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Antimicrobial consumption: Comparison of three different data collection methods

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ABSTRACT

The increasing incidence of antimicrobial resistance represents a global threat. As a result, surveillance programmes monitoring antimicrobial consumption and resistance in animals have been implemented in several countries throughout the world. However, such programmes depend on the accurate and detailed collection of data on antimicrobial consumption. For this reason, the aim of this longitudinal study was to compare the consistency of data on antimicrobial consumption between three different data collection methods.

Antimicrobial consumption data associated to udder health were collected from 20 veterinary practices and 92 dairy farms for 18 months. The compared data sources were: 1) data extracted from veterinary practice software 2) farm treatment journals and 3) on-farm discarded drug packages (garbage). Two different procedures were chosen to analyse the data issued from treatment journals: 1) only complete entries were analysed 2) entries with missing dosage were supplemented with the information provided by the Swiss Compendium of Veterinary Medicinal Products. The antimicrobial data were divided into intramammary preparations used during lactation (IMM), intramammary preparations used for dry off (DRY) and systemic treatments (SYS). We compared the quantities of injectors (IMM and DRY), the quantities of active substances (SYS) and the treatment incidences (TI) for the defined daily dose (DDD) per 1000 cow-days (IMM and SYS) and the defined course dose (DCD) per 1000 cow-days (DRY). Additionally, the variety of antimicrobial products among the different data sources was compared.

The highest quantity of antimicrobials for IMM, DRY and SYS could be collected with the software data. The lowest quantity was collected by using the data of the treatment journal with only complete entries. For IMM and DRY, software and garbage performed similar, with agreement on the number of injectors used in 56.1% of the analysed cases. The widest variety of intramammary antimicrobial preparations was found in the garbage whilst most systemic preparations were collected using software data. The results of the study show a lack of data consistency between the three different data sources. None of the methods was able to collect the integral antimicrobial consumption in the participating farms. Finally, the results emphasise the need to implement a standardised system to quantify and assess the antimicrobial consumption at veterinary practice and farm level.

1. Introduction

Antimicrobial resistance (AMR) represents an undeniable threat to Public Health (Ferri et al., 2017). As inappropriate antimicrobial usage (AMU) is reinforcing AMR (Hoelzer et al., 2017), one important approach towards combatting this issue is the prudent and responsible use of antimicrobials. For this aim, good surveillance systems need to be in place.

In April 2010, the European Medicines Agency (EMA) launched a project to develop a harmonised approach for the recording and reporting of AMU data in animals. This European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) project aims at collecting sales data of veterinary antimicrobials, allowing the European Union Member States and the European Economic Area to enhance policies on

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AMU in veterinary medicine. Furthermore, the EMA published in February 2018 guidelines for reporting data on antimicrobial consumption by animal species. These data allow the identification of species with the highest AMU and the monitoring and tracking of AMU within a given species. In addition, benchmarking of farms is possible, and use of antimicrobials in species for which they are not licensed can be identified (Edo, 2017; European Medicines Agency, 2020).

At international level, several countries implemented monitoring systems to quantify antimicrobial consumption in food animals (Bager, 2000; Veterinary Medicines Directorate, 2018; The Netherlands Veterinary Medicines Institute (SDa), 2020; AACTING, 2020; Government of Canada, 2020). These systems are based on either voluntary or mandatory records of antimicrobial usage from different stakeholders. Most of the time, veterinarians are the ones who report antimicrobial prescriptions (AMP) intended for diseased animals. However, feed mills, pharmaceutical companies, pharmacies as well as farmers also contribute to the antimicrobial data collection. Only very few systems use veterinary prescriptions extracted from the practice management software as an information base. All these aspects make the different monitoring systems inconsistent and not comparable (AACTING, 2020). Even within the same country, there can be large discrepancies between different data sources on antimicrobial consumption (Spycher et al., 2002).

In Switzerland, the National Strategy on Antibiotic Resistance (StAR) was launched in 2015 (Nationale Strategie Antibiotikaresistenzen Schweiz (StAR), 2015) with the aim to prevent the development and the spread of AMR. One strategic approach was to establish and monitor the consumption of antimicrobials on a comprehensive basis. At the time of this study, the only estimation of antimicrobial data in veterinary medicine was based on antimicrobial sales provided by the Marketing Authorization Holders and published annually in the ARCH-Vet-Report from the Federal Food Safety and Veterinary Office (FSVO) (Federal Food Safety and Veterinary Office, 2017).

