillins (aminopenicillins)	High priority	77.6 (32.1%) (2.58 ± 4.20)	62.2 (30.7%) (2.07 ± 4.10)	6.4 (32.3%) (0.20 ± 0.31)	9.0 (45.1%) (0.30 ± 0.88)	9.8 (20.2%) (0.33 ± 0.59)	6.9 (23.7%) (0.23 ± 0.47)	2.1 (13.3%) (0.07 ± 0.17)	0.8 (22.8%) (0.02 ± 0.09)
Aminoglycoside		12.2 (5%) (0.40 ± 0.60)	9.4 (4.7%) (0.31 ± 0.59)	1.6 (8.3%) (0.05 ± 0.11)	1.2 (5.6%) (0.04 ± 0.08)	8.3 (17.2%) (0.28 ± 0.44)	4.9 (17%) (0.16 ± 0.21)	3.2 (20%) (0.10 ± 0.32)	0.2 (6.9%) (0.01 ± 0.01)
Phosphonic acid derivatives		0.2 (0.1%) (0.01 ± 0.03)	0.2 (0.09%) (0.01 ± 0.03)	0	0	0	0	0	0
Ansamycins		0	0	0	0	0.03 (0.1%) (0.00 ± 0.01)	0	0.03 (0.2%) (0.00 ± 0.01)	0
Sulfonamide	Highly important	34.5 (14.3%) (1.15 ± 2.10)	33.7 (16.7%) (1.12 ± 2.10)	0.5 (2.6%) (0.02 ± 0.04)	0.3 (1.5%) (0.01 ± 0.03)	6.4 (13.2%) (0.20 ± 0.57)	2.8 (9.6%) (0.09 ± 0.20)	3.6 (22.3%) (0.12 ± 0.45)	0
Tetracyclines		34.3 (14.2%) (1.14 ± 1.90)	28.3 (14.0%) (0.94 ± 1.79)	2.8 (14.2%) (0.09 ± 0.30)	3.2 (16.0%) (0.10 ± 0.31)	7.2 (14.8%) (0.24 ± 0.33)	5.5 (19%) (0.18 ± 0.28)	1.5 (8.8%) (0.05 ± 0.10)	0.2 (6.9%) (0.01 ± 0.03)
Amphenicols		24.5 (10.1%) (0.82 ± 1.70)	19.9 (9.8%) (0.66 ± 1.69)	2.7 (13.8%) (0.09 ± 0.26)	1.9 (9.5%) (0.06 ± 0.26)	2.7 (5.5%) (0.09 ± 0.18)	1.2 (4.0%) (0.04 ± 0.08)	1.4 (8.6%) (0.05 ± 0.16)	0.1 (4.1%) (0.00 ± 0.01)
Cephalosporin 1 and 2 generation		8.0 (3.3%) (0.27 ± 0.76)	7.85 (3.9%) (0.26 ± 0.76)	0.07 (0.4%) (0.00 ± 0.01)	0.08 (0.4%) (0.00 ± 0.02)	0.7 (1.5%) (0.02 ± 0.10)	0.69 (2.4%) (0.02 ± 0.10)	0	0.01 (0.2%) (0.00 ± 0.00)
Lincosamides		4.8 (2.0%) (0.16 ± 0.27)	2.4 (1.2%) (0.08 ± 0.18)	0.9 (4.3%) (0.03 ± 0.10)	1.5 (7.8%) (0.05 ± 0.20)	1.5 (3.1%) (0.05 ± 0.08)	0.6 (2.1%) (0.02 ± 0.04)	0.6 (3.6%) (0.02 ± 0.05)	0.3 (9%) (0.01 ± 0.04)
Penicillins (narrow spectrum)		0.4 (0.2%) (0.01 ± 0.03)	0	0.2 (0.8%) (0.01 ± 0.02)	0.2 (1%) (0.01 ± 0.03)	1.0 (2.1%) (0.03 ± 0.06)	0.7 (2.4%) (0.02 ± 0.06)	0.27 (1.9%) (0.01 ± 0.04)	0.03 (0.8%) (0.00 ± 0.00)
Polypeptides	Important	4.0 (1.6%) (0.13 ± 0.55)	4.0 (2.0%) (0.66 ± 0.55)	0	0	1.2 (2.5%) (0.04 ± 0.14)	0.7 (2.4%) (0.02 ± 0.11)	0	0.5 (15.6%) (0.02 ± 0.09)
Aminocyclitols		3.9 (1.6%) (0.13 ± 0.27)	2.4 (1.2%) (0.08 ± 0.17)	1.3 (6.8%) (0.04 ± 0.21)	0.2 (1%) (0.01 ± 0.01)	1.0 (2%) (0.03 ± 0.07)	0.75 (2.5%) (0.02 ± 0.06)	0.2 (1.5%) (0.01 ± 0.01)	0.05 (1.5%) (0.00 ± 0.01)
Pleuromutilin		1.1 (0.4%) (0.04 ± 0.09)	0	1 (5.1%) (0.03 ± 0.09)	0.1 (0.5%) (0.00 ± 0.01)	0.4 (0.8%) (0.01 ± 0.06)	0.01 (0.03%) (0.00 ± 0.00)	0.39 (2.4%) (0.01 ± 0.06)	0
Total		242.0	202.2	19.8	20.0	48.4	28.9	16.0	3.5

