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Quantifying antimicrobial resistance in food-producing animals in North America

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The global misuse of antimicrobial medication has further exacerbated the problem of antimicrobial resistance (AMR), enriching the pool of genetic mechanisms previously adopted by bacteria to evade antimicrobial drugs. AMR can be either intrinsic or acquired. It can be acquired either by selective genetic modification or by horizontal gene transfer that allows microorganisms to incorporate novel genes from other organisms or environments into their genomes. To avoid an eventual antimicrobial mistreatment, the use of antimicrobials in farm animal has been recently reconsidered in many countries. We present a systematic review of the literature discussing the cases of AMR and the related restrictions applied in North American countries (including Canada, Mexico, and the USA). The Google Scholar, PubMed, Embase, Web of Science, and Cochrane databases were searched to find plausible information on antimicrobial use and resistance in food-producing animals, covering the time period from 2015 to 2024. A total of 580 articles addressing the issue of antibiotic resistance in food-producing animals in North America met our inclusion criteria. Different AMR rates, depending on the bacterium being observed, the antibiotic class being used, and the farm animal being considered, have been identified. We determined that the highest average AMR rates have been observed for pigs (60.63% on average), the medium for cattle (48.94% on average), and the lowest for poultry (28.43% on average). We also found that Cephalosporines, Penicillins, and Tetracyclines are the antibiotic classes with the highest average AMR rates (65.86%, 61.32%, and 58.82%, respectively), whereas the use of Sulfonamides and Quinolones leads to the lowest average AMR (21.59% and 28.07%, respectively). Moreover, our analysis of antibiotic-resistant bacteria shows that *Streptococcus suis* (*S. suis*) and *S. auerus* provide the highest average AMR rates (71.81% and 69.48%, respectively), whereas *Campylobacter spp.* provides the lowest one (29.75%). The highest average AMR percentage, 57.46%, was observed in Mexico, followed by Canada at 45.22%, and the USA at 42.25%, which is most probably due to the presence of various AMR control strategies, such as stewardship programs and AMR surveillance bodies, existing in Canada and the USA. Our review highlights the need for better strategies and regulations to control the spread of AMR in North America.

KEYWORDS

antibiotics, antimicrobial use, antimicrobial resistance, farm animals, food-producing animals, North America

1 Introduction

The increasing demand for meat around the globe has led to a significant rise in livestock breeding (Graham and Nachman, 2010; Chriki and Hocquette, 2020). Livestock are usually fed with drinkable water and food mixed with antimicrobial drugs (Sapkota et al., 2007; Brown et al., 2019). The availability and the use of antimicrobials have transmuted the practice of veterinary medicine (Lees et al., 2021; Schwarz et al., 2017; Drouillard, 2018; Prescott, 2017; Paulson et al., 2015). Several fatal animal infections have now become treatable as the antimicrobial use (AMU) has led to significant advances in global health, animal health, food safety, and food security. However, the abuse and misuse of antimicrobials have contributed significantly to the emergence and expansion of antimicrobial resistance (AMR), posing a serious threat to human and animal health as well as to the global ecosystem (Kahn, 2017; Mehrotra M, 2017; Thakur and Gray, 2019; McCubbin et al., 2021; Otto et al., 2022; Cobo-Angel and Gohar, 2022; Xu et al., 2022). Approximately, 700,000 people around the globe die every year because of antimicrobial misuse. It has been estimated that this number will increase to 10 million people by 2050 (O'Neill, 2016). According to Nathan (2020), the development of new antibiotics is declining, but the global antimicrobial consumption in food animals is accelerating. Several studies have shown that AMR of animal origin can be transmitted to humans through food production (Ribeiro et al., 2024; Martak et al., 2024) as well as to the environment (Graham et al., 2009; Fujita et al., 2022). Evidence linking AMR between animals and humans is particularly strong for common foodborne pathogens resistant to Quinolones, such as *Campylobacter spp.* and *Salmonella spp.* (Engberg et al., 2001). Nowadays, antimicrobial resistance became a major public health challenge, which requires deeper study and immediate action to combat it (World Health Organization, 2012). Van Boeckel et al. (2015) have discussed the relationships between AMU and AMR in farmed animals in a systematic review covering the period from 2000 to 2018. Following multiple international calls for urgent action, the North American countries (Canada, Mexico, and the USA) reacted to protect their population by introducing several antibiotic restriction policies discussed below.

The observation of antimicrobial use in farm animals in Canada started with the report of Health Canada in 2002 (Uses of Microbalances in Food Animals in Canada: Impact on Resistance and Human Health).¹ The Canadian Integrated Program for Antimicrobial Resistance (CIPARS) was launched

to better understand the antimicrobial resistance in livestock and its impact on human health. Since 2005, CIPARS has been publishing an annual report presenting the current situation in the field (Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS)).² In 2014, Health Canada announced some important actions, including the strict restriction and veterinary prescription of all antimicrobial drugs. Several actors have been engaged in these actions, including the Canadian Food Inspection Agency and Agriculture and Agri-Food Canada (Antimicrobial Resistance and Use in Canada: A Federal Framework for Action).³ In 2017, the Canadian government started working with provincial partners to monitor antimicrobial use. Since 2018, the importation and self-manufacturing of antimicrobials have been banned in Canada. These actions were supported by the Canadian Animal Health Institute.⁴ The exact restriction policy being applied in each case differs with respect to the Canadian province, which takes full responsibility for regulatory actions. For example, in Ontario, the College of Veterinarians of Ontario, in collaboration with veterinarians and farmers, has identified the standardization of laboratory reporting as a major AMR preventing priority (College of Veterinarians of Ontario, 2017). Other associations and voluntary organizations, as for example the Canadian Cattlemen's Association, have been also involved in the establishment of the AMR restriction policies. For instance, the Canadian chicken farms have been actively involved in this work due to the spread of ceftiofur-resistant *Salmonella Heidelberg* pathogen (Dutil et al., 2010).

A survey conducted between 2013 and 2015 in the United States showed that 88% of veterinarians are ignorant of any veterinary professional guidelines related to AMU and AMR, thus raising the government's concern about this issue (International Society for Companion Animal Infectious Diseases).⁵ The American Food and Drug Administration (FDA) Center for Veterinary Medicine proposed some suggestions specifying the duration of AMU in food and water under veterinary oversight and providing a comprehensive AMU data collection for companion animals, thus increasing AMU data sharing. We can mention that California was the first USA state that required the use of medically important antimicrobials (Antimicrobial Use and Stewardship (Aus) Program Report to the Legislature, California, USA, 2019). Moreover, the American Veterinary Medical Association (AVMA) created an antimicrobial committee made up of the American Animal Hospital Association (AAHA) and the American Association of Swine Veterinarians (AASV) (Antimicrobial Stewardship in Companion Animal Practice, 2015). AVMA's activities involve

Abbreviations: AMU, Antimicrobial use; AMR, Antimicrobial resistance; ARG, Antimicrobial resistance gene; *E. coli*, *Escherichia coli*; *C. jejuni*, *Campylobacter jejuni*; *S. aureus*, *Staphylococcus aureus*; *S. suis*, *Streptococcus suis*; *C. coli*, *Campylobacter coli*; WGS, Whole-genome sequencing; MLST, Multi-locus sequence typing; PCR, Polymerase Chain Reaction; PFGE, Pulse-field gel electrophoresis; qPCR, Quantitative PCR; NGS, Next generation sequencing; NAS, Non-aureus staphylococci; CI, Confidence Interval; STD, Standard Deviation.

1 <https://www.canada.ca/en/health-canada/services/drugs-health-products/reports-publications/veterinary-drugs/uses-antimicrobials-food-animals-canada-impact-resistance-human-health-health-canada-2002.html> (accessed June, 2024).

2 www.Canada.ca/en/public-health/services/surveillance/canadian-integrated-program-antimicrobial-resistance-surveillance-cipars/cipars-reports/2016-annual-report-summary.html (accessed March, 2024).

3 www.Canada.ca/en/public-health/services/antibiotic-antimicrobial-resistance/antimicrobial-resistance-use-Canada-federal-framework-action.html (accessed February, 2024).

4 <https://www.cahi-icsa.ca/policy-and-outreach/antimicrobial-stewardship> (accessed March, 2024).

5 Antimicrobial Use Guidelines (Davis, CA: ISCAID). Available online at: www.iscaid.org/ (accessed May, 2024).

creating and sharing guidelines as well as promoting stewardship for companion animal practice. Recently, a national veterinary regulation action plan for 2020–2025, intended to combat antibiotic-resistant bacteria and restrict the antimicrobial use in the United States, has been adopted by the Presidential Advisory Council (National Action Plan for Combating Antibiotic-Resistant Bacteria).⁶

In Mexico, a national initiative for the containment of antimicrobial resistance was endorsed by major medical, veterinary, and public health institutions to better control the situation with antimicrobial use in food-producing animals (Zaidi et al., 2015). This initiative consists in establishing of effective surveillance systems. Furthermore, the Mexican Ministry of Health issued a decree enforcing some regulations that require medical prescriptions.