Under Swiss legislation, antimicrobials for animal treatments may only be prescribed and sold by veterinarians. If farmers want to administer antimicrobials to animals, they need to have a veterinary medicines contract with a veterinarian who performs regular farm visits. Furthermore, only antimicrobials for treatment of individual animals or groups of animals for a defined indication for a maximum duration of three months may be stored on the farm. Since 2016, on-farm storing of antimicrobials used for prophylactic treatments as well as Highest Priority Critically Important Antimicrobials (HPCIAs), except essential HPCIA quantities for ongoing treatments, is prohibited by law (Verordnung über die Tierarzneimittel (TAMV) AS 2016 97 961, 2016). Pharmacies may not sell antimicrobials directly to farmers without a prescription by a veterinarian. Prescription can be done electronically or on paper, and data on prescriptions are not assembled centrally. However, the legislation in Switzerland requires a precise documentation of AMU at farm level in the form of a treatment journal, indicating the date, animal identification number, treatment indication/diagnosis, substance, dosage, treatment duration and withdrawal period. The farmer has the responsibility and duty to keep the treatment journal up to date and to store it for three years (Verordnung über die Tierarzneimittel (TAMV) SR 812.212.27, 2004). At the time of data collection for this study, this could be done electronically or on paper. Since 2019, all antimicrobial treatments need to be recorded in a national database (Federal Food Safety and Veterinary Office, 2020).

Switzerland had the highest sale (in weight of active substances) of intramammary antimicrobial preparations per population correction unit (biomass of livestock and slaughtered animals) in 2015 and 2016 in comparison to 29 other European countries (Wagemann, 2005; European Medicines Agency, 2017, 2018; Bundesamt für Statistik, 2018; Swissmilk, 2018). These antimicrobial preparations are used for the treatment of mastitis and dry cow therapy, which are the most common indications for AMU in dairy farms (Thomson et al., 2008; Menéndez González et al., 2010; De Briyne et al., 2014; Kuipers et al., 2015). For this reason, there is a special interest to quantify and monitor the actual AMU for both intramammary and systemic treatments of mastitis in Switzerland, requiring an accurate record of AMU at practice and farm level. Data quality of recording systems can best be assessed by comparing different methods of recording, on farm level as well as on veterinary practice level. Data on AMU in dairy farms can also be collected by analysing discarded drug packages, which has the advantage that the farmer does not need to keep written records (Nobrega et al., 2017).

Therefore, the aim of the study was to compare the data consistency between three different data collection methods: 1) data from the veterinary practice software 2) farm treatment journal and 3) on-farm collection of discarded drug packages.

2. Material und methods

2.1. Study population

Twenty-one veterinary practices were recruited in Switzerland during a previous study (Pucken et al., 2019). Participating practices were informed about the project through newsletters in January 2016 via the Swiss Cattle Health Service and a newspaper article published in the Swiss Archive for Veterinary Medicine (Pucken et al., 2016). In addition, the project was presented at the continuous education for farm animal practitioners in Berne and Zurich in January 2016. Eligible veterinarians had to be members of the Swiss Association for Ruminant Health and had to work with one of the three most common veterinary practice management software to allow automated extraction of prescription data. Veterinarians were asked to provide a list of all eligible dairy clients having a veterinary medicines contract with the practice. This contract ensures that the veterinarian is the main farm veterinarian and performs regular farm visits. Five farms per veterinarian were then selected using the random number function of Excel. Farmers who refused participation (29), did not answer (14) or were not eligible for the study (9) were replaced with the next farmer on the list. In total 105 dairy farms participated at the beginning of the study (Nägele et al., 2019).

2.2. Data collection and cleaning

From August 2016 until January 2018 (18 months), data on antimicrobial sales and use were collected with three different methods: data extracted from veterinary practice software, discarded drug packages collected on farms (from custom garbage bins on the farms) and farm treatment journals. The participating veterinarians and farmers signed an agreement allowing the authors to collect antimicrobial data from the different data sources. In order to record the collected data, spreadsheets were prepared (Microsoft Excel, Microsoft Corp., Redmond, WA), with the identity of the participating farmers, the months of data collection and a list of all antimicrobial products approved in Switzerland for mastitis treatment. If antimicrobials not yet included in the table were found in the data sources, the list was complemented with these. The data from every collection source was cleaned according to defined rules available as supplementary material (see Supplementary Material Fig. S1-S5).

2.2.1. Data from practice software

The participating veterinary practices were asked to share the files of all prescriptions and treatments for cattle of the participating five clients for the collection period. The data were provided either as PDF files or as Excel spreadsheets or on paper.

Six veterinary practices preselected the provided software files. These files either only contained the prescribed antimicrobials used for mastitis treatment or the antimicrobials prescribed for mastitis treatment were marked. In the second case, only the marked ones were considered. For the other practices, one of the authors (FMS) scanned each file individually and each antimicrobial used for udder health was identified. The information considered from the software files was the following: date of prescription, name of the drug prescribed, amount of drug prescribed and the cow identification number, if present. Systemically administered antimicrobials approved in Switzerland for mastitis treatment were considered if they were allocated to a clearly identified cow diagnosed with mastitis, or if it was declared as being used for mastitis treatment. If no indication was given, it was strictly decided according to the decision tree available in the supplementary material whether the drug was considered or not (see Supplementary Material Fig. S1). In case of any ambiguity regarding the amount of antimicrobials prescribed or the treatment indication, the respective veterinarian was contacted for verification (see Supplementary Material Fig. S2). Previously dispensed antimicrobials subsequently returned to the veterinarian were removed from the dataset. If a drug was identified as not being registered for mastitis or if a drug was used in a manner contrary to its approved method of application, it was not considered due to off-label use. Even though information on off label use is relevant, the number of off label treatments was too small to allow for a meaningful comparison between the data sources.