The figures in parenthesis indicate the average sale per shop over the 3-week study period, alongside the Standard Deviation (SD) corresponding to data from each province.

significant differences for poultry (W = 679.5; $p < 0.001$) and ruminants (W = 650.5; $p = 0.002$) but not for pigs (W = 421.5; $p = 0.678$).

Crude AAI Sales

A total of 242.0 and 48.4 kg of AAI were, respectively, sold in study shops in Bac Giang and Dong Thap over the 3-week period. In Bac Giang, 202.2 kg (83.6%), 19.8 kg (8.1%), and 20.0 kg (8.3%) of antibiotics sold were intended for poultry, pigs, and ruminants, respectively. In Dong Thap, the equivalent figures were 28.9 kg for poultry (59.7%), 16.0 kg for pigs (33.1%), and 3.5 kg (7.2%) for ruminants (**Table 2**). AAIs belonging to the "highly important" class were sold the most (44.0 and 40.2% of total AAIs sold) in Bac Giang and Dong Thap, respectively, followed by those belonging to the "high priority, critically important" group (37.2 and 37.5%, respectively), "highest priority, critically important" (15.2 and 16.9%, respectively) and "important" groups (3.6 and 5.4%, respectively). In Bac Giang, the aminopenicillin class was the largest amount of agent sold (32.1%), followed by sulfonamides (14.3%). In Dong Thap, aminopenicillins represented the AAI class most sold (20.2%) followed by aminoglycosides (17.2%). In Bac Giang, 111.4 kg (46.0%), 58.1 kg (24.0%), and 72.5 kg (30.0%) of AAIs were, respectively, sold in Luc Nam, Tan Yen, and Yen The districts over the 3-week study period. In Dong Thap, 13.3 kg (27.5%), 23.5 kg (48.6%), and 11.6 kg (23.9%) of

TABLE 3 | Animal population denominators used for AMU calculations in two pilot provinces (based on population estimates provided by SDAH in Dong Thap and Bac Giang in 2020).

Province	Denominator used (kg)	Sampled districts			Whole province		
		Standing body weight	Biomass	PCU	Standing body weight	Biomass	PCU
Bac Giang	All species	39,873,009	93,751,783	70,775,081	83,380,307	180,317,741	137,905,141
	Poultry	9,606,520	31,302,954	17,364,211	17,549,337	57,054,508	31,655,100
	Pigs	23,179,551	57,046,129	48,842,310	43,048,207	105,944,123	90,708,268
	Ruminants	7,086,938	5,402,700	4,568,560	22,782,763	17,319,110	15,541,773
Dong Thap	All species	3,619,388	7,356,626	5,354,826	15,864,580	29,707,964	21,086,746
	Poultry	1,609,653	3,128,486	1,723,806	7,422,613	14,843,190	8,187,699
	Pigs	1,516,297	3,697,840	3,169,385	4,416,926	10,771,441	9,232,129
	Ruminants	493,438	530,300	461,635	4,025,041	4,093,333	3,666,918

antibiotics were, respectively, sold in Cao Lanh, Lai Vung, and Thap Muoi districts. Detailed overall AMU sales per district are presented in **Supplementary Material 3**.

Animal Population Denominators

Animal population denominators in the two provinces differed considerably, with the sampled districts in the northern province of Bac Giang having ∼11 times higher animal standing bodyweight than the districts in Dong Thap (39873.0 vs. 3619.4 tons); with regards to pigs and ruminants, the differences were, respectively, 15.3 (23179.6 vs. 1516.3 tons) and 14.4 times higher (7086.9 vs. 493.4 tons) (**Table 3**).

Antimicrobial Use (mg/kg) by Species Group

The total annual AMU in Bac Giang (three districts) was estimated at 1,129.2 mg/kg standing animal bodyweight, 480.2 mg/kg biomass and 636.1 mg/kg PCU. For Dong Thap these figures were slightly higher in all three metrics at 1211.0 mg/kg standing body weight, 595.8 mg/kg biomass and 818.5 mg/kg PCU (**Table 4** and **Figure 2**). In Bac Giang, poultry where the target of the highest amounts of antimicrobials related to standing bodyweight (3917.1 mg/kg), followed by ruminants (522.3 mg/kg) and pigs (159.3 mg/kg). In relation to biomass, the equivalent amounts were 1202.1 mg/kg (poultry), 685.1 mg/kg (ruminants), and 64.7 mg/kg (pigs). Similarly, in relation to PCU, the highest amounts were in poultry (2167.1 mg/kg) followed by ruminants (810.2 mg/kg) and pigs (75.6 mg/kg) (**Table 4** and **Figure 2**).