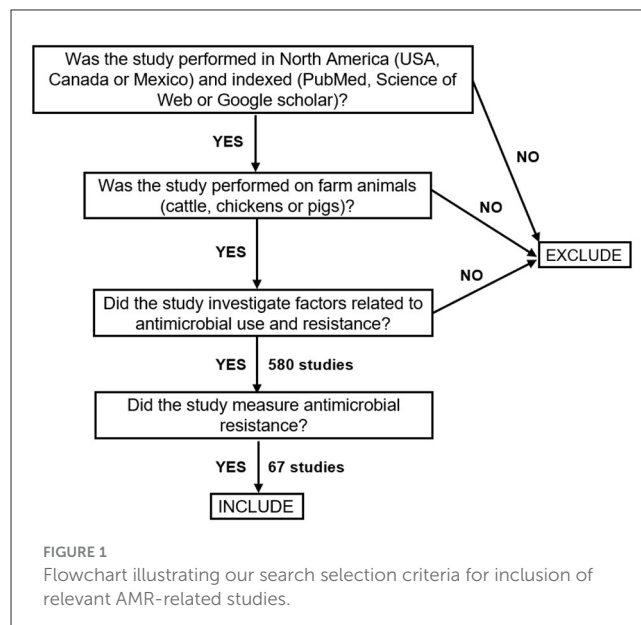
Several studies have been conducted regarding the global issue of antimicrobial resistance in farm animals, and different solutions have been proposed depending on national strategies and regulations maintained by each country. In this context, we will perform a meta-analysis to identify the main AMR trends typical for the three largest North American countries Canada, Mexico, and the USA.

2 Methods

2.1 Search strategy and selection criteria

Google Scholar, PubMed, EMBASE, MEDLINE, Web of Science Core Collection (Science Citation Index and Emerging Sources Citation Index), and Cochrane Library have been searched to gather information on antimicrobial resistance on North American farms. Articles written in English and covering the time period from 2015 to 2024 have been selected for our review study. Search terms for our investigation included the following keywords: “antibiotic(s)”, “antimicrobial(s)”, “food animals”, “food-producing animal”, “farm animal”, “environment”, “bacteria”, “virus”, “water”, “soil”, “manure heaps”, “ponds”, “barns”, “calf hutches”, “straw and other bedding”, “feed and feed trough”, “water and water troughs”, “farm equipment”, “ground and pasture”, “watercourses”, “USA”, “Canada”, “Mexico”, “cattle”, “poultry”, and “pig(s)”. The reference list of all plausible articles (published between 2015 and 2024) has been established, and the most cited articles have been considered first. In some cases, the authors, including students, professors, veterinarians, and experts in epidemiology have been contacted for some clarification about the results. The retained papers focused on the three types of food-producing animals: cattle, poultry, and pigs. As our study aims at quantifying and understanding the impact of AMR in North America, our search was limited to the studies concerning the three largest American countries: Canada, Mexico, and the USA. No search restrictions have been applied to bacterial species under study. Figure 1 shows the flowchart presenting our main search selection criteria.

6 www.hhs.gov/sites/default/files/carb-national-action-plan-2020-2025.pdf (accessed May, 2024).

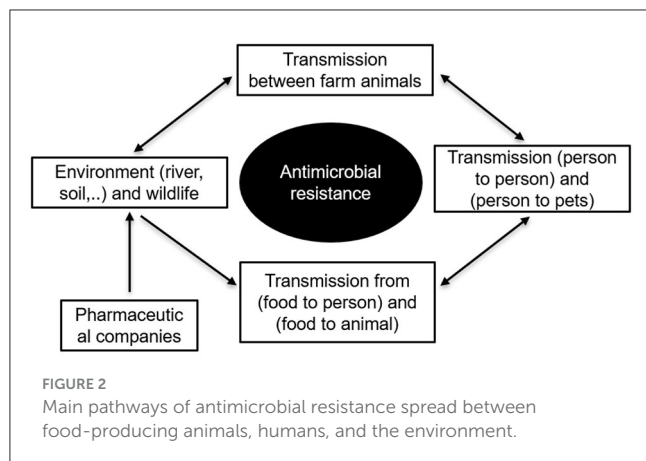


2.2 Data analysis

Different relevant meta-data were extracted from each of the selected papers, including: Country, farm animal(s), sample type (e.g., meat or fecal matter), sampling environment (e.g., river, soil, or feedlot), living animal specimen type (e.g., swab, nasopharynxes lungs and joints, blood, vaginal, paw, tissue, or saliva) or carcass specimen type (e.g., tissue or corpse). Meta-analysis has been conducted for food-producing animals only, and not for humans or the environment. Regarding food-producing animals, we limited our investigation to cattle (cow and bovine), poultry (chicken and turkey), and pigs. Regarding antimicrobials, the 11 following groups of antibiotic classes were considered: Penicillins, Tetracyclines, Sulphonamides, Macrolides, Pleuromutins, Lincosamides, Aminoglycosides, Amphenicols, Chloramphenicol, Cephalosporins, and Quinolones.

2.3 Main pathways of antimicrobial resistance

Minimizing the transmission of antibiotic-resistant bacteria remain a very relevant and challenging issue. Unfortunately, no universal solution has been proposed to solve it. Figure 2 presents the main pathways of antimicrobial resistance spread between animals, humans, and the environment. In many occasions, the transmission is direct, but some intermediate, often unknown, zoonotic hosts may also be involved in the chain of transmission. Direct contacts with animals can accelerate the spread of resistant bacteria as it was for example the case of the methicillin-resistant *Staphylococcus aureus* (*S. aureus*) bacterium isolated from the US swine population (Hau et al., 2017). Farmers, their families, and veterinarians are the most vulnerable people to be infected by antibiotic-resistant bacteria. These bacteria can be transferred to the food products at the stage of livestock slaughter as well.



Obviously, humans can be also contaminated by bacteria through the meat, if it is not cooked properly (Heiman et al., 2015; Christidis et al., 2020).

Bacteria that come from animals, which can be their healthy or asymptomatic carriers, are generally pathogenic for humans, increasing the human mortality rate (Smith et al., 2020; Anomaly, 2015; Dalton et al., 2020; Rodríguez-Medina et al., 2019). Moreover, unwashed fruits or vegetables can be another path of bacterial contamination (Rahman et al., 2021; Dharmarha et al., 2019; Godínez-Oviedo et al., 2023). Vegetables can be easily contaminated through human/animal feces or wastewater (Huang et al., 2015; Huijbers et al., 2015; Ibekwe et al., 2023). The environment often plays a connection role between different farm compartments, and especially between animals compost, soil, water, sediments, and sewage. Generally, antibiotics are used for therapeutic purposes and livestock receive antibiotics in their feed for disease prevention. According to many authors, the non-therapeutic use occurs later in animals, when they reach the feedlot (Veterinary Feed Directive (VFD)).⁷ Manure is the predominant propagation pathway of AMR in farms (Dungan et al., 2018). Table 1 presents some typical examples of antibiotic resistance genes (ARGs) detected on North American farm animals, the environments, and humans. We can observe that phenotypic and molecular characterization sequencing methods, such as Polymerase Chain Reaction (PCR) and Whole Genome Sequencing (WGS), have been widely used to identify ARGs. Such a variety of studies and methods being used reveal that North American countries are very concerned with AMR detected in livestock and search for effective solutions to address this important challenge. However, the sampling and design variation makes the comparison between the resulting data fairly complicated. The global expansion of the pharmaceutical industry, driven by the rising demand for antibiotics, plays a significant role in environmental challenges. Pharmaceutical wastewater contains high concentrations of antibiotics and antibiotic resistance genes, making these areas hotspots for environmental pollution and the spread of AMR. Poor treatment and improper discharge of such wastewater into the environment result in significant antibiotic

contamination, whereas its prolonged presence in the environment can alter bacterial genomes, contributing to the rise and spread of AMR (Kotwani et al., 2021).

3 Results

A total of 580 articles met the inclusion criteria mentioned above. Most of these studies discuss the use of antimicrobials and the resistance to them with respect to sample type. Table 2 presents the classification of data collections according to sample type and approach used for data analysis. The data available in this table suggest that 34% of studies have been based on the analysis of fecal or urine material used as a sample for AMR analysis. Moreover, 92% of the selected studies have been based on a laboratory analysis as an approach to detect antimicrobial resistance. We also report typical cases of antimicrobial resistance in Canada, the USA, and Mexico which were taken from the 67 articles (taken from the original list of 580 articles) that provided numerical estimates of antimicrobial resistance on North American farms. Tables 3–5, based on these 67 studies, present the AMR estimates (shown in percentages) reported for the 10 most frequent bacterial types detected and the 11 most used antibiotic classes used on North American farms. We can observe that *E. coli* and *Salmonella* were the most frequent bacteria affecting North American livestock in terms of AMR, and Penicillins and Tetracyclines were among the most used antibiotic classes triggering AMR.

Comparing the average AMR rates across the three largest North American countries (see Tables 3–6 as well as Figures 3–5), one can observe the following trends: Regarding cattle, the USA have the lowest average AMR rate of 35.67%, followed by Canada with the average AMR rate of 49.60%, and Mexico with the highest average AMR rate of 64.45%. In contrast, in pig farming, Canada shows the highest average AMR rate of 67.86%, compared to Mexico with 55.80%, and the USA with 57.62%. Finally, for poultry, Canada shows the lowest average AMR rate at 25.31%, while the USA and Mexico have much higher average AMR rates of 42.96% and 42.45%, respectively. The related confidence intervals of the observed AMR cases are generally much longer for cattle than for pigs, and especially than for poultry that provide the lowest estimates. Obviously, the observed AMR rate depends highly on the antibiotic type being used and the bacterium being treated.

Furthermore, we conducted a detailed analysis to compare separately, for cattle, poultry, and pigs raised on North American farms, the average AMR rates per antibiotic class (Figure 4) and per bacterium being treated (see Figure 5). A 90% confidence interval (CI) was calculated for each AMR estimate considered.

Figure 4 illustrates the average AMR rates for each antibiotic class in cattle (a), poultry (b), and pigs (c) farms across North America. For cattle, the highest value of antibiotic resistance is observed with Cephalosporins – 71.42% on average [90% CI: 56.62% to 86.22%], for poultry, the highest AMR is observed with Tetracyclines – 51.21% on average [90% CI: 43.94% to 58.48%], while for pigs, the highest AMR is found with Penicillins – 74.7% on average [90% CI: 58.51% to 90.89%].