2.2.2. Discarded antimicrobial drug packages from garbage bins

Eight-litre receptacles with swing and flap tops (Robert Thoma GmbH, 79733 Görwihl, Germany) and 20 suitable 10-litre garbage bags were placed on each of the participating farms for the collection of discarded antimicrobial packages (tubes, bottles, syringes). Farmers were asked to put the empty packages of all antimicrobials used for mastitis treatment into these bags, including dry cow treatments and drugs given as parenteral treatment for mastitis, regardless of the person who administered the antimicrobial. One garbage bag, labelled with the name of the farmer, the address of the farm, and the month of collection was provided for every month of data collection. In addition, two spare garbage bags were given as replacements. The bags were exchanged on the first day of every month by the farmer during the collection period. In order to ensure the monthly bag replacement, a reminder via phone or text message was sent to the farmer. The filled bags were collected in December 2016, July 2017 and February 2018 and the gathered drug packages were recorded in the corresponding spreadsheet. Intramammary injectors were counted and the volumes of systemic preparations were summed. If an empty bottle or syringe was found in one of these bags, the data of amount used was supplemented either with the information given in the treatment journal or according to the information given from the Swiss Compendium of Veterinary Medicinal Products (Swiss Compendium of Veterinary Medicinal Products, 2020). A decision tree was created to ensure that all data was entered uniformly (see Supplementary Material Fig. S3 and Fig. S4).

2.2.3. Treatment journal

In addition to the collection of discarded drug packages, the data of the treatment journals were analysed. The treatment journals were available either in electronic or paper format and were collected as photocopies or photographed.

Only entries clearly assigned to mastitis treatment were considered. If the cow treatment was carried out across two months, all related medications were assigned to the first month (of treatment). Entries with missing drug names were discarded. In addition, missing cow identification number(s) and missing prescription date(s) were ignored. If the dose was missing, but all other relevant information was available, two different procedures were chosen to handle this missing data. Each procedure ended in a separate spreadsheet, and was therefore regarded as a separate method of data collection. (1) The entry was deleted and therefore not further included in the database. This data source is referred to as treatment journal. (2) Either the drug was also found in the garbage bag and the entry was supplemented with the garbage dosage, or the drug was not found in the garbage and the entry was added with the information provided by the Swiss Compendium of Veterinary Medicinal Products (Swiss Compendium of Veterinary Medicinal Products, 2020). This data source is referred to as treatment journal added. If the dose was missing for intramammary antimicrobials used during lactation, one udder quarter was considered as affected and treated. If the dose was missing for intramammary antimicrobials used for dry off, the entire udder (both front and hind quarters) was considered as treated. If the Swiss Compendium of Veterinary Medicinal Products proposed different treatment protocols for different types of mastitis, the most common mastitis type was taken into account. If several treatment days were indicated, the shortest treatment duration was chosen (see Supplementary Material Fig. S5) (Swiss Compendium of Veterinary Medicinal Products, 2020).

2.3. Analysis

The collected data on antimicrobials were classified into three groups according to their indication and application route: intramammary antimicrobials used during lactation (IMM), intramammary antimicrobials used for dry off (DRY) and antimicrobials used for systemic treatment (SYS). In addition, the antimicrobials were grouped into three different categories based on the WHO list of Critically Important Antimicrobials for Human Medicine (WHO CIA list): Highest Priority Critically Important Antimicrobials (HPCIAs), High Priority Critically Important Antimicrobials (CIAs) and Highly Important Antimicrobials (HIAs) (WHO | Critically important antimicrobials for human medicine, 6th revision, 2018).

2.3.1. Comparison of antimicrobial quantities and antimicrobial products

We compared the quantity of antimicrobials between the three different data sources: 1) data from the practice software (software); 2) discarded drug packages from garbage bins (garbage); 3) treatment journal and 4) treatment journal added. The quantity was measured by the total number of injectors (IMM and DRY), the quantity (in mg) of active substances (SYS) and in a standardised manner by calculating the treatment incidence (TI) for the defined daily dose (DDDvet) per 1,000 cow-days (IMM and SYS) and the defined course dose (DCDvet) per 1,000 cow-days (DRY). As the TI can be used to consider times with varying population size, it provides a more precise picture of the population under study (Werner et al., 2018). The formula of More et al. (2017) was amended in this study for the calculation of TI for intramammary antimicrobials (More et al., 2017). For intramammary products for lactating cows, the unit for the DDDvet is unit dose per teat (UD/teat). As one quarter per cow affected by mastitis was assumed, this corresponds to one injector per cow per day. For dry cow treatments, the unit for the DCDvet is unit dose per udder (UD/udder), which corresponds to four injectors per cow (European Surveillance of Veterinary Antimicrobial Consumption (ESVAC), 2016). For systemic antimicrobials, the formula used by Svetlana et al. (2019) was modified (Kasabova et al., 2019). An estimated standard body weight for a cow was chosen at 600 kg (Menéndez González et al., 2010). The observation period was set at 549 days. The number of cows on each farm was determined at the beginning of the study by each farmer using a questionnaire. One farmer reported a variation in his herd size of over 50 % during the study. This variation was included in the calculation of the number of cows (3360.5 cows in total).