In Dong Thap, poultry was the target of the highest amounts of antimicrobials (1639.5 mg/kg), followed by pigs (958.3 mg/kg) and ruminants (589.9 mg/kg) (all related to standing bodyweight). However, using biomass metrics, the highest sales were still for poultry (843.5 mg/kg), followed in second position by ruminants (548.8 mg/kg) and pigs (393.0 mg/kg). The extrapolated AMU result for poultry using standing bodyweight was slightly higher than that estimated using PCU metric and roughly two times higher than that of biomass metric. For pigs, the extrapolated sales of standing body weight metrics were two times higher than those of both biomass and PCU metrics. The figures of the three metrics were similar for ruminants (**Table 4** and **Figure 2**).

AMU by AAI Class

AMU for aminopenicillins (high priority antimicrobials) were the highest in both provinces. These figures were recorded with 362.0, 154.0, and 204.0 mg/kg when expressed in relation to standing animal bodyweight, animal biomass, and PCU metrics, respectively, in Bac Giang province. In Dong Thap province, those figures were slightly lower with 245.0, 120.5, and 165.6 mg/kg when expressed in relation to standing animal bodyweight, animal biomass, and PCU metrics The second most consumed AAI class in Bac Giang province were sulfonamides (highly important class), with 68.5 mg/kg (animal biomass metric). However, in latter province was aminoglycoside, classified as the high priority antimicrobial class, with 102.7 mg/kg in the same metric (**Figure 3**).

The detailed extrapolation of AMU in the six surveyed districts are shown in **Supplementary Material 4** (Bac Giang) and **Supplementary Material 5** (Dong Thap). Overall, highly important AAI classes was predominantly sold in Yen The and Luc Nam districts in Bac Giang province and Cao Lanh and Lai Vung districts in Dong Thap province, while high priority class AAIs were more commonly retailed in Tan Yen district (Bac Giang) and Thap Muoi (Dong Thap). Penicillins (aminopenicillins) were the most frequently sold class in the five studied districts.

DISCUSSION

This is the first attempt to collect retail data and explore the feasibility for AMU surveillance in Vietnam. In Vietnam veterinary drug shop owners are the main source that provide antimicrobials containing products to farmers for their different purposes (Phu et al., 2019; Truong et al., 2019); therefore, targeting this stakeholder is imperative to minimize unnecessary prescriptions of antimicrobials. Owners of vet drug shops are required to have at least a vocational (animal science) qualification obtained in a technical college to be allowed to operate vet drug shops. However, antimicrobials are more

TABLE 4 | Total annual AMU sales following species in three districts of Bac Giang and Dong Thap province (Unit: mg/kg).