⁷ www.fda.gov/animalveterinary/development-approval-process/veterinary-feed-directive-vfd

TABLE 1 Typical examples of antimicrobial resistance genes (ARG) detected in animals, the environment, and humans (for studies conducted in Canada, the USA, and Mexico).

Country	Methodology	AMR genes			Reference
		Animals	Environment	Humans	
Canada	WGS	blaCMY-2, aac(3)-VIa, aac(3)-IIId ant(2'')-Ia, aac(6')-Ib3, ant(3'')-Ia aadA2,aadA2		blaCTX-M, blaCMY-2, aac(3)-VIa, aac(3)-IIId aac(3)-Id, aac(3)IIa, ant(2'')-Ia aac(6')-Ib-cr, ant(3'')-Ia, aadA2 aadA7, aadA1, aadA17, aadA5 aadA22	(Cox et al., 2021)
	WGS	erm(B, tet(M), ant(6)-Ia, aph(3')-IIIa, sat4, tet(L), tet(M, bcrB, bcrC	erm(B), tet(M), ant(6)-Ia, aph(3')-IIIa, sat, tet(L), tet(M), ant(6)-Ia, sat4, aph(3')-IIIa		(Zaheer et al., 2020)
	qPCR		erm(A), erm(B), erm(F), erm(X), sul(1), sul(2),tet(B), tet(C), tet(H), tet(L), tet(M), tet(W)		(Holman et al., 2016)
	PCR	blaCTX-M, blaCMY-2, blaSHV, blaTEM, qnrB, qnrS			(Awosile et al., 2018)
	WGS	VmacAB, IbblaCMY-2	M,Baph(6)-Id, aph(6)-Id, tet(C) E2,J25bmrA, M,VblaCTX-M-55		(Cameron et al., 2019)
	qPCR		tet(B), tet(C), tet(L), tet(M), tet(W), erm(A),erm(B), erm(F), erm(X), sul(1), and sul(2).		(Xu et al., 2016)
	NGS	TETA, TETB, TET32, TETW, TET40, TET44, TETO, TETQ, TETX, MEFA, LNUC, APH3',ANT6, CFX, ACI	TETA, TETB, TET32, TETW, TET40, TET44, TETO, TETQ, TETX, MEFA, LNUC, APH3', ANT6, CFX, ACI, TETH, TET36, TETZ, TETS, TETT, APH6, MPHE,MPHB, MSRD ERMA, MPHE, MEL, ERM, ERM, ERM		(Zaheer et al., 2019)
	PCR, WGS	blaCTX-M-55, blaCTX-M-32, blaCTX-M-27 blaCTX-M-15, blaCTX-M-14	blaCTX-M-55, blaCTX-M-32 blaCTX-M-27, blaCTX-M-15, blaCTX-M-14		(Cormier et al., 2020)
USA	WGS		blaIMP-27		(Mollenkopf et al., 2017)
	PCR		mphA, aadA, aphA1, blaTEM, tet(B), strA, penA, ampC, lde, ermB, tet(O), aadB, blaOXA-61, tet(O), and aadE		(Hailu et al., 2021)
	WGS	aac(6)-Iaa, PBR, floR, CMY, tet (A), tet (R) sul2, strA, strB, aadA, sul1, aph(3'')-Ia, tet(A) tet(R), aadA, dfrA, blaTEM-1D		aac(6)-Iaa, PBR, floR CMY, tet(A) tet(R), sul2, strA, strB, aadA, sul1 aph (3'')-Ia, aadA, dfrA, blaTEM-1D	(Carroll et al., 2017)
	WGS	blaCMY-2, blaCMY-130, blaCMY-132,blaTEM-1A, blaTEM-1B,blaTEM-150, floR, cmlA5, qnrB19, ant(2'')-Ia, aph(3'')-Ib, aph(6)-Id (strB), aph(3')-Ia,sul1, sul2, tetA			(Srednik et al., 2021)
	PCR, PFGE		blaCMY-2		(Hsieh et al., 2016)
Mexico	PCR	tetA, tetB, strA, aadA, blaTEM, blaSHV			(Martínez-Vázquez et al., 2021)
	PCR		blaCTX-M9, blaTEM blaCTX-M151, blaCTX-M1-8 blaCTX-M-9,aac(6')-IB-cr, qepA		(Enciso-Martínez et al., 2022)
	PCR	blaCMY		blaCMY	(Aguilar-Montes de Oca et al., 2018)

TABLE 2 Main sample types and approaches considered to investigate antimicrobial use and resistance on North American farms.

Sample type	Approach	Number of studies
Animal food (meat, milk, eggs, ...)	Laboratory analysis of antimicrobial susceptibility and resistance	144
Environment (water, soil, manure, litter and feedlot)	Laboratory analysis	123
Fecal matter, urine	Laboratory analysis	197
Living animal (swab, nasopharynxes lungs and joints, blood, vaginal, paw, tissue, saliva) or Carcass (tissue, corpse,...)	Laboratory analysis	71
	Discussions and in-depth observations, group discussions, and interviews	45

Figure 5 shows the average AMR rates per bacterium, characteristic for the cattle (a), poultry (b), and pig (c) farms in North America. The highest AMR for cattle is found with *S. aureus* – 69.02% on average [90% CI: 55.2% to 82.84%], for poultry, the highest AMR percentage is found with *Enterococcus* – 42.0% on average [90% CI: 34.26% to 49.74%], while for pigs, the highest AMR is observed with *Streptococcus suis* (*S. suis*) – 71.91% on average [90% CI: 53.45% to 90.37%].

Moreover, we determined that the highest average AMR rates have been observed for pigs – 60.63%, on average, the medium for cattle – 48.94%, on average, and the lowest for poultry – 28.43%, on average. The presented results indicate that Cephalosporines, Penicillins, and Tetracyclines are the antibiotic classes with the highest average AMR rate – 65.86%, 61.32%, and 58.82%, respectively, whereas the use of Sulfonamides and Quinolones leads to the lowest average AMR – 21.59% and 28.07%, respectively. Regarding antibiotic-resistant bacteria, we found that *S. suis* and *S. aureus* provide the highest average AMR rates – 71.81% and 69.48%, respectively, while *Campylobacter* spp. provides the lowest average AMR of 29.75%.

Table 6 reports the average AMR rates along with the corresponding standard deviations (STD) and 90% confidence intervals (CI) obtained for the 2015–2024 time period. The most important AMR percentage variations are observed for Cattle, followed by Pigs, and then by Poultry that correspond to the lowest AMR scores and STD values.

Figure 3a presents the average AMRs over two-year periods (from 2015 to 2024) in North American farms. The averages were calculated over all types of livestock and antimicrobials considered. We can observe an important trend consisting in the decrease of an average AMR from 57.5 % in 2015–2016 to 39.25% in 2019–2020. However, this trend was reversed in 2021–2022 and 2023–2024 as the AMR rate increased again, reaching the level of 52%. Figure 3b illustrates the spatial AMR pattern characteristic for North American food-producing animal farms. The highest average AMR percentage, 57.46%, was observed in Mexico, followed by Canada at 45.22%, and the USA at 42.25%. This trend can be explained by a better AMR control, carried out through different programs and strategies

discussed above, existing in Canada and the USA, compared to Mexico.

4 Discussion

Nowadays, the use of antibiotics on farms to prevent bacterial propagation is a topic of discussion around the world (Holmes et al., 2016; Wu et al., 2023; Galiot et al., 2023; Mohsin et al., 2023; Gao et al., 2023). Obviously, antibiotics given to livestock have the benefits of treating, reducing, and preventing bacterial infections. However, the downside is also evident. Antibiotics impose strong selective pressure on microbial populations so that their excessive use in food-producing animals makes the targeted bacteria not only resistant to antimicrobials but also transferable to humans, thus contributing to the emergence of new antibiotic-resistant human pathogens (e.g., antibiotic-resistant bacteria can be easily transferred to humans through the consumption of meat, fruits, or vegetables) (O'Neill, 2016; Manyi-Loh et al., 2018; Salam et al., 2023; Kaur et al., 2024).

Several studies have suggested that AMU in animals can bring resistance to various zoonotic pathogens (Dutil et al., 2010; Rhouma et al., 2021; Innes et al., 2020; Huber et al., 2021; Ekakoro et al., 2019; Léger et al., 2022). Moreover, the transmission of antibiotic-resistant bacteria can go in the opposite direction, i.e., from humans to animals. This kind of transmission is much less studied, however. Some recent works in the field have been devoted to the investigation of different cases of human-to-animal transmission of antimicrobial resistance, involving pets (Haenni et al., 2012; Redding et al., 2023; Roken et al., 2022) and livestock (Khanna et al., 2008). Yet, AMR can be transmitted from humans to animals, and then be back to humans. Weese et al. indicated the presence of human clones of methicillin-resistant *S. aureus* in horses (Weese et al., 2005). Dierikx et al. discussed the presence of common human clones of multidrug-resistant *Enterococcus* in pets (Dierikx et al., 2012). Several recent studies argued that AMU in different animals can contribute to AMR to several animal pathogens (Beck et al., 2012; Agunos et al., 2019; Pinto et al., 2023; Ida et al., 2023; Ekhlal et al., 2023). A number of recent studies discussed the facts of transmission of antimicrobial resistance genes from animals to soil pathogens through manure and wastewater irrigation (Sanchez et al., 2016; Williams-Nguyen et al., 2016; Scott et al., 2018; Murray et al., 2019; Mays et al., 2021). For instance, antimicrobial resistance genes in surface and groundwater can propagate to indigenous organisms through horizontal gene transfer (HGT) (Boc and Makarenkov, 2011; Gou et al., 2018; Makarenkov et al., 2021). According to Dungan et al. (2018), manure containing antibiotic resistance genes (ARGs) is the most important propagation pathway in the environment. According to Qian et al. (2018), pig and chicken manures show a greater ARG diversity than cow manures. This can be explained by the fact that over their lifetime pigs and chickens usually receive a higher dosage of antibiotics than cows (Dunlop et al., 1998; Dewey, 1999). However, no qualitative or quantitative studies have been conducted so far to explain in detail the relationships between AMU and the emergence of ARG.