$$TI_{IMM} = \frac{\sum \mathit{Intramammary\ AM\ injectors\ during\ lactation}}{DDD_{vet}[UD/teat] \times \mathit{number\ of\ cows} \times \mathit{observation\ period\ (days)}} \times 1000$$

$$TI_{DRY} = \frac{\sum \mathit{Intramammary\ AM\ injectors\ for\ dry\ off}}{DCD_{vet}[UD/udder] \times \mathit{number\ of\ cows} \times \mathit{observation\ period\ (days)}} \times 1000$$

$$TI_{SYS} = \frac{\sum \text{systemic AM for mastitis treatment (mg)}}{DDD_{vet} \times \text{number of cows} \times \text{kg per cow} \times \text{observation period (days)}} \times 1000$$

TI was calculated for each farm, antimicrobial product, and data source, respectively. Comparison of TIs between the different data sources was done at the level of overall sums over all farms. Number of injectors was also compared at the level of the individual farm. Individual treatments could not be matched between the different data sources, because information on the treated animal and the date of treatment was only available in the treatment journal. In the practice software, dates of treatment were only available for treatments administered by the veterinarian. For garbage, only the month of treatment, and not the exact date was known.

2.3.2. Statistical analysis

For the statistical analysis at the level of the farm, only a subset of all antimicrobial products could be used. SYS were recorded in the veterinary software and sometimes in the treatment journal, but very rarely in the garbage. Of 54 product used, 23 had to be excluded because they did not occur in all data sources. Furthermore, 21 products were used in less than 10 farms. For the 10 remaining IMM and DRY products, differences between the number of injectors for a given antimicrobial product and farm were compared between the four data sources. Statistical analyses were performed with STATA (StataCorp LCC, College Station, Texas, USA). First, the maximum number of injectors recorded in the four data sources in the respective farm was determined, assuming that it was more likely for a recording to be forgotten than for antimicrobials that had not been used to be falsely recorded. For each data source, the difference between the maximum number and the number in that data source was calculated. This was expressed as a relative error by dividing the difference by the maximum number recorded for that farm and product, respectively. The relative errors of the different data sources were compared with descriptive statistics.

The relative errors had a bimodal distribution, with the peaks at values of 0 and 100 %. They were therefore classified into four categories. A relative error of 0 (corresponding to the maximum TI recorded in the respective data source) was classified as 0. An error >0 and less than 50 % was coded 1, 50 % to less than 100 % was coded 2, and an error of 100 % (corresponding to a completely missing entry in the respective data source) was coded 3.

These error categories were further analysed in a mixed ordinal logistic regression model (Stata command meologit) with farm and product as random effects, and data source as fixed effect. Because this analysis requires a minimum sample size per cluster (Bell et al., 2010), we only included antimicrobial products, which had been used on at least 10 farms, and were present in all four data sources.

In addition, TIs for all antimicrobial products were summed according to their application (IMM, DRY and SYS) and the different WHO categories (HPCIAs, CIAs and HIAs). These sums were compared descriptively between the four data sources. Finally, the total number of different products found in the four data sources was compared. In the treatment journal, all registered antimicrobials used for udder health were included, irrespective of whether a dosage was given or not. Therefore, only three data sources were evaluated for the comparison of the total number of different products (software, garbage and treatment journal).

3. Results

Initially, 21 veterinary practices and 105 farms participated in the study. The antimicrobial consumption data of 20 veterinary practices and 92 farms could be analysed. Their geographical distribution was uneven within Switzerland, with most of them being located in the canton Berne. As one participating veterinarian left the practice during the study and the software data was consequently no longer available, this veterinary practice had to be excluded from the analysis. Of the remaining 100 farms, two changed their veterinarian, two stopped dairy farming during the intervention and one left the study. Moreover, one farmer did not store the garbage bags, resulting in only two collected bags within 18 months, one farmer refused to provide access to his treatment journal, and for another farmer the data of the treatment journal were obviously incomplete. These three farms were excluded from the final analysis.

3.1. Data quality

3.1.1. Data from practice software

The software data of 49 and 43 farms could be extracted as Excel sheets and as PDF files, respectively. In total, 4249 entries could be clearly assigned to antimicrobials used for udder health. From these entries, 3991 (93.1 %) were further analysed and 258 (6.1 %) entries were considered implausible because of off-label use and therefore not included in the final analysis.

3.1.2. Discarded drug packages from garbage bins

On the 92 farms included in the analysis, 1656 garbage bags should have been gathered during the 18 months of collection period. In the end, 1646 garbage bags were collected, of which 1141 (69.3 %) bags contained discarded antimicrobial packages. 10 bags (0.6 %) could not be collected because they were lost by the farmers.