Province	Districts	Denominator used (kg)	Poultry	Pigs	Ruminants	Total species
Bac Giang	Three districts	Standing body weight	3,917.1 (CI: 3,845.2–3,989.1)	159.3 (CI: 156.1–162.4)	522.3 (CI: 510.9–533.8)	1129.2 (CI: 1,111.9–1,146.5)
		Animal biomass	1,202.1 (CI: 1,180.0–1224.2)	64.7 (CI: 63.4–66)	685.1 (CI: 670.1–700.1)	480.2 (CI: 472.9–487.6)
		PCU	2,167.1 (CI: 2,127.3–2,206.9)	75.6 (CI: 74.1–77.1)	810.2 (CI: 792.5–828)	636.1 (CI: 626.4–645.9)
	Luc Nam	Standing body weight	7,747.3 (CI: 7,316.8–8,177.8)	258.7 (CI: 229.7–287.7)	70.6 (CI: 64.5–76.2)	1,824.2 (CI: 1,745.0–1,903.4)
		Biomass	2382.4 (CI: 2,250.0–2,514.8)	105.1 (CI: 93.3–116.9)	94.9 (CI: 87.3–102.5)	812.2 (CI: 776.9–847.5)
		PCU	4,294.1 (CI: 4,055.5–4,532.7)	122.8 (CI: 109.0–136.6)	117.0 (CI: 107.7–126.3)	1,069.9 (CI: 1,023.4–1,116.4)
	Tan Yen	Standing body weight	1,916.8 (CI: 1,850.7–1,982.9)	119.6 (CI: 114.5–124.7)	772.3 (CI: 727.4–817.2)	473.8 (CI: 458.9–488.7)
		Biomass	576.8 (CI: 556.9–596.7)	48.6 (CI: 46.5–50.7)	1,021.6 (CI: 962.2–1,081.0)	204.2 (CI: 197.8–210.6)
		PCU	1,041.6 (CI: 1,005.7–1,077.5)	56.7 (CI: 54.3–59.1)	1,034.5 (CI: 974.3–1,094.7)	254.7 (CI: 246.7–262.7)
	Yen The	Standing body weight	4,154.1 (CI: 3,216.8–5,091.4)	45.1 (CI: 36.5–53.7)	672.5 (CI: 568.9–776.1)	1,963.3 (CI: 1,542.5–2,384.1)
		Biomass	1,288.0 (CI: 997.4–1,578.6)	18.3 (CI: 14.8–21.8)	846.4 (CI: 716.0–976.7)	783.7 (CI: 615.8–951.6)
		PCU	2,319.8 (CI: 1,796.3–2,843.2)	21.4 (CI: 17.3–25.5)	1247.9 (CI: 1,055.6–1,440.1)	1,159.6 (CI: 911.1–1,408.2)
Dong Thap	Three districts	Standing body weight	1,639.5 (CI: 1,616.8–1,662.2)	958.3 (CI: 934.3–982.4)	589.9 (CI: 575.0–604.7)	1,211.0 (CI: 1,193.5–1,228.5)
		Animal biomass	843.5 (CI: 831.9–855.2)	393.0 (CI: 383.1–402.8)	548.8 (CI: 535.0–562.6)	595.8 (CI: 587.2–604.4)
		PCU	1,530.9 (CI: 1,509.7–1,552.1)	458.5 (CI: 447–470)	630.4 (CI: 614.5–646.2)	818.5 (CI: 806.7–830.4)
	Cao Lanh	Standing body weight	1,609.3 (CI: 1,500.9–1,717.7)	205.9 (CI: 191.4–220.4)	729.0 (CI: 649.5–808.5)	871.7 (CI: 816.5–926.9)
		Biomass	823.1 (CI: 767.6–878.6)	84.4 (CI: 78.5–90.3)	703.7 (CI: 627.0–780.5)	415.8 (CI: 389.5–442.1)
		PCU	1,493.4 (CI: 1,392.8–1,594.0)	98.5 (CI: 91.6–105.4)	747.7 (CI: 666.1–829.3)	565.5 (CI: 529.7–601.3)
	Lai Vung	Standing body weight	2,095.5 (CI: 1,979.2–2,211.8)	2,490.1 (CI: 2,248.9–2,731.4)	539.8 (CI: 496.6–583.0)	1,734.2 (CI: 1,627.0–1,841.3)
		Biomass	1,056.7 (CI: 998.1–1,115.3)	1021.5 (CI: 922.6–1,120.4)	484 (CI: 445.3–522.7)	940.3 (CI: 882.2–998.4)
		PCU	1,916.3 (CI: 1,810.0–2,022.6)	1,191.8 (CI: 1,076.4–1,307.2)	598.2 (CI: 550.3–646.1)	1,334.9 (CI: 1,252.4–1,417.4)
	Thap Muoi	Standing body weight	1,247 (CI: 1,110.1–1,383.9)	1,155.8 (CI: 981.9–1,329.7)	9.8 (CI: 7.1–12.5)	1,112.7 (CI: 983.0–1,242.4)
		Biomass	654.2 (CI: 582.4–726.0)	473.9 (CI: 402.6–545.2)	9.6 (CI: 6.9–12.3)	531.8 (CI: 469.8–593.8)
		PCU	1,188.1 (CI: 1,057.7–1,318.5)	553.0 (CI: 469.8–636.2)	10.0 (CI: 7.2–12.8)	724.5 (CI: 640.1–808.9)

often than not sold without providing a diagnostic service. According to a new regulation, antimicrobial should be sold with a prescription that made by registered veterinarian (shops owners or qualified staff) (The Government of the Socialist Republic of Vietnam, 2020). However, in reality antimicrobials are sold without prescription in most cases, and drug shop owners play a role in the final decision as to the type of antimicrobial to be dispensed. Although this study is based on a limited sample size, we found considerable differences between species and study sites with regards to volumes