Today, many public and governmental organizations in North America continue to argue for reducing the use of antibiotics in

TABLE 3 Typical cases of antimicrobial resistance (AMR) on Canadian farms (cattle, poultry, and pigs).

Livestock	Antibiotic class	Active ingredient	Bacterium	(%) AMR	Sample type	Reference
Cattle	Penicillins	Ampicillin	<i>E. coli</i>	11.5	Mastitis	(Majumder et al., 2021)
		Ampicillin	<i>E. coli</i>	98.0	Manure	(Massé et al., 2023)
	Tetracyclines	Tetracycline	<i>E. coli</i>	26.0	Fecal	(Massé et al., 2021)
		Oxytetracycline	<i>S.aureus</i>	96.0	Milk	(Awosile et al., 2018)
		Doxycycline	<i>Enterococcus</i>	31.0	Fecal	(Davedow et al., 2020)
		Tetracycline	<i>E. coli</i>	15.9	Mastitis	(Majumder et al., 2021)
		Tetracycline	<i>E. coli</i>	80.0	Manure	(Massé et al., 2023)
		Tetracycline	<i>Salmonella</i>	17.0	Fecal	(Fonseca et al., 2023)
		Sulfisoxazole	<i>Salmonella</i>	13.0	Fecal	(Fonseca et al., 2023)
	Sulphonamides	Sulfisoxazole	<i>E. coli</i>	23.0	Fecal	(Massé et al., 2021)
		sulfonamide	<i>S.Aureus</i>	7.0	milk	(Naushad et al., 2020)
		Sulfisoxazole	<i>E. coli</i>	88.0	Manure	(Massé et al., 2023)
	Macrolides	Tylosin	<i>Enterococcus</i>	86.0	Fecal	(Davedow et al., 2020)
		Clindamycin	NAS	4.0	Milk	(Nobrega et al., 2018a)
		Erythromycin	NAS	100.0	Milk	(Nobrega et al., 2018b)
		Clindamycin	NAS	99.9	Milk	(Nobrega et al., 2018b)
		Erythromycin	NAS	8.0	Milk	(Nobrega et al., 2018a)
		Erythromycin	<i>Enterococcus</i>	84.0	Fecal	(Davedow et al., 2020)
	Aminoglycosides	Streptomycin	<i>E. coli</i>	19.0	Fecal	(Massé et al., 2021)
		Kanamycin	<i>E. coli</i>	15.0	Fresh colostrum	(Awosile et al., 2017)
		Streptomycin	<i>E. coli</i>	20.0	Fresh colostrum	(Awosile et al., 2017)
		Streptomycin	<i>E. coli</i>	17.7	Mastitis	(Majumder et al., 2021)
		Streptomycin	<i>E. coli</i>	73.8	Fecal	(Adator et al., 2022)
		Neomycin	<i>E. coli</i>	3.7	Fecal	(Adator et al., 2022)
		streptomycin	<i>Campylobacter</i>	3.0	Fecal	(Waldner et al., 2019)
		Streptomycin	<i>Salmonella</i>	13.0	Fecal	(Fonseca et al., 2023)
	Cephalosporins	Ceftriaxone	<i>E. coli</i>	90.0	Manure	(Massé et al., 2023)
		Ceftriaxone	<i>E. coli</i>	80.0	Fresh colostrum	(Awosile et al., 2017)
		Cephalosporin	<i>E. coli</i>	80.0	fecal	(Salaheen et al., 2019)
		Ceftiofur	<i>E. coli</i>	80.0	Fresh colostrum	(Awosile et al., 2017)
		Cefoxitin	<i>E. coli</i>	100.0	Fresh colostrum	(Awosile et al., 2017)
		Ceftiofur	<i>E. coli</i>	70.2	Manure	(Adator et al., 2022)
		Ceftiofur	<i>E. coli</i>	84.0	Manure	(Massé et al., 2023)
Poultry	Penicillins	Ampicillin	<i>E. coli</i>	16.0	Cecal	(Varga et al., 2019)
		Ampicillin	<i>E. coli</i>	44.0	Broiler	(Varga et al., 2018)
		Beta-lactam	<i>E. coli</i>	31.2	Fecal	(Shrestha et al., 2022)
	Tetracyclines	Tetracycline	<i>E. coli</i>	43.0	Fecal	(Varga et al., 2019)
		Tetracycline	<i>Salmonella</i>	42.9	Cecal	(Romero Barrios et al., 2020)
		Tetracycline	<i>Campylobacter</i>	39.0	Slaughterhouse	(Draméet al., 2020)
		Tetracycline	<i>Campylobacter</i>	48.1	Retail meats	(Narvaez-Bravo et al., 2017)
		Tetracycline	<i>E. coli</i>	57.0	Broiler	(Varga et al., 2018)
		Tetracycline	<i>E. coli</i>	61.7	Fecal	(Shrestha et al., 2022)

(Continued)

TABLE 3 (Continued)

Livestock	Antibiotic class	Active ingredient	Bacterium	(%) AMR	Sample type	Reference
	Sulphonamides	Sulphonamide	<i>E. coli</i>	17.0	Cecal	(Varga et al., 2019)
		Sulfisoxazole	<i>Salmonella</i>	6.2	Cecal	(Romero Barrios et al., 2020)
		Sulfamethoxazole	<i>E. coli</i>	18.0	Broiler	(Varga et al., 2018)
	Macrolides	Azithromycin	<i>Campylobacter</i>	1.78	Retail meats	(Narvaez-Bravo et al., 2017)
		Erythromycin	<i>Campylobacter</i>	1.78	Retail meats	(Narvaez-Bravo et al., 2017)
	Aminoglycosides	Streptomycin	<i>E. coli</i>	29.0	Cecal	(Varga et al., 2019)
		Gentamicin	<i>Salmonella</i>	2.1	Cecal	(Romero Barrios et al., 2020)
		Streptomycin	<i>Salmonella</i>	41.5	Cecal	(Romero Barrios et al., 2020)
		Gentamicin	<i>E. coli</i>	50.0	Broiler	(Varga et al., 2018)
		Kanamycin	<i>E. coli</i>	11.0	Broiler	(Varga et al., 2018)
		Apramycin	<i>E. coli</i>	3.0	Broiler	(Varga et al., 2018)
		Aminoglycoside	<i>E. coli</i>	45.0	Fecal	(Shrestha et al., 2022)
	Cephalosporins	Ceftriaxone	<i>Salmonella</i>	31.4	Cecal	(Romero Barrios et al., 2020)
		Ceftiofur	<i>E. coli</i>	15.0	Broiler	(Varga et al., 2018)
	Quinolones	quinolone	<i>Campylobacter</i>	3.5	slaughterhouse	(Draméet al., 2020)
		Ciprofloxacin	<i>Campylobacter</i>	5.5	Retail meats	(Narvaez-Bravo et al., 2017)
		Nalidixic acid	<i>Campylobacter</i>	5.5	Retail meats	(Narvaez-Bravo et al., 2017)
Pigs	Penicillin	ampicillin	<i>E.coli</i>	100.0	diseased pigs	(Jahanbakhsh et al., 2016b)
		amoxicillin	<i>E.coli</i>	96.5	diseased pigs	(Jahanbakhsh et al., 2016b)
	Tetracyclines	tetracycline	<i>S. suis</i>	84.2	Nasal and vaginal swabs	(Arndt et al., 2019)
		tetracycline	<i>S. suis</i>	98.0	different sites of pigs	(Aradanas et al., 2021)
	Macrolides	Macrolide	<i>S. suis</i>	90.0	Different sites of pigs	(Aradanas et al., 2021)
	Aminoglycosides	Spectinomycin	<i>S. suis</i>	40.4	Nasal and vaginal swabs	(Arndt et al., 2019)
		Streptomycin	<i>E. coli</i>	89.4	Diseased pigs	(Jahanbakhsh et al., 2016b)
		Streptomycin	<i>E. coli</i>	91.6	Fecal	(Jahanbakhsh et al., 2016a)
		Gentamicin	<i>E. coli</i>	84.0	Diseased pigs	(Jahanbakhsh et al., 2016b)
		Kanamycin	<i>E. coli</i>	50.6	Diseased pigs	(Jahanbakhsh et al., 2016b)
	Cephalosporins	Cefoxitin	<i>E.coli</i>	96.5	Diseased pigs	(Jahanbakhsh et al., 2016a)
		Cefoxitin	<i>E.coli</i>	20.0	Diseased pigs	(Jahanbakhsh et al., 2015)
		Ceftriaxone	<i>E.coli</i>	20.0	Diseased pigs	(Jahanbakhsh et al., 2015)
		Ceftiofur	<i>E.coli</i>	20.0	Diseased pigs	(Jahanbakhsh et al., 2015)
		Ceftiofur	<i>E.coli</i>	100.0	Diseased pigs	(Jahanbakhsh et al., 2016b)
	Quinolone	Nalidixic acid	<i>E.coli</i>	4.7	Different sites of pigs	(Jahanbakhsh et al., 2016b)

TABLE 4 Typical cases of antimicrobial resistance (AMR) on the US farms (cattle, poultry, and pigs).