One farmer did not replace the garbage bag at the beginning of every month and collected all antimicrobials in one garbage bag. However, as it is assumed that all discarded antimicrobial drug packages used for udder health were collected, the content of this unique garbage bag was included in the analysis.

3.1.3. Treatment journal

The treatment journal was either digital (50 farms) or paper based (41 farms). One farmer worked with both types of recordings. Altogether, 2728 entries issued from treatment journals could be assigned to udder health. Out of these, 1444 (52.9 %) entries were complete and 1284 (47.1 %) lacked at least one required data field, whereby large differences existed between the individual farmers regardless of whether the treatment journal was kept electronically or in paper form. As we only included antimicrobials that are registered for mastitis treatment, it was possible to supplement a total of 32 entries with missing indications as well as eight entries with missing cow identification numbers and prescription dates. As a result, a total of 1484 entries could be included in the recording of drugs from the treatment journal. Furthermore, a total of 1177 entries where the dosage was missing, but containing all other relevant information, could be supplemented with the dosage details issued from the Swiss Compendium of Veterinary Medicinal Products and used as treatment journal added.

67 entries with missing drug names had to be completely discarded from the analysis (Table 1). Finally, a total of 2661 entries issued from the treatment journal added could be analysed.

3.2. Comparison of antimicrobial quantities

For every type of treatment (IMM, DRY and SYS), the highest recorded quantity of antimicrobials was reported with the veterinary practice software and the lowest quantity with the treatment journal. Almost as many udder injectors for IMM and DRY treatments were gathered with the garbage bags as were recorded with the veterinary practice software. However, a huge difference could be observed for the SYS group between the preparations recorded in the garbage bags compared to the software records. The treatment journal added recorded the second-highest quantity for systemic preparations, but represented only slightly more than half of the quantity collected with the veterinary practice software (Table 2).

Table 1
Overview of entries in the treatment journal, how missing entries were handled and for which data source they could still be used.

<table>
<tr><td rowspan="2">Complete entries</td><td colspan="8">Missing information (n = 1284)</td></tr>
<tr><td>Cow identification</td><td>Date</td><td>Indication</td><td>Indication and other[a]</td><td>Dosage</td><td>Dosage and other[a]</td><td>Drug</td><td>Drug and dosage</td></tr>
<tr><td>1444</td><td>7</td><td>1</td><td>25</td><td>7</td><td>1151</td><td>26</td><td>65</td><td>2</td></tr>
<tr><td>Entries could be used directly</td><td colspan="2">Missing information was ignored</td><td colspan="4">Information could be supplemented</td><td colspan="2">Entries had to be discarded</td></tr>
<tr><td colspan="7">Treatment journal added (n = 2661)</td></tr>
<tr><td colspan="5">Treatment journal (n = 1484)</td></tr>
</table>

[a]Other = date, product or animal identification number.

Table 2
Comparison of antimicrobials quantities collected from different data sources.

Data source	Intramammary preparations				Systemic preparations	
	during lactation		for dry off			
	Quantity of injectors	TI (DDD per 1000 cow-days)	Quantity of injectors	TI (DCD per 1000 cow-days)	Quantity (in mg of active substances)	TI (DDD per 1000 cow-days)
Software	12,916.00	7.00	8,353	1.13	12,920,272	1.07
Garbage	11,294.60	6.12	8,235	1.12	4,285,987	0.34
Treatment journal	5,326.60	2.89	3,355	0.45	3,101,505	0.20
Treatment journal added	7,815.60	4.24	6,286	0.85	7,280,302	0.58

TI: Treatment incidence.
Software: Antimicrobial data extracted from veterinary practice software.
Garbage: Discarded drug packages collected on farms.
Treatment journal: Data from treatment journals collected on farms without supplemented missing dosage.
Treatment journal added: Data from treatment journals collected on farms with the missing dosage records supplemented with information issued from the Swiss Compendium of Veterinary Medicinal Products.

The differences between the recording systems were similar when TI was analysed separately for the different WHO categories (HPCIAs, CIAs and HIAs).

Across all data sources, the highest quantity of IMM preparations were CIAs like penicillin, penicillin combinations as well as aminoglycosides, followed by HPCIAs. Only a few preparations were assigned to the HIAs category (Fig. 1).

On the other hand, no product containing HPCIAs was used in the DRY group (Fig. 2). Based on the analysis of the software and garbage data, CIAs were the most used dry off preparations.

Regarding systemic preparations, the most frequently used antimicrobials belonged to the CIAs group. Similar to the overall distribution of systemic antimicrobials, most of CIAs were recorded with the practice software followed by the treatment journal added, the lowest quantity being recorded in the treatment journal. Conversely, the fewest HPCIAs, CIAs and HIAs were found in the garbage (Fig. 3).

3.3. Comparison of the variety of products

For both garbage and treatment journal, 23 IMM preparations and 10 DRY preparations were collected. The lowest variety of intramammary preparations was found in the software (Table 3).