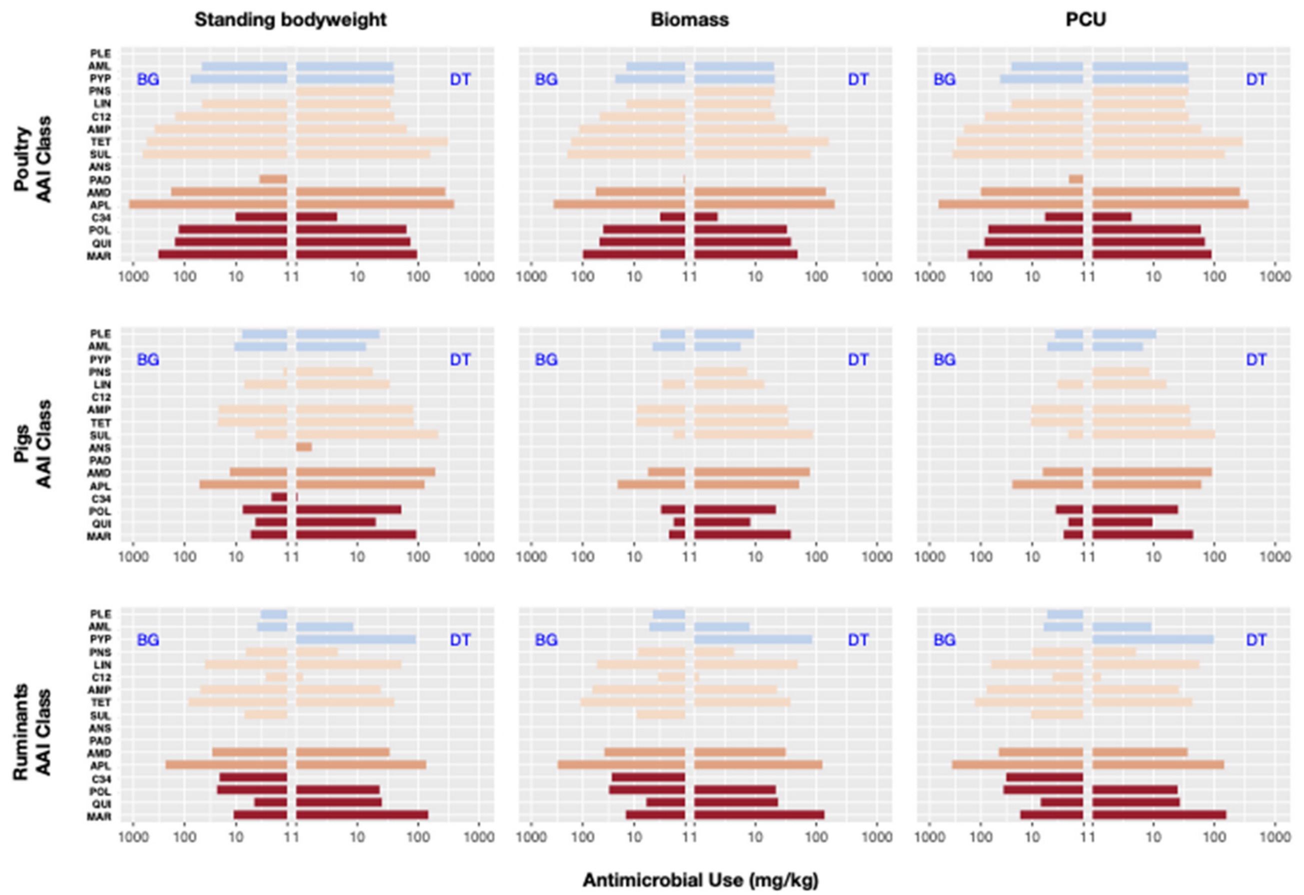

FIGURE 2 | Estimation of annual AMU sales for poultry, pigs and ruminants by three different metrics in surveyed districts in Bac Giang and Dong Thap provinces. x-axis: estimation of annual AMU sales (mg/kg) by three different metrics; y-axis: the surveyed districts in Bac Giang and Dong Thap provinces; Blue, important antimicrobial group; Light Brown, highly important antimicrobial group; Brown, high priority antimicrobial group; Red, highest priority antimicrobial group; BG, Bac Giang province; DT, Dong Thap province; PCU, Population Correction Unit; AAI, active antimicrobial ingredient; PLE, pleuromutilins; AML, aminocyclitols; PYP, polypeptides; PNS, penicillins (narrow spectrum); lin, lincosamides; C12, 1st-2nd generation cephalosporins; AMP, amphenicols; TET, tetracyclines; SUL, sulphonamides; ANS, ansamycins; PAD, phosphonic acid derivatives; AMD, aminoglycoside; APL, aminopenicillins; C34, 3th−4th generation cephalosporins; POL, polymyxins; QUI, quinolone; MAR, macrolide.

and classes of antimicrobials sold, as well as by type of metric chosen.

Overall quantities of antimicrobial sales in Bac Giang province (242.0 kg) were 5 times higher than those in Dong Thap province (48.4 kg). However, animal populations were also considerably greater in Bac Giang (**Supplementary Material 1**). Among the six districts of the two provinces, sales in Luc Nam district (Bac Giang) and Lai Vung district (Dong Thap) were particularly high. A potential reason for the disparities in AMU across districts may be due to some of the purchases not corresponding to retail sales to farmers in their district, but to wholesales intended for further retailing in veterinary drug shops not based in the province/study districts.

