Metrics for measuring veterinary antimicrobial use data – a Canadian perspective

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Abstract

In order to understand how antimicrobial use (AMU) in animals contributes to antimicrobial resistance in both animals and humans, it is essential to measure AMU in animals. The results obtained from applying different metrics to an AMU dataset may have different implications on decision-making surrounding AMU in animals. The objectives of this study were to compare the utility and implications of three AMU metrics applied to 2011 to 2015 AMU data from the Canadian Integrated Program for Antimicrobial Resistance Surveillance's Farm-Swine surveillance program. The metrics used were the defined daily dose vet (DDD_{vet}) per population correction unit (PCU), milligrams of antimicrobial used per PCU, and the proportion of farms using an antimicrobial. The DDD_{vet}/PCU was estimated using Canadian (DDD_{vet}CA) and European (DDD_{vet}EU) standards. Differences in trends over time were observed across the metrics when applied to aggregate AMU data. The DDD_{vet}CA/PCU, based on the average Canadian labelled daily dose and accounting for population biomass, provides an estimate of AMU in a specifically Canadian context.

Keywords: *Antimicrobial use, metrics, defined daily dose, Canada*

Introduction

Information about antimicrobial use (AMU) in food animal production is essential for a comprehensive understanding of the contribution of veterinary use of antimicrobials to the problem of antimicrobial resistance (AMR) (1).

In human medicine, one of the metrics used to express AMU is the number of defined daily doses (DDD) per 1000 patient-days (2). The DDD is a standardized unit of measurement that, when applied to AMU data, takes into account differences in doses between antimicrobial active ingredients (AI). In 2013, the European Surveillance of Veterinary Antimicrobial Consumption committee (ESVAC) of the European Medicines Agency adopted the use of the DDD by developing the DDD_{vet} (3,4). The DDD_{vet} is standardized for each antimicrobial AI, and is stratified by route of administration and animal species. The DDD_{vet} standard for an antimicrobial is used to estimate the number of DDD_{vet}, which describes the number of DDD "units" or doses of an antimicrobial AI used in a particular species, and can be expressed as a treatment incidence rate (per animal-time, e.g. per 1000 pig-days) or per population correction unit (PCU). The PCU is a measurement of the biomass of animals that are at risk of exposure to the antimicrobial of interest. These measures of AMU can be applied to assess temporal (e.g. yearly) and spatial (e.g. provincial or regional) trends. In this study, the PCU was chosen as the denominator for the number of DDD_{vet} and mg of antimicrobial used. In an effort to reflect veterinary AMU accurately in a specifically Canadian context, the Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) of the Public Health Agency of Canada assigned Canadian specific DDD_{vet}s (called DDD_{vet}CAs). Since 2006, the farm component of CIPARS has collected AMU data from grower-finisher swine herds in the five major pig producing provinces in Canada (6).

Other AMU metrics that are in use in veterinary medicine include the milligrams of active ingredient sold or used per PCU (mg/PCU) and the proportion of farms using an active ingredient, among others. Different metrics are useful in different contexts and there is no one metric that adequately reflects the complexity of AMU (5). The results obtained from each metric may have different implications when used to inform interventions/policies supporting greater antimicrobial stewardship.

The objectives of this study were to compare results obtained from applying different metrics to 2011 to 2015 AMU data collected by the CIPARS Farm-Swine surveillance program and to assess the utility and implications of each metric in reporting trends over time and between regions.

Materials and methods

The three metrics were applied to data from two Canadian provinces for bacitracin, chlortetracycline and tylosin use in feed (Table 1). The data were collected from grower-finisher swine herds participating in CIPARS from 2011-2015. Data on AMU were collected once a year on each farm, for a single grower-finisher period. The names of the provinces were anonymized as province A and province B. The number of DDD_{vet}/PCU was calculated using ESVAC (4) and Canadian DDD_{vet} standards.

Table 1. Metrics applied to antimicrobial use in feed data from the CIPARS Farm-Swine surveillance program, 2011-2015.

Metric	Calculation
Number of DDD_{vet}CA/PCU	$\left[\frac{Mg\ used}{DDD_{vet}CA \times animal\ weight\ (kg)}\right] / PCU$
Number of DDD_{vet}EU/PCU	$\left[\frac{Mg\ used}{DDD_{vet}EU \times animal\ weight\ (kg)}\right] / PCU$
Milligrams of active ingredient used / PCU	$Mg\ used\ /\ PCU$
Proportion of farms	$\frac{Number\ of\ farms\ using\ antimicrobials}{Total\ number\ of\ participating\ farms}$

The DDD_{vet}CA standards were assigned following ESVAC's principles (3), with a few exceptions. The DDD_{vet}CAs were assigned based on labelled doses of Canadian approved antimicrobial products. While ESVAC used the maximum and minimum product doses to calculate the mean active ingredient dose, CIPARS used every unique product dose to calculate the mean (7,8). Additionally, the DDD_{vet}CAs were stratified by four routes of administration (feed, water, injectable and bolus), while ESVAC's DDD_{vet}s were stratified (for all species) by oral (combining feed, water and bolus routes) and parenteral routes (4).