Most of the systemic preparations were captured by the veterinary practice software (83.8 %), followed by the treatment journal (72.1 %) with the garbage (54.0 %) having the least. The widest variety of intramammary preparations was found in the garbage (88.5 % of IMM and 90.1 % of DRY), followed by the treatment journal (80.8 % of IMM and 90.1 % of DRY). The veterinary practice software captured only 69.2 % and 63.6 % of the IMM and DRY preparations, respectively.

Based on the number of different preparations present across all data

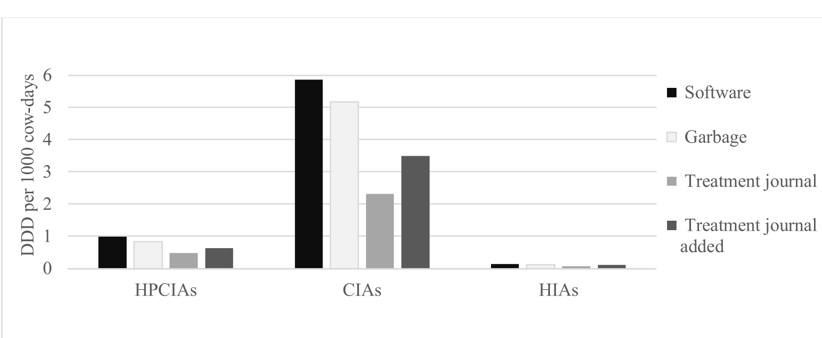

Fig. 1. Comparison of treatment incidence of intramammary antimicrobials used during lactation (TI_{IMM}) according to WHO categorisation.
DDD: Defined daily dose.
Software: Antimicrobial data extracted from veterinary practice software.
Garbage: Discarded drug packages collected on farms.
Treatment journal: Data from treatment journals collected on farms without supplemented missing dosage.
Treatment journal added: Data from treatment journals collected on farms with the missing dosage records supplemented with information issued from the Swiss Compendium of Veterinary Medicinal Products.
HPCIAs: Highest Priority Critically Important Antimicrobials (according to WHO).
CIAs: High Priority Critically Important Antimicrobials (according to WHO).
HIAs: Highly Important Antimicrobials (according to WHO).

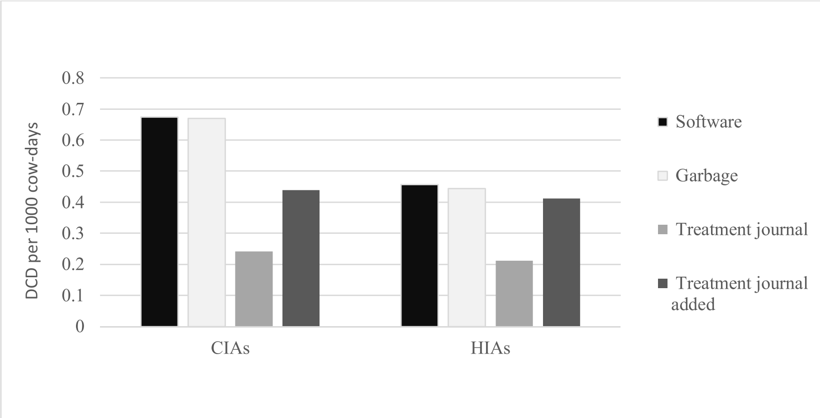

Fig. 2. Comparison of treatment incidence of intramammary antimicrobials used for drying off (TI_{DRY}) according to WHO categorisation.
DCD: Defined course dose.
Software: Antimicrobial data extracted from veterinary practice software.
Garbage: Discarded drug packages collected on farms.
Treatment journal: Data from treatment journals collected on farms without supplemented missing dosage.
Treatment journal added: Data from treatment journals collected on farms with the missing dosage records supplemented with information issued from the Swiss Compendium of Veterinary Medicinal Products.
CIAs: High Priority Critically Important Antimicrobials (according to WHO).
HIAs: Highly Important Antimicrobials (according to WHO).

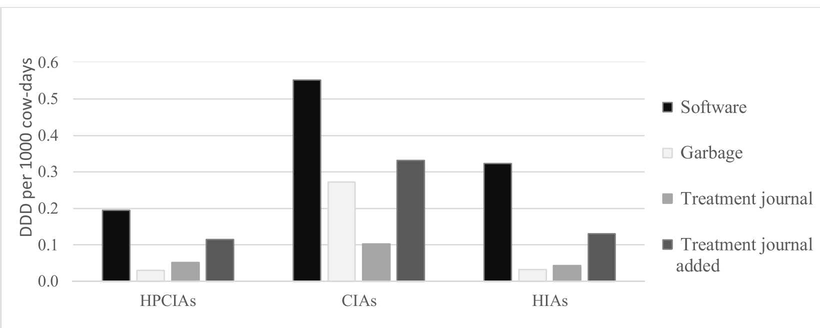

Fig. 3. Comparison of treatment incidence of systemic antimicrobials used for mastitis treatment (TI_{SYS}) according to WHO categorisation.
DDD: Defined daily dose.
Software: Antimicrobial data extracted from veterinary practice software.
Garbage: Discarded drug packages collected on farms.
Treatment journal: Data from treatment journals collected on farms without supplemented missing dosage.
Treatment journal added: Data from treatment journals collected on farms with the missing dosage records supplemented with information issued from the Swiss Compendium of Veterinary Medicinal Products.
HPCIAs: Highest Priority Critically Important Antimicrobials (according to WHO).
CIAs: High Priority Critically Important Antimicrobials (according to WHO).
HIAs: Highly Important Antimicrobials (according to WHO).