Livestock	Antibiotic class	Active ingredient	Bacterium	(%) AMR	Sample type	Reference
Cattle	Penicillins	beta lactam	<i>Salmonella</i>	85.0	Living animal and fecal	(Srednik et al., 2021)
		Pencillin	<i>S. aureus</i>	63.2	Beef	(Rao et al., 2021)
		Ampicillin	<i>E. coli</i>	100.0	Fecal	(Morris et al., 2023)
		Ampicillin	<i>Enterococcus</i>	0.4	Fecal	(Morris et al., 2023)
	Tetracyclines	Tetracycline	<i>E. coli</i>	27.5	Fecal	(Jeamsripong et al., 2021)
		tetracycline	<i>Campylobacter</i>	88.1	Feedlot	(Tang et al., 2017b)
		tetracycline	<i>E. coli</i>	74.8	Feedlot	(Tang et al., 2017b)
		tetracycline	<i>Salmonella</i>	21.74	Fecal	(Dargatz et al., 2016)
	Sulphonamides	sulphonamide	<i>E. coli</i>	22.5	Fecal	(Jeamsripong et al., 2021)
		sulphadimethoxine	<i>S.aureus</i>	25.0	Milk	(Abdi et al., 2018)
		sulphadimethoxine	<i>E. coli</i>	32.4	Fecal	(Abdelfattah et al., 2021)
		sulfadimethoxine	<i>E. coli</i>	25.4	fecal	(Morris et al., 2023)
		Sulfisoxazole	<i>Salmonella</i>	12.4	Fecal	(Dargatz et al., 2016)
	Macrolides	Macrolide	<i>Enterococcus</i>	77.6	Fecal	(Jeamsripong et al., 2021)
		Macrolide	<i>Salmonella</i>	77.0	Manure	(Hailu et al., 2021)
		Macrolide	<i>E.coli</i>	73.0	Manure	(Hailu et al., 2021)
		Erythromycin	<i>S. aureus</i>	15.8	Beef	(Rao et al., 2021)
		Erythromycin	<i>Enterococcus</i>	14.9	Retrail	(Tate et al., 2021)
		Azithromycin	<i>C. jejuni</i>	0.3	Feedlot	(Tang et al., 2017b)
		Azithromycin	<i>E.coli</i>	0.04	Fecal	(Levent et al., 2022)
		Clindamycin	<i>C. jejuni</i>	0.3	Feedlot	(Tang et al., 2017b)
		Clindamycin	<i>C. coli</i>	4.3	Feedlot	(Tang et al., 2017b)
		Azithromycin	<i>C. coli</i>	0.0	Feedlot	(Tang et al., 2017b)
		Erythromycin	<i>C. jejuni</i>	0.3	Feedlot	(Tang et al., 2017b)
	Aminoglycosides	Aminoglycoside	<i>Salmonella</i>	95.0	Living animal and fecal	(Srednik et al., 2021)
		Streptomycin	<i>E. coli</i>	49.45	Retrail	(Tate et al., 2021)
		Aminoglycoside	<i>E. coli</i>	7.2	Fecal	(Doster et al., 2022)
		Streptomycin	<i>Enterococcus</i>	19.0	Retrail	(Tate et al., 2021)
	Cephalosporins	Ceftiofur	<i>E. coli</i>	0.4	Fecal	(Morris et al., 2023)
	Quinolones	ciprofloxacin	<i>C. jejuni</i>	35.6	Feedlot Cattle	(Tang et al., 2017b)
		Quinolone	<i>C. coli</i>	60.0	Retail meat	(Hull et al., 2021)
		Ciprofloxacin	<i>C. coli</i>	74.4	Feedlot cattle	(Tang et al., 2017b)
		Nalidixic acid	<i>C. jejuni</i>	34.3	Feedlot cattle	(Tang et al., 2017b)
		Nalidixic acid	<i>C. coli</i>	82.6	Feedlot cattle	(Tang et al., 2017b)
Poultry	Penicillin	Penicillin	<i>C. coli</i>	63.6	Fresh poultry products	(Hull et al., 2021)
	Tetracyclines	Tetracycline	<i>Salmonella</i>	63.0	Cloacal swabs	(Velasquez et al., 2018)
		Tetracycline	<i>C. coli</i>	64.3	Fresh poultry products	(Hull et al., 2021)
		Tetracycline	<i>Salmonella</i>	13.9	Environment and carcasses	(Liljebyelke et al., 2017)
		Tetracycline	<i>Salmonella</i>	76.0	broiler farm	(Rama et al., 2022)
		Tetracycline	<i>Salmonella</i>	52.17	Retail chicken	(Lee et al., 2018)

(Continued)

TABLE 4 (Continued)

Livestock	Antibiotic class	Active ingredient	Bacterium	(%) AMR	Sample type	Reference
	Macrolides	Macrolide	<i>C. coli</i>	34.8	Cloacal swabs	(Velasquez et al., 2018)
	Aminoglycosides	Aminoglycoside	<i>C. coli</i>	38.6	Fresh poultry products	(Hull et al., 2021)
		Streptomycin	<i>Salmonella</i>	30.9	Environment and carcasses	(Liljebjelke et al., 2017)
		Gentamicin	<i>Salmonella</i>	12.6	Environment and carcasses	(Liljebjelke et al., 2017)
		Streptomycin	<i>Salmonella</i>	70.0	Broiler farm	(Rama et al., 2022)
		Streptomycin	<i>Salmonella</i>	52.17	Retail chicken	(Lee et al., 2018)
	Quinolones	nalidixic acid	<i>Salmonella</i>	5.0	Cloacal swabs	(Velasquez et al., 2018)
		Quinolone	<i>C. coli</i>	24.4	Fresh poultry products	(Hull et al., 2021)
Pigs	Pencillin	Ampicillin	<i>E. coli</i>	21.1	cecal	(Sodagari and Varga, 2023)
		penicillin	<i>S. aureus</i>	72.0	Fecal	(Beier et al., 2021)
	Tetracyclines	Tetracycline	<i>Salmonella</i>	57.6	Manure and soil	(Pornsukarom and Thakur, 2016)
		tetracycline	<i>S. suis</i>	97.0	Swine	(Nicholson and Bayles, 2022)
		Tetracycline	<i>E. coli</i>	65.3	Cecal	(Sodagari and Varga, 2023)
		Tetracycline	<i>S. aureus</i>	50.0	Pig pens	(Randad et al., 2021)
	Sulphonamides	Sulfisoxazole	<i>Salmonella</i>	67.2	Manure and soil	(Pornsukarom and Thakur, 2016)
	Macrolides	Tilmicosin	<i>S. aureus</i>	78.5	Nasal swabs and environment	(Hau et al., 2018)
		Macrolide	<i>S. suis</i>	72.0	Swine	(Nicholson and Bayles, 2022)
		Macrolide	<i>S. aureus</i>	56.0	Pig pens	(Randad et al., 2021)
	Aminoglycosides	Streptomycin	<i>Salmonella</i>	88.3	Manure and soil	(Pornsukarom and Thakur, 2016)
		Streptomycin	<i>E. coli</i>	20.4	Cecal	(Sodagari and Varga, 2023)
		Aminoglycoside	<i>S. aureus</i>	62.0	Pig pens	(Randad et al., 2021)
	Cephalosporins	Ceftiofur	<i>E. coli</i>	82.1	Diseased pigs	(Hayer et al., 2020b)
		Ceftiofur	<i>E. coli</i>	34.1	Diseased pigs	(Hayer et al., 2020a)
	Quinolones	Enrofloxacin	<i>E. coli</i>	81.8	Diseased pigs	(Hayer et al., 2020b)
		Quinolone	<i>S. suis</i>	21.8	Pig	(Hayer et al., 2020b)
		Quinolone	<i>Salmonella</i>	10.1	Pig	(Pires et al., 2021)

livestock. According to Moreno (2012), a referendum involving 1,000 US residents showed that 72% of them were apprehensive about the excess of antibiotics in animal feed. In 2012, the US Food and Drug Administration forbade unapproved doses of cephalosporins (Cephalosporin Order of Prohibition Goes Into Effect).⁸ Still in 2012, Barbara Sibbald (Deputy Editor of Canadian Medical Association journal) raised a danger alert for stricter regulations on antibiotic use in farm animals in Canada

⁸ www.albertaanimalhealthsource.ca/content/cephalosporin-order-prohibition-goes-effect (accessed March, 2024).

(Sibbald, 2012). In the province of Quebec (Canada), the resistance of porcine *Escherichia coli* (*E. coli*) isolates to ceftiofur has increased from 0% in 1994 to 20% in 2011 (*Surveillance de l'antibiorésistance-Rapport Annuel*, 2011). Moreover, according to Park et al. (2013), 97% of the *Staphylococcus hyicus* isolates from pigs in the province of Ontario (Canada) have been resistant to penicillin G and ampicillin, whereas 71% of these isolates have been resistant to ceftiofur. A study conducted in the USA in 2023 revealed that *Salmonella* found in American poultry show a high resistance (73.1% on average) to multiple antibiotics, including fluoroquinolones and extended-spectrum cephalosporins. It poses

TABLE 5 Typical cases of antimicrobial resistance (AMR) on Mexican farms (cattle, poultry, and pigs).