In order to compare trends in overall use, the number of DDD_{vet}CA/PCU for each antimicrobial were summed. This process was repeated for the mg/PCU. The total proportion of farms using antimicrobials was calculated by dividing the number of farms using one or more of the antimicrobials by the total number of participating farms in each surveillance year. The relative percent change in use from one year to the next, and from 2011 to 2015 was determined for each metric using Equation One.

$$Relative\ percent\ change = \left[\frac{Year\ B - Year\ A}{Year\ A}\right] \times 100$$

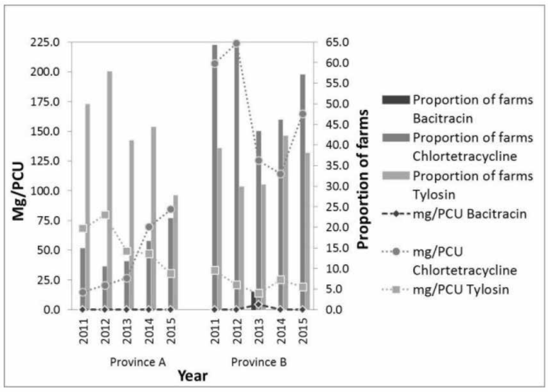
SAS (version 9.3) was used to collate and tabulate the mg used and population numbers from the surveillance herds in each province by year. This information was exported into Microsoft Excel 2010, where the metrics were applied and figures created.

Results

The oral DDD_{vet}EU for chlortetracycline (31.0mg/kg-pig) and tylosin (12.0mg/kg-pig) were three to four times higher than the DDD_{vet}CA in feed (10.4 and 3.1mg/kg-pig, respectively). As no corresponding DDD_{vet}EU for bacitracin exists, it was not possible to compare DDD_{vet} standards for this antimicrobial.

The trend in the proportion of farms using each antimicrobial deviated on occasion from the trend in mg/PCU (Figure 1). For example, in province B from 2013 to 2014, the proportion of farms using tylosin increased, while the mg/PCU decreased (Figure 1).

Figure 1. Trends in antimicrobial use in feed in two Canadian provinces, using different AMU metrics Source: CIPARS Farm-Swine surveillance program, 2011-2015.



Since the DDD_{vet}EU standards for chlortetracycline and tylosin were higher than the DDD_{vet}CA standards, when the DDD_{vet}EU standards were applied to the AMU data, the number of DDD_{vet}EU/PCU were smaller than the number of DDD_{vet}CA/PCU (Figure 2). The trends for the number of DDD_{vet}CA/PCU and the number of DDD_{vet}EU/PCU, however, were identical (Figure 2). Since no DDD_{vet}EU standard for bacitracin exists, the number of DDD_{vet}EU/PCU could not be determined (Figure 2).

When comparing use between provinces, all metrics showed a higher use of chlortetracycline and bacitracin in province B. Use of tylosin was higher for all metrics in province A, except for proportion of farms in 2015, which showed a higher use of tylosin in province B (Figures 1, 2).

Figure 2. Trends in antimicrobial use in feed in two Canadian provinces, using different AMU metrics. Source: CIPARS Farm-Swine surveillance program, 2011-2015.

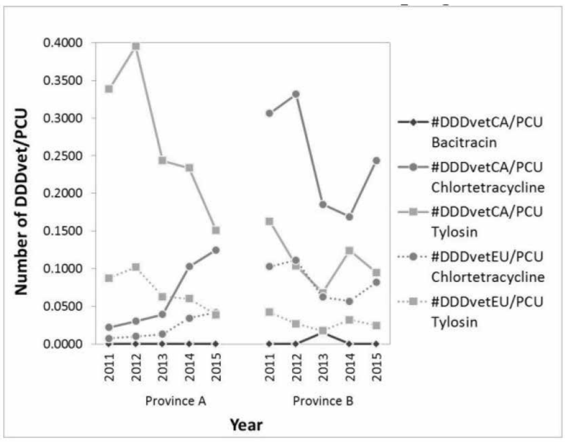
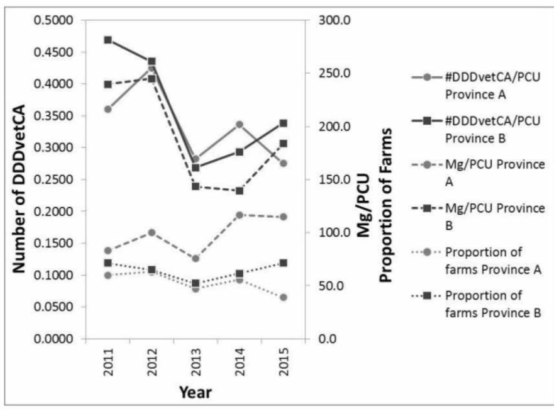


Figure 3. Trends in total consumption of bacitracin, chlortetracycline and tylosin in feed in two Canadian provinces, using different AMU metrics. Source: CIPARS Farm-Swine surveillance program, 2011-2015.