Of the three species groups, poultry was quantitatively associated with the highest total AMU. These results were consistent with data on small-scale chicken farms in Mekong Delta of Vietnam, where total AMU was 791.8 (SEM ± 16.7) mg of AAI per kg (treatment weight) and 323.4 (SEM ± 11.3) mg (related to kilogram sold) (Cuong et al., 2019). Many chicken farms are run by farmers with inadequate training and experience in disease prevention and control (Cuong et al., 2019). Aminopenicillins, sulphonamide, tetracyclines, amphenicols were the antimicrobial classes most sold for the three species in Bac Giang province. The most common antimicrobial classes in Dong Thap province were aminopenicillins, aminoglycosides, sulphonamide, and tetracyclines. Our findings were consistent with a previous study on chicken farms in the Mekong Delta region where the most common antimicrobials used were polypeptides, tetracyclines, penicillin, and aminoglycosides with 18.6, 17.5, 11.3, and 10.1% of the farms, respectively (Carrique-Mas et al., 2015).

The standing animal bodyweight and weight at the time of treatment denominators were always lower than the weight at slaughter since animals weigh the most at the end of their production cycle (European Surveillance of Veterinary Antimicrobial Consumption, 2016). The higher denominators,

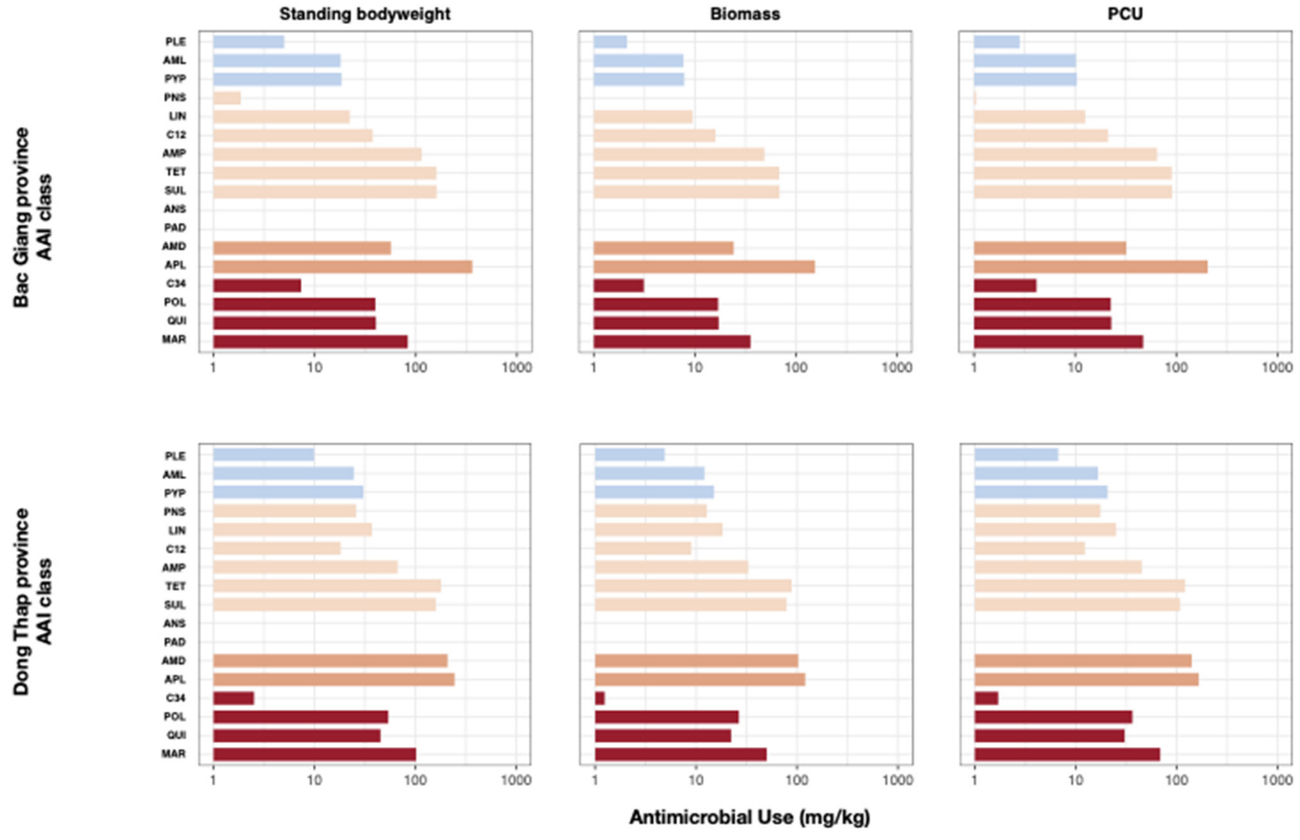

FIGURE 3 | Comparison of AMU sales following antimicrobial classes by three metrics (Standing bodyweight, Bioomas, and PCU) in the two study provinces (Bac Giang and Dong Thap). x-axis, estimation of annual AMU sales (mg/kg) by three different metrics; y-axis, the surveyed districts in Bac Giang and Dong Thap provinces; Blue, important antimicrobial group; Light Brown, highly important antimicrobial group; Brown, high priority antimicrobial group; Red, highest priority antimicrobial group; PCU, Population Correction Unit; AAI, active antimicrobial ingredient; PLE, pleuromutilins; AML, aminocyclitols; PYP, polypeptides; PNS, penicillins (narrow spectrum); lin, lincosamides; C12, 1st-2nd generation cephalosporins; AMP, amphenicols; TET, tetracyclines; SUL, sulphonamides; ANS, ansamycins; PAD, phosphonic acid derivatives; AMD, aminoglycoside; APL, aminopenicillins; C34, 3th−4th generation cephalosporins; POL, polymyxins; QUI, quinolone; MAR, macrolide.

the lower estimation of antimicrobial use. Although we used our own estimates, they do not differ from official Vietnamese government estimates of bodyweight of livestock (Anonym, 2020). As a result, relating weight of AAIs to the weight of standing animal bodyweight results in quantitative the largest magnitude of AMU, followed by PCU and biomass for pigs and poultry. In contrast, for ruminants, the highest estimates were obtained using PCU, followed by animal biomass and standing animal bodyweight metrics, respectively. A previous study reported that in chickens AMU related to the animal weight of treatment (i.e., equivalent PCU metric) was 2–3 times higher than AMU related to animal biomass (Cuong et al., 2019).