Livestock	Antibiotic class	Active ingredient	Bacterium	(%) AMR	Sample type	Reference
Cattle	Penicillins	Penicillin G	<i>S. aureus</i>	36.8	Composite milk and hand swabs	(Salgado-Ruiz et al., 2015)
		ampicillin	<i>S. aureus</i>	83.3	milk	(Guzmán-Rodríguez et al., 2021)
		Oxacillin	<i>S. aureus</i>	36.6	milk	(Guzmán-Rodríguez et al., 2021)
		Penicillin	<i>S. aureus</i>	100.0	Milk	(Varela-Ortiz et al., 2018)
		Ampicillin	<i>Salmonella</i>	40.9	Fecal, carcass, cut and ground beef	(Delgado-Suárez et al., 2019)
		Carbenicillin	<i>Salmonella</i>	29.5	Fecal, carcass, cut and ground beef	(Delgado-Suárez et al., 2019)
		Benzylpenicillin	<i>S. aureus</i>	97.0	milk	(Mora-Hernández et al., 2021)
		Ampicillin	<i>E. coli</i>	94.0	Irrigation water, harvesting melons, hands of workers. and boxes	(Enciso-Martínez et al., 2022)
		Ampicillin	<i>E. coli</i>	83.0	Feces and carcass	(Martínez-Vázquez et al., 2021)
		Ampicillin	<i>Salmonella</i>	94.73	Retail beef	(Nova Nayarit-Ballesteros et al., 2016)
		Carbenicillin	<i>Salmonella</i>	84.21	Retail beef	(Nova Nayarit-Ballesteros et al., 2016)
	Tetracyclines	Tetracycline	<i>S. aureus</i>	77.0	Cow Milk	(Varela-Ortiz et al., 2018)
		Tetracycline	<i>Salmonella</i>	90.9	Fecal, carcass, cut and ground beef	(Delgado-Suárez et al., 2019)
		tetracycline	<i>E. coli</i>	69.0	Fecal, carcass, cut and ground beef	(Martínez-Vázquez et al., 2021)
		Tetracycline	<i>Salmonella</i>	40.2	Fecal	(Maradiaga et al., 2019)
		Tetracycline	<i>E. coli</i>	86.6	Fecal	(Mandujano et al., 2023)
		Tetracycline	<i>Salmonella</i>	68.42	Retail beef	(Nova Nayarit-Ballesteros et al., 2016)
	Aminoglycosides	Streptomycin	<i>Salmonella</i>	36.3	Fecal, carcass, cut and ground beef	(Delgado-Suárez et al., 2019)
		Streptomycin	<i>E.coli</i>	83.3	Fecal	(Mandujano et al., 2023)
		Aminoglycoside	<i>Salmonella</i>	7.8	Lymph nodes	(Delgado-Suárez et al., 2021)
		Gentamicin	<i>E. coli</i>	93.3	Fecal	(Mandujano et al., 2023)
	Cephalosporins	Cephalothin	<i>S. aureus</i>	100.0	cow Milk	(Varela-Ortiz et al., 2018)
		Cephalothin	<i>E. coli</i>	76.0	Feces and carcass	(Martínez-Vázquez et al., 2021)
		Cefotaxime	<i>S. aureus</i>	86.6	Milk	(Guzmán-Rodríguez et al., 2021)
		ceftazidime	<i>S. aureus</i>	80.0	Milk	(Guzmán-Rodríguez et al., 2021)
		Ceftazidime	<i>E. coli</i>	1.3	Carcasse	(Aguilar-Montes de Oca et al., 2015)
	Quinolones	Nalidixic acid	<i>E. coli</i>	64.0	Carcasse	(Aguilar-Montes de Oca et al., 2015)

(Continued)

TABLE 5 (Continued)

Livestock	Antibiotic class	Active ingredient	Bacterium	(%) AMR	Sample type	Reference
Poultry		Ciprofloxacin	<i>E. coli</i>	10.0	carcasse	(Aguilar-Montes de Oca et al., 2015)
		Nalidixic acid	<i>Salmonella</i>	21.1	Fecal	(Maradiaga et al., 2019)
	Penicillins	Ampicillin	<i>E. coli</i>	80.7	cloacal swab	(Talavera-González et al., 2021)
		Carbenicillin	<i>E. coli</i>	56.3	Cloacal swab	(Talavera-González et al., 2021)
		Carbenicillin	<i>Salmonella</i>	26.0	Ground beef	(Delgado-Suárez et al., 2021)
		Amoxicillin-clavulanic acid	<i>Salmonella</i>	20.8	Ground beef	(Delgado-Suárez et al., 2021)
	Tetracyclines	Tetracycline	<i>E. coli</i>	64.4	cloacal swab	(Talavera-González et al., 2021)
		Tetracycline	<i>Salmonella</i>	40.3	Ground beef	(Delgado-Suárez et al., 2021)
	Aminoglycosides	amikacin	<i>Enterococcus</i>	42.0	Chicken	(almada Corral et al., 2023)
		Kanamycin	<i>Enterococcus</i>	38.0	chicken	(almada Corral et al., 2023)
		Streptomycin	<i>Enterococcus</i>	55.0	Chicken	(almada Corral et al., 2023)
	Macrolides	Erythromycin	<i>Enterococcus</i>	33.0	Chicken	(almada Corral et al., 2023)
	Quinolones	Nalidixic acid	<i>E. coli</i>	26.9	Cloacal swab	(Talavera-González et al., 2021)
		Ciprofloxacin	<i>Salmonella</i>	26.0	Ground beef	(Delgado-Suárez et al., 2021)
Pigs	Penicillins	Penicillin	<i>E. coli</i>	92.0	meat	(Martínez-Vázquez et al., 2018)
		Ampicillin	<i>S. aureus</i>	85.0	Meat	(Martínez-Vázquez et al., 2021)
		Penicillin	<i>S. aureus</i>	86.2	Meat	(Martínez-Vázquez et al., 2021)
		Penicillin	<i>E. coli</i>	44.8	Water	(Canizalez-Roman et al., 2019)
	Tetracyclines	Tetracycline	<i>E. coli</i>	75.0	Meat	(Martínez-Vázquez et al., 2018)
		Tetracycline	<i>E. coli</i>	37.9	Water	(Canizalez-Roman et al., 2019)
		Tetracycline	<i>Salmonella</i>	73.7	Slaughterhouse	(Vega-Sánchez et al., 2020)
	Sulphonamides	Sulfamethoxazole-trimethoprim	<i>E. coli</i>	13.8	Water	(Canizalez-Roman et al., 2019)
	Aminoglycosides	Gentamicin	<i>E. coli</i>	6.9	Water	(Canizalez-Roman et al., 2019)
		Aminoglycoside	<i>Salmonella</i>	100.0	Slaughterhouse	(Vega-Sánchez et al., 2020)
	Cephalosporins	Cefazolin	<i>E. coli</i>	92.0	Meat	(Martínez-Vázquez et al., 2018)
		Cefotaxime	<i>E. coli</i>	78.0	Meat	(Martínez-Vázquez et al., 2018)
	Quinolones	Ciprofloxacin	<i>E. coli</i>	3.5	Water	(Canizalez-Roman et al., 2019)
		Nalidixic acid	<i>E. coli</i>	3.5	Water	(Canizalez-Roman et al., 2019)
		Ciprofloxacin	<i>Salmonella</i>	44.7	Slaughterhouse	(Vega-Sánchez et al., 2020)

(Continued)

TABLE 6 Average AMR rates (in %) and the corresponding standard deviations (STD) obtained for food-producing animals in North America during the 2015–2024 time period.

	Livestock		Average	STD	CI
Antibiotics	Cattle	Penicillins	66.94	33.66	13.42
		Tetracyclines	54.30	30.78	12.28
		Sulfonamides	29.46	24.95	14.50
		Macrolides	37.96	41.66	16.62
		Aminoglycosides	34.78	33.14	13.63
		Cephalosporins	71.42	32.46	14.80
		Quinolones	42.32	26.19	15.23
	Poultry	Penicillins	42.32	22.98	13.31
		Tetracyclines	51.21	15.94	7.27
		Sulfonamides	13.73	6.54	6.21
		Macrolides	17.84	18.55	15.26
		Aminoglycosides	34.72	19.98	8.84
		Quinolones	13.82	11.21	6.96
	Pigs	Penicillins	74.70	27.84	16.19
		Tetracyclines	70.96	20.46	11.12
		Macrolides	74.12	14.19	11.67
		Aminoglycosides	59.54	33.56	16.64
		Cephalosporins	60.30	35.77	19.6
Bacteria	Cattle	Quinolones	24.30	29.38	18.26
		<i>E. coli</i>	52.14	34.90	8.96
		<i>Enterococcus</i>	44.70	36.58	22.74
		<i>Salmonella</i>	47.12	32.94	12.77
		<i>Campylobacter</i>	31.93	35.61	16.91
		<i>S. aureus</i>	69.02	30.30	13.82
	Poultry	<i>E. coli</i>	37.17	21.79	8.45
		<i>Salmonella</i>	32.28	23.11	8.72
		<i>Campylobacter</i>	27.57	23.86	11.33
		<i>Enterococcus</i>	42.00	9.41	7.74
	Pigs	<i>E. coli</i>	54.48	35.89	11.15
		<i>Salmonella</i>	63.08	29.73	18.48
		<i>S. aureus</i>	69.55	13.78	8.56
		<i>S. suis</i>	71.91	29.69	18.46

Confidence intervals (CI) computed for the alpha parameter of 0.1 (i.e. 90%) are reported.

a significant public health concern as these antibiotics are also commonly used to treat *Salmonella* infections in humans (Mujahid et al., 2023). Besides the commonly discussed antibiotics, antimicrobial resistance to pleuromutilins (Hayer et al., 2020a), lincosamides (Abdelfattah et al., 2021), amphenicols (Nobrega et al., 2018b), and chloramphenicols (Vounba et al., 2019) has also been observed in food-producing animals across North America. Although these antibiotics have been used less frequently, they still contribute to a broader issue of the AMR spread in livestock.