Looking at total AMU, the trends over time for each province were different for each metric (Figure 3). The relative percent change in use from one year to the next showed differences in the magnitude of change and, in some cases, the direction of change (Table 2). For example, for province A, from 2013 to 2014, the magnitude of change in mg/PCU was almost three times higher than the magnitude of change in the number DDD_{vet}CA/PCU and proportion of farms. For province B, from 2012 to 2013, the magnitude of change for mg/PCU was in the opposite direction of the magnitude of change in the number of DDD_{vet}CA/PCU and the proportion of farms.

Table 2. The temporal relative percent change in the total consumption of bacitracin, chlortetracycline and tylosin in feed in two Canadian provinces. Source: CIPARS Farm-Swine surveillance program, 2011-2015.

Province	Years	Relative Percent Change		
		#DDDvetCA /PCU	Mg/PCU	Proportion of farms
Province A	2011-2012	18.0	20.5	5.3
	2012-2013	-33.6	-24.5	-25.5
	2013-2014	19.1	54.4	18.1
	2014-2015	-18.2	-1.7	-30.0
	2011-2015[1]	-23.6	38.2	-35.2
Province B	2011-2012	-7.2	-47.0	-9.0
	2012-2013[1]	-38.3	13.1	-19.7
	2013-2014[1]	9.1	-2.9	17.9
	2014-2015	15.5	31.9	16.1
	2011-2015[1]	-27.8	-23.4	0.0

[1]At least one metric resulted in a different direction in relative percent change.

For province A, the relative percent change in mg/PCU for 2011 to 2015 was positive, while the relative percent change in the number of DDD_{vet}CA/PCU and the proportion of farms was negative (Table 2). Depending on which metric was applied, use appeared to increase, decrease, or stay the same over the five-year period in provinces A and B.

Discussion

Differences in Canadian and European DDD_{vet} standards have implications in terms of reporting AMU using the number of DDDvet/PCU, as Canada's AMU appears higher or lower depending on the standard chosen. Potential reasons for the differences in standards could include differences in labelled doses between Canada and Europe and differences in how routes of administration are stratified. However, while the magnitude of the number of DDDvet/PCU changed with the standard used, the overall trend over time for this metric did not, leaving the overall AMU message the same (e.g. use is increasing or decreasing). For a single antimicrobial, the mg/PCU also yielded a similar trend line as the number of DDDvet/PCU, providing the same overall AMU message. By its nature, the proportion of farms using an AI (use frequency), cannot be adjusted by the biomass of animals at risk of exposure to the antimicrobial. Changes in the population of animals at risk of exposure will need to accompany text in any interpretation of data using this metric. Changes in temporal and spatial trends will always require additional information on animal health status to help explain some of the possible drivers of shifting AMU patterns.

The choice of metric can affect decisions made based on the results when measuring the aggregate use of antimicrobials over time. In this situation, the DDD_{vet}/PCU has the advantage over the other metrics, as it not only adjusts for the biomass of the population at risk; it also adjusts for differences in doses between the antimicrobials under consideration. As a result, it provides a more accurate representation of the trend in aggregated AMU data over time.

In terms of communication, the proportion of farms and mg/PCU are simpler metrics that have been in use for longer in Canada than the number of DDD_{vet}. However, the number of DDD_{vet}/PCU, by adjusting for both biomass and dose, is more robust than other metrics. Since this metric is relatively new to stakeholders, it will need to be clearly explained (1). Over time, familiarity and acceptance of the metric is expected to increase. Adopting a DDD_{vet}CA metric, based on Canadian labelled doses, provides findings of greater internal and external validity, in a Canadian context. This makes the DDD_{vet}CA useful for reporting trends in AMU, and for interprovincial/regional comparisons in use within Canada. When reporting and comparing AMU internationally, it is important to use the same metric as other countries do. Hence, there is a need to have both a Canadian DDD_{vet} standard as well as a standard that reflects antimicrobial doses globally and is accepted internationally.

In conclusion, AMU data comes with many attributes, and analysis and reporting of AMU data is not simple. The DDD_{vet}CA/PCU has advantages over other metrics in terms of accuracy and robustness, providing a valid measure of AMU in a Canadian context.

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