Table 3
Comparison of number of antimicrobial preparations collected from different data sources.

Data source	Intramammary preparations						Systemic preparations		
	during lactation			for dry off					
	recorded preparations	%	recorded preparations from abroad	recorded preparations	%	recorded preparations from abroad	recorded preparations	%	recorded preparations from abroad
Software	18	69.23	0	7	63.64	0	31	83.78	0
Garbage	23	88.46	3	10	90.91	1	20	54.05	0
Treatment journal	23	88.46	1	10	90.91	1	27	72.97	0
Common in all data sources	17	65.38	1	7	63.64	1	16	44.44	0
Total different preparations	26	100	3	11	100	1	36	100	0

Garbage: Discarded drug packages collected on farms.
Treatment journal: Data from treatment journals.
Software: Antimicrobial data extracted from veterinary practice software.

sources, only 65.4 % and 63.6 % of intramammary preparations and 44.4 % of systemic preparations were found in every data source. Consequently, preparations were found in the software that could not be found in the garbage or treatment journal and vice versa.

Finally, the analysis of the data issued from the garbage and the treatment journal demonstrated the on-farm usage of intramammary antimicrobials, which are not approved in Switzerland for mastitis treatments and dry cow therapy (preparations from abroad). In the garbage, 23 of the 11294.6 injectors for intramammary treatment during lactation and 4 of the 8235 injectors for dry cow therapy could be assigned to a product not approved in Switzerland. In the treatment journal, three entries out of a total of 2728 entries could be assigned to a preparation from abroad.

3.4. Agreement of data sources on the farm level

From 460 combinations of farm and antimicrobial product, the maximum number of injectors of all four data sources was recorded in the veterinary software in 258 combinations (56.1 %). In 231 combinations, the maximum number was found in the garbage (50.2 %). In the treatment journal and treatment journal added, the maximum number was only recorded in 94 (20.4 %) and 56 (12.2 %) combinations, respectively. In 63 combinations (13.7 %), no treatment had been recorded in the practice software, even though usage of the product on the respective farm was recorded in another data source. Completely missing entries were found for 49 combinations (10.7 %) in the garbage, 212 combinations (46.1 %) in the treatment journal, and 97 combinations (21.1 %) in the treatment journal added.

There was perfect agreement between garbage and veterinary software in 258 combinations (56.1 %). Garbage agreed perfectly with treatment journal in 32 combinations (7.0 %), and with treatment journal added in 39 combinations (8.5 %). Veterinary software agreed perfectly with treatment journal in 32 combinations (7.0 %), and with treatment journal added in 39 combinations (8.5 %). Treatment journal and treatment journal added agreed perfectly with each other in 56 combinations (12.2 %).

The effect of the data source on the relative error category was further analysed with a mixed ordinal regression model. The random effect for product was not significant (chi-square for the likelihood ratio test = 1.9, $p = 0.12$, ICC = 0.007), and was therefore removed from the model. The random effect for farm was relatively small (0.16, 95 % CI 0.08−0.30), but significant (chi-square for the likelihood ratio test = 22.2, $p < 0.001$, ICC = 0.08). In a two-level model correcting for clustering on the level of the farm, treatment journal added was significantly less likely to be in a category with a greater relative error (OR = 0.4, 95 % CI = 0.3−0.5) compared to treatment journal. Garbage (OR = 0.11, 95 % CI = 0.08−0.14) and veterinary software (OR = 0.10, 95 % CI = 0.07−0.13) were also significantly less likely than the treatment journal to have a large relative error.

4. Discussion

The purpose of this study was to compare data on antimicrobial consumption between three different collection methods: treatment journal records, data from veterinary practice software and on-farm discarded drug packages. The highest antimicrobial consumption was recorded with the veterinary practice software. The lowest quantity was gathered with the treatment journal. The largest variety of intramammary preparations was found with the garbage and the treatment journal. On the other hand, the veterinary practice software gathered most of the systemic preparations.

4.1. Comparison of used quantity of antimicrobials

As the current Swiss legislation requires a precise documentation of each antimicrobial treatment at farm level, treatment journals are assumed to reflect the integral AMU on farms. However, our results showed that the treatment journal recorded the lowest quantity of antimicrobials. This suggests that either the farmers or the veterinarians forgot to record entries in the treatment journals, and controls by the veterinary authorities failed to identify these missing data. Furthermore, this under-recording could be also due to poor compliance from the farmers' side. In line with our results, previous studies suggested that the calculated AMU based on the treatment journal records was lower than the calculated AMU based on the data issued from empty drug containers (Nobrega et al., 2017) as well as the antimicrobial data obtained from veterinary prescription records (Menéndez González et al., 2010; Kuipers et al., 2015). The comparably low antimicrobial quantity gathered with the treatment journal was partly due to the fact that the used dosage was missing in around half of the entries. Previous studies faced similar issues (Menéndez González et al., 2010; Stevens et al., 2016; Nobrega et al., 2017). By supplementing the dosage with the information given in the Swiss Compendium of Veterinary Medicinal Products (treatment journal added), there might be a risk of over- or underestimation of the actual antimicrobial usage (Regula et al., 2009; Echtermann et al., 2019).