The calculations using production data (i.e., animal biomass and PCU metric) do not take into account mortality, since dead animals are not included; therefore, situations of high mortality may result in higher than expected estimated values. In addition, the estimated volume of antimicrobial sales for ruminants was lowest in the standing bodyweight metric. Since the number of annually slaughtered ruminants referring to denominator was often lower than the number from census data, the smaller the denominator, the higher the antimicrobial sales estimates. We suggest using the animal denominator obtained in the standing animal bodyweight metric which is based on census data (not production data) as it is often the easiest parameters to calculate. It also allows direct comparison with AMU data in humans which are often based on census populations.

A major limitation of this study is that it is not based on a true random sample. Therefore, quantitative AMU results are only hypothetical and need to be taken with caution. As the study is not representative, we did not use the conventional statistics to compare between provinces or species. The non-random choice of establishments and the potential for inaccurate animal production statistics may also be a source of errors. A possible limitation of the study is the potential seasonality of AMU. In southern Vietnam, for example, the incidence of disease in poultry is greater during the rainy season (authors' observation). Therefore, we propose that data collection is collected over the year, with random allocation to provinces/districts by month. The calculation of AMU in each study unit (district) should be used to calculate overall country-level AMU by species group;

the data from individual districts/provinces is subject to a large error given the small number of drug and shop and should not used for local AMU estimations. It is also likely that farmers procure antimicrobials from vet drug shops located not in their immediate vicinity (Phu et al., 2019).

We noticed a slight reduction in the number of antimicrobial sales transactions recorded in drug shops over the 3-week period (data not shown). Because of this, we propose 1-week data collection slots per shop. A small number of veterinary drug shop owners objected to using the tablet. An alternative for these would be to allow a computer-based spreadsheet or even hand note-taking in such cases.

Monitoring of sales through veterinary drug shops excluded any antimicrobials in commercial feed rations. However, antimicrobial growth promoters (AGP) have been banned in Vietnam since January 2018 (National Assembly of the Socialist Republic of Vietnam, 2018). Monitoring of sales through retail veterinary drug shops may also miss antimicrobials targeting the increasingly important larger industrial sector, operated through contract farmers with their independent pharmaceutical suppliers. Engaging with this sector, as well as with the large aquaculture sector in Vietnam, is essential to enable comprehensive AMU data collection on animal production. The country has outlined a roadmap to gradually ban AMU for livestock prophylactic purposes: "critically important" antimicrobials will be banned from 2021; "highly important" from 2022; "important" antimicrobials from 2023 and any other antimicrobial classes from 2026 (The Government of the Socialist Republic of Vietnam, 2020).