Certainly, the use of antibiotics in livestock around the world needs to be better analyzed and characterized by conducting new quantitative or qualitative studies and surveys as it has been recently done by Kimera et al. (2020) in an African perspective. Real-life data should be made available to allow decision-makers to know where we currently stand. This kind of studies can be used not only to compare the AMU and AMR relationships in different countries, but also to take action and help reduce unnecessary antimicrobial use. Denmark and the Netherlands are examples of countries that applied different AMR prevention approaches to reduce antibiotic usage in farm animals (Aarestrup et al., 2010). For example, by 2008 in Denmark, pig production was using less than 50% of antibiotics of the total they were using in 1992. The Netherlands launched, in 2009, a project intended to minimize the antibiotic use by 50% in three years. The proposed measures helped reduce sales of antibiotics in the Netherlands by 32% (Trends in Veterinary Antibiotic Use in the Netherlands 2005-2011, 2011). Since 2020, Norway has been implementing a cyclical approach to combat antimicrobial resistance based on a new national strategy (Rørtveit and Simonsen, 2020). Rørtveit and Simonsen explored the key elements and the effectiveness of this approach, and described primary care perspective on the Norwegian national strategy against antimicrobial resistance (Rørtveit and Simonsen, 2020).

The spread of antimicrobial resistant genes in livestock and their transfer to humans become more and more challenging issues not only in North America, but in many countries around the globe. The need for understanding how to reduce the transmission of ARG from food-producing animals to humans has become a topic of major importance.

To effectively address the potential health risks related to AMR, it is crucial to adopt the OneHealth approach (Asaaga et al., 2022) that highlights the need for collaboration between human, animal, and environmental health sectors to effectively mitigate AMR risks. This approach aims at tackling AMR by encouraging global collaboration, innovation, and accountability. It includes using antibiotics only when necessary for treatment, avoiding their use as growth promoters, and regulating their use in both humans and animals. By offering a comprehensive strategy, the OneHealth framework promotes stronger global governance, sustainable practices, and monitoring to control the spread of resistant bacteria. This integrated approach is essential to reduce AMR risks and ensure long-term health for all.

Some specific approaches have already shown their effectiveness in reducing the use of AMR in farms (Aarestrup et al., 2010; Trends in Veterinary Antibiotic Use in the Netherlands 2005-2011, 2011; Rørtveit and Simonsen, 2020). They include creating a private place for infected animals, minimizing contacts between humans and animals, and optimizing waste collection. A deep understanding of the mechanisms related to animal maintenance is fundamental for understanding how livestock waste can accelerate the spread of AMR. Obviously, farmers should pay particular attention when they use antibiotics because not all bacterial infections need antibiotic treatment (Ventola, 2015). Thus, the increase in the number of sick animals on a farm is not a cause for antimicrobial misuse. Sometimes, inflammatory conditions, such as pancreatitis or neoplasia are considered and

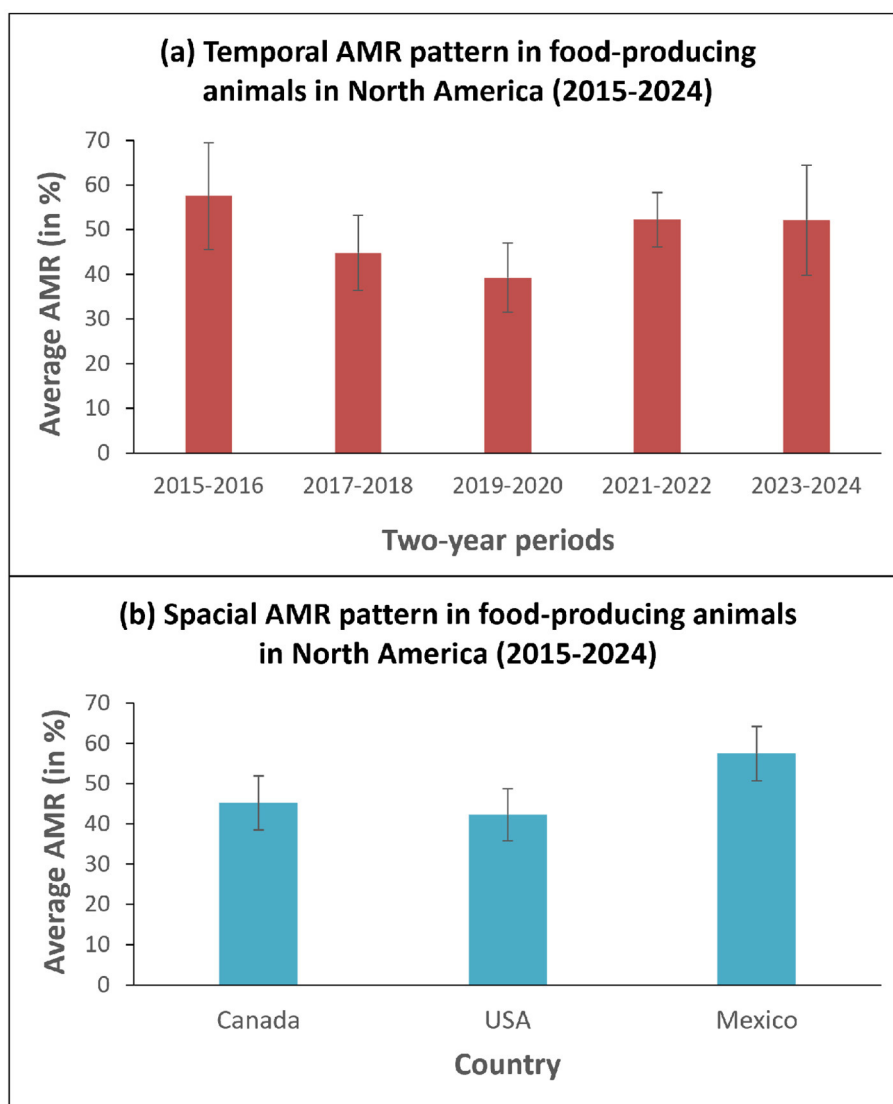


FIGURE 3

Average AMR rates on: (a) the temporal (by a two-year period within 2015–2024) and (b) the spatial (by North American country) scales. The associated 90% confidence intervals (CI) are shown.

treated as bacterial infections. In many cases, incision and drainage represent an alternative for treatment of localized abscesses. Prevention in early times can also help heal a secondary bacterial infection without antimicrobials (Lhermie et al., 2018).

Spatio-temporal factors provide important information that can help policymakers, researchers, and veterinarians take action to reduce or prevent the spread of AMR (Asaduzzaman et al., 2022). For instance, a study by Sodagari et al. revealed higher levels of antimicrobial resistance in *Escherichia coli* isolates from eggs produced in cage-free systems compared to cage systems, particularly after the tetracycline and amoxicillin treatment (Sodagari et al., 2023). A study conducted by Novoa Rama examined the impact of housing systems on the prevalence and AMR of *Campylobacter jejuni* (*C. jejuni*). The results showed a higher prevalence of bacteria in hens from cage-free systems, with high resistance to tetracycline (67%) (Novoa Rama et al., 2018). These findings highlight the significance of housing systems

as an environmental factor in the spatial distribution of AMR. In addition, the rearing period of animals plays a role in AMR development. Montoro-Dasi et al. (2020) compared two breeds of hens—one with rapid growth and the other with slow growth. The results suggest that fast-growing hens had higher AMR rates at the beginning of their rearing period. However, by the end of the growth period, no significant difference was observed between the two groups, indicating that AMR can develop rapidly under certain production conditions, even without antibiotic use. Thus, AMR dynamics are obviously influenced by both environmental and temporal factors, which should be considered when developing strategies to reduce AMR spread. This understanding can help inform more targeted intervention efforts and policies aimed at controlling AMR in agricultural settings.

AMU data can be considered as well to explore the relationship between the use of antimicrobials and the emergence of antimicrobial resistance to specific bacterial strains (Holmer

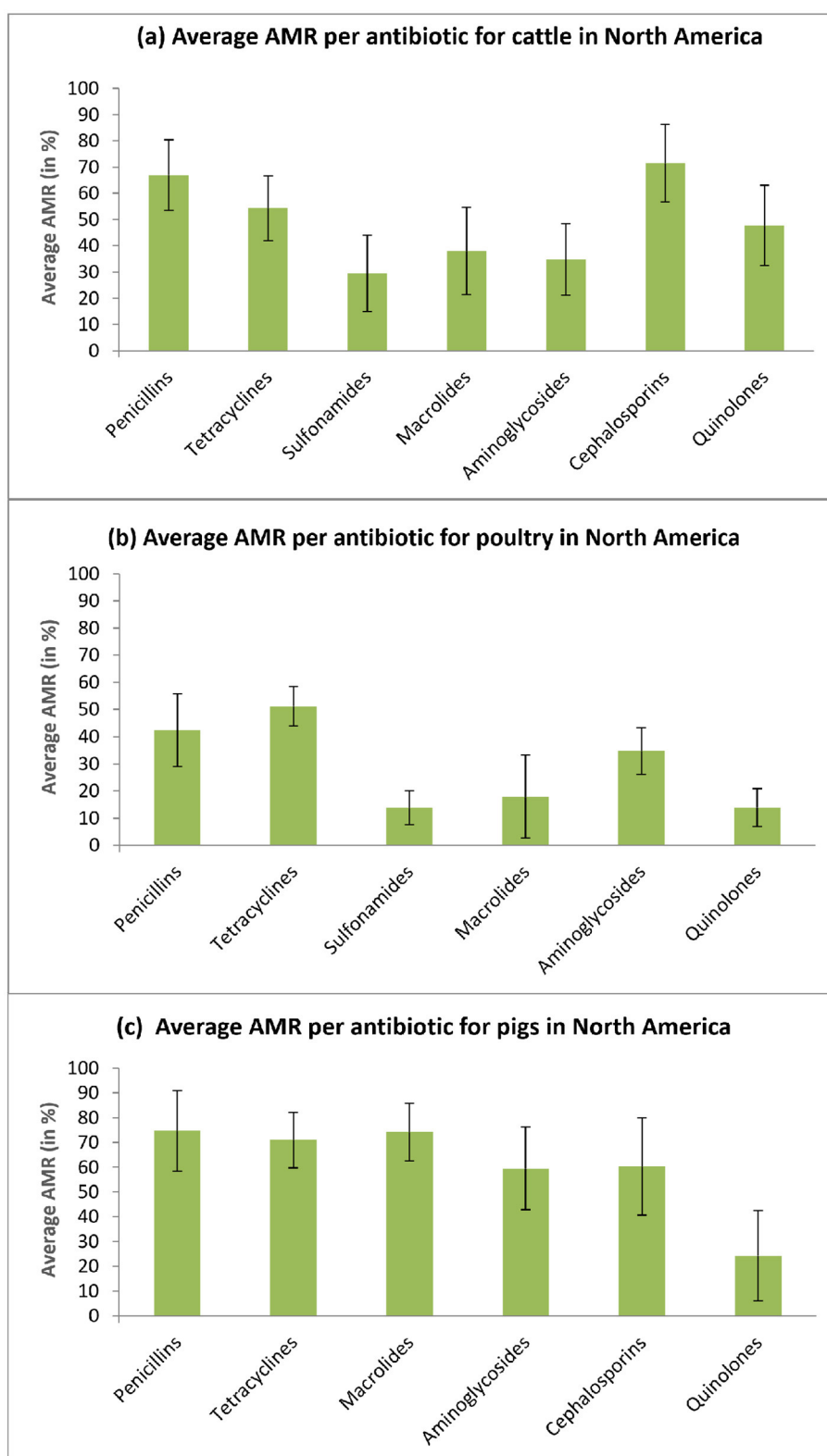


FIGURE 4

Average AMR per antibiotic class rates for cattle, poultry, and pig farms in North America. The associated 90% confidence intervals are reported. **(a)** Average AMR per antibiotic for cattle in North America. **(b)** Average AMR per antibiotic for poultry in North America. **(c)** Average AMR per antibiotic for pigs in North America.

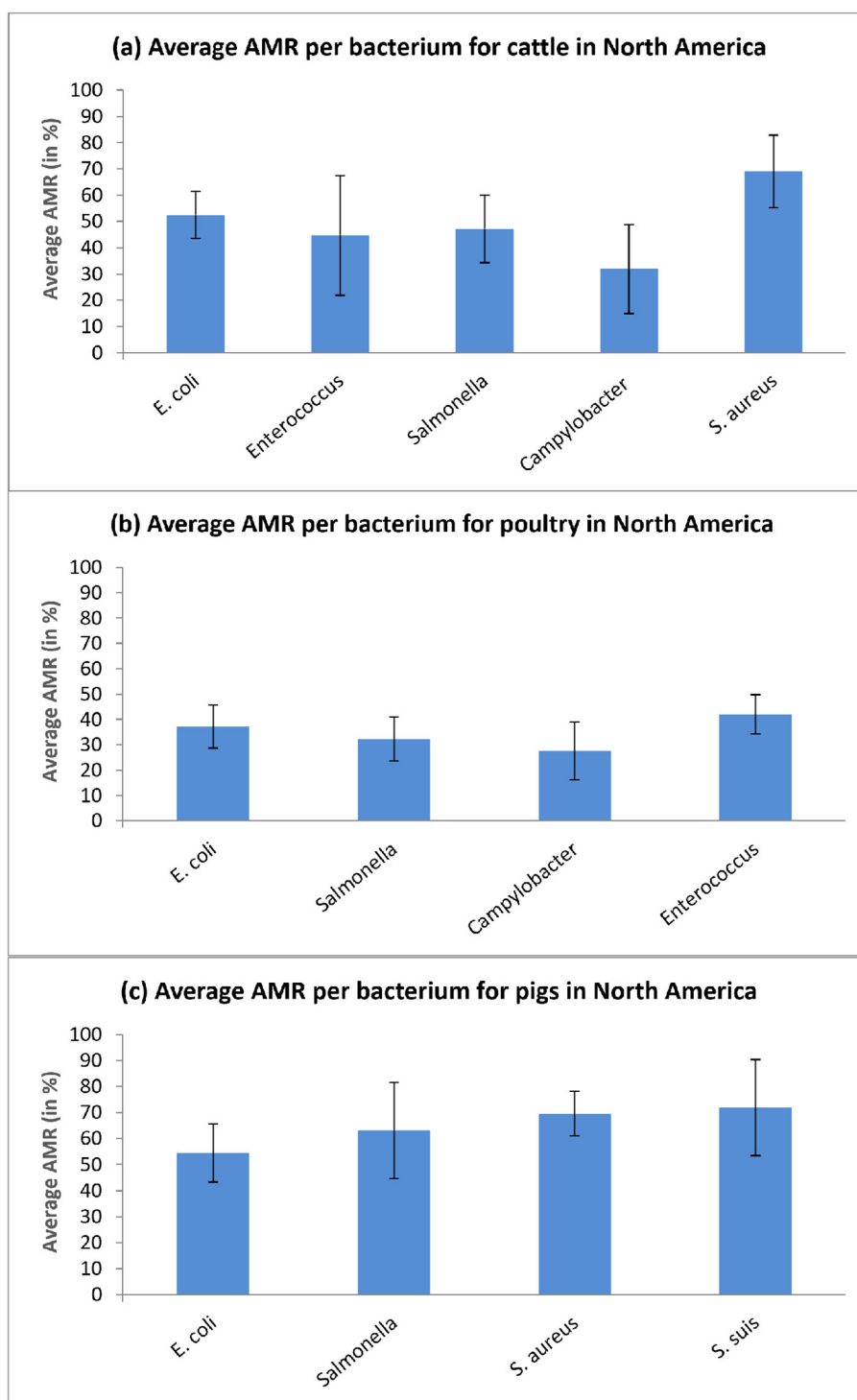


FIGURE 5

Average AMR rates per bacterium for cattle, poultry, and pig farms in North America. The associated 90% confidence intervals are reported. **(a)** Average AMR per bacterium for cattle in North America. **(b)** Average AMR per bacterium for poultry in North America. **(c)** Average AMR per bacterium for pigs in North America.

et al., 2019). For example, the administration of ceftiofur in-ovo or to day-old chicks in hatcheries was associated with the emergence of the ceftiofur resistance in *Salmonella* Heidelberg found in the chicken meat. A noticeable reduction of this kind of AMR was observed when hatcheries in Quebec voluntarily

ceased the in-ovo use of ceftiofur (Dutil et al., 2010). It has been shown that infections caused by antibiotic-resistant *Campylobacter* strains may lead to more frequent and prolonged hospitalizations compared to infections caused by non-resistant strains (Igwaran and Okoh, 2019). *Campylobacter* is one of the

main source of bacterial foodborne and waterborne infections, including diarrhoeal diseases. Although most pig herds carry *Campylobacter coli* (*C. coli*), limited research has explored the relationship between AMU and AMR to *Campylobacter* in pigs (Tang et al., 2017a). This gap may be attributed to the prevailing focus on poultry as a primary source of human exposure to *Campylobacter* (Igwaran and Okoh, 2019). While campylobacteriosis is a less common cause of clinical illness in pigs, they still pose a potential risk for foodborne campylobacteriosis, environmental contamination, and exposure of farm workers to *Campylobacter*.

It is worth noting that the decrease in antibiotic use does not always decrease AMR. For example, Borgen et al. (2000) observed the persistence of vancomycin-resistant *Enterococcus* on Norwegian poultry farms even after the prohibition of the avoparcin. According to Lopatkin et al. (2017), the conjugation of plasmids carrying an antimicrobial gene can result in plasmid maintenance in a microbial community in the absence of antibiotics. It is imperative to embrace a fresh perspective that not only aims at decreasing antibiotic usage but also focuses on preventing the unification of resistance as well as on promoting the preservation of plasmids. Several alternatives to combat antimicrobial resistance have been proposed in the literature, including prebiotics (Hume, 2011; Cunningham et al., 2021; Yang et al., 2019), antimicrobial peptides (Rima et al., 2021; rudzynski K, 2015), and probiotics (Yaqoob et al., 2022; Lone et al., 2022). For example, prebiotics can help modify the animal's gut by regulating its immune systems (Pourabedin and Zhao, 2015). Ghosh et al. (2019) discussed the current state of these alternatives and highlighted the main difficulties of their implementation.

Furthermore, some strategies should be implemented to limit the transmission of antimicrobial resistance through the environment. For example, some preventive measures must be applied to manure storage and disposal. Farm workers should pay attention to conventional waste treatment. Disinfection with chlorine is a fundamental step to treat the wastewater on farms (Yuan et al., 2015). In addition, farmers need to stop applying livestock waste-amended manure to soils to prevent the transfer of AMR from soil pathogens to humans (National Antimicrobial Resistance Monitoring System (NARMS)).⁹

5 Conclusion

Food-producing animals have been identified as a significant contributor to the dissemination of antimicrobial resistance as indicated by the high levels of AMR observed in livestock in the three largest North American countries. High AMR rates, observed especially for cattle and pigs, can be a cause of transmission of AMR to humans who come in contact with farm animals, directly or indirectly through contaminated food products or the environment.

Our review only touches the surface of a vast global issue, which requires urgent attention and coordinated efforts of

farmers and veterinarians. It is important to note that our study was not designed to recommend any specific type or level of restriction on antibiotic use. Our research is rather focused on quantifying and comparing AMR rates in food-producing animals, including cattle, poultry, and pigs, in North America. We reviewed the proposed solutions to combat AMR in the three largest North American countries and suggested some complementary strategies which could aid to reduce antimicrobial resistance in livestock. Our findings can be used to develop new policies and approaches to address this pressing global concern.

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.

Author contributions

MM: Writing – original draft, Writing – review & editing. AD: Writing – original draft, Writing – review & editing. VM: Writing – original draft, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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⁹ www.cdc.gov/narms/index.html (accessed June, 2024).

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