This study highlights the potential of AMU surveillance at retail. Using the methodologies developed here, the Government of Vietnam should be able to collect data on AMU rolling out data collection rounds on randomly selected provinces/districts. This information is essential to highlight hotspots of AMU as well as to set benchmarks and reduction targets.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the study obtained ethics approval from OxTREC (Oxford University Review Board) No. 551-20. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

JC-M, LTH, PP, and BDT conceived and designed the study. LTTH and BDT conducted the field survey. NG, DT, BTK, VH, LTH, and PP designed and aided data collection. LTTH, DP, BDT, and JC-M contributed to data analyses. LTTH, CR, DP, LTH, PP, BDT, and JC-M contributed to writing up and editing the manuscript. All authors contributed to the article and approved the submitted version.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fsufs.2021.784500/full#supplementary-material

Supplementary Material 1 | Supplementary Table S1: Estimation of animal "standing bodyweight," "animal biomass," and animal "PCU" in three districts combined of Bac Giang province. The figures were extrapolated from number of animals in the census (1), estimated production data (2) and estimated weight of animals from their estimated mid-age weight (3), slaughter weight (based on OIE) (4), or treatment weight (based on ESVAC) (5). Mid-age standing bodyweight of meat animals was taken as 50% of their weight at slaughter.
Supplementary Table S2: Estimation of animal "standing bodyweight," "animal biomass," and animal "PCU' in three districts combined of Dong Thap province. The figures were extrapolated from number of animals in the census (1), estimated production data (2) and estimated weight of animals from their estimated mid-age weight (3), slaughter weight (based on OIE) (4), or treatment weight (based on ESVAC) (5). Mid-age standing bodyweight of meat animals was taken as 50% of their weight at slaughter. **Supplementary Table S3**: Estimation of animal "standing bodyweight," "animal biomass," and animal "PCU" in Luc Nam district (Bac Giang). **Supplementary Table S4**: Estimation of animal "standing bodyweight," "animal biomass," and animal "PCU" in Tan Yen district (Bac Giang).
Supplementary Table S5: Estimation of animal "standing bodyweight," "animal biomass," and animal "PCU" in Yen The districts (Bac Giang).
Supplementary Table S6: Estimation of animal "standing bodyweight," "animal biomass," and animal "PCU" in Cao Lanh district (Dong Thap).
Supplementary Table S7: Estimation of animal "standing bodyweight," "animal biomass" and animal "PCU" in Lai Vung district (Dong Thap).
Supplementary Table S8: Estimation of animal "standing bodyweight," "animal biomass," and animal "PCU" in Thap Muoi district (Dong Thap).

Supplementary Material 2 | Number of products by AAI content in the database ($n = 3,778$) and identified in the 60 shops surveyed ($n = 2,843$) by species group and WHO Critical Importance Antimicrobial (CIA) criteria (Góchez et al., 2019). The first figure in each cell represents products identified in the survey; the second, products in the database.

Supplementary Material 3 | Sales over the 3-week study period in shops in six study districts in Bac Giang and Dong Thap provinces. The data indicate total numbers and sales by shop (alongside the SD by province).

Supplementary Material 4 | Annual antimicrobial use sales following antimicrobial classes by three metrics in each study district in Bac Giang province. x-axis, estimation of annual AMU sales (mg/kg) by three different metrics; y-axis, the surveyed districts in Bac Giang provinces; Blue, important antimicrobial group;

Light Brown, highly important antimicrobial group; Brown, high priority antimicrobial group; Red, highest priority antimicrobial group; PCU, Population Correction Unit; AAI, active antimicrobial ingredient; PYP, polypeptides; PLE, pleuromutilins; AML, aminocyclitols; TET, tetracyclines; SUL, sulphonamides; PNS, penicillins (narrow spectrum); LIN, lincosamides; C12, 1st-2nd generation cephalosporins; AMP, amphenicols; PAD, phosphonic acid derivatives; APL, aminopenicillins; ANS, ansamycins; AMD, aminoglycoside; QUI, quinolone; POL, polymyxins; MAR, macrolide; C34, 3th−4th generation cephalosporins.

Supplementary Material 5 | Annual antimicrobial use sales by antimicrobial classes and by three metrics in each study district in Dong Thap province. x-axis: estimation of annual AMU sales (mg/kg) by three different metrics; y-axis, the surveyed districts in Dong Thap provinces; Blue, important antimicrobial group; Light Brown, highly important antimicrobial group; PCU, Population Correction Unit; AAI, active antimicrobial ingredient; Brown, high priority antimicrobial group; Red, highest priority antimicrobial group; PYP, polypeptides; PLE, pleuromutilins; AML, aminocyclitols; TET, tetracyclines; SUL, sulphonamides; PNS, penicillins (narrow spectrum); LIN, lincosamides; C12, 1st-2nd generation cephalosporins; AMP, amphenicols; PAD, phosphonic acid derivatives; APL, aminopenicillins; ANS, ansamycins; AMD, aminoglycoside; QUI, quinolone; POL, polymyxins; MAR, macrolide; C34, 3th−4th generation cephalosporins.

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