As prescribed antimicrobials are not necessarily used, antimicrobial sales or prescription data do not reflect the true AMU on farms. For this reason, the calculated treatment incidences based on the software data can possibly overestimate the actual AMU on farms. We tried to minimise this bias by subtracting AM which had been returned from the farmer to their veterinarian. For intramammary preparations, the second highest quantity was recorded by garbage bags. These preparations are usually prescribed and delivered by veterinarians after examination of diseased cows and administered by farmers themselves, who afterwards dispose the discarded drug packages in these bags. However, this collection method could lead to an underestimation of the AMU if farmers did not discard the empty drug packages in the garbage bags. In particular, this might have happened if a diseased cow was treated directly by the veterinarian. Moreover, this could also explain the comparably low quantities of antimicrobials for systemic use collected in the garbage. Veterinarians routinely administer systemic antimicrobials themselves after examination of cows affected by acute mastitis. These antimicrobials are most of the time available in bottles containing volumes of either 50 mL or 100 mL (Swiss Compendium of Veterinary Medicinal Products, 2020). As veterinarians keep leftovers for the next antimicrobial treatment, some of these treatments could not be collected with the garbage.

Based on the WHO categorisation of antimicrobials according to their importance for human health, the most frequently used intramammary antimicrobials belonged to the category "critically important" (CIAs). Critically important substances like penicillin and penicillin combinations as well as aminoglycosides are in fact first-line antimicrobials for the treatment of acute mastitis (Antibiotika-Scout, 2020). The absence of dry off preparations belonging to the HPCIAs category is due to the fact that such preparations were neither available on the Swiss market (Swiss Compendium of Veterinary Medicinal Products, 2020) nor imported from abroad.

Similarly, the most frequently used systemic preparations belonged to the CIAs category. Substances of the category HPCIAs were the least frequently used systemic antimicrobials. As only a few HPCIAs preparations were found in the garbage, this suggests that veterinarians are mostly administering these products themselves.

4.2. Comparison of preparations

Surprisingly, the widest variety of intramammary preparations was found in the garbage and in the treatment journal. As a veterinary medicines contract was a prerequisite for the participation to the study, which ensures that only one veterinary practice supplies the farmer with antimicrobial preparations, the authors expected to find the same intramammary preparations in every data source. However, during emergency services, a different veterinary practice may treat the cows. Moreover, a few intramammary antimicrobial preparations were recorded, which are not approved in Switzerland for mastitis or dry off treatments, but contain antimicrobial substances which can legally be used in dairy cows. The occasional acquisition of those drugs from abroad (France) is a commonly known practice among the sector (Pucken et al., 2019). As the number of different intramammary preparations found in the software was lower than the number found in garbage and treatment journal, the calculated antimicrobial consumption based on the veterinary software might underestimate the use of intramammary preparations.

In contrast to intramammary preparations, systemic preparations are usually prescribed and used by the contractual veterinarian after examination of diseased cows. This explains that the widest variety of these preparations was gathered with the veterinary practice software. The lowest systemic preparations variety was found in the garbage and in the treatment journal. Therefore, the calculated AMU based on both methods might underestimate the use of systemic preparations.

4.3. Strengths and limitations

This study had to rely on the voluntary participation of a small number of veterinary practices and dairy farms. This selection bias was unavoidable, as the support of farmers and veterinarians was needed to conduct the study. Since the participants were interested in the study, they might be more likely to record antimicrobial treatments accurately, and therefore have data quality above-average. We also had to exclude farmers with very poor recordings, and records with implausible data. Volunteer farmers and veterinarians might use antimicrobials more prudently than those who chose not to participate, resulting in a lower antimicrobial consumption. For the farmers, this bias is likely to be small because of the high participation rate for this study. This descriptive study is not representative of the population and the results on antimicrobial usage cannot be extrapolated to the Swiss dairy production.

4.4. Data quality

Despite the mandatory documentation of antimicrobial treatments at farm level in Switzerland, the recorded data from farm treatment journals were often inaccurate and incomplete: around half of the entries lacked at least one piece of critical information.

The collection of discarded drug packages with the help of garbage bags was convenient and easy to implement. Around 30 % of the provided garbage bags were discarded at collection, suggesting no AMU during the respective month. Even though it cannot be excluded that farmers forgot to put some of the discarded antimicrobial packages into these bags, this collection method on AMU seems to be reliable for DRY and SYS, and is recommended by the authors of previous studies (Carson et al., 2008; Saini et al., 2012).

As a moderate number of entries issued from veterinary practice software had to be excluded from the analysis, it is assumed that the software data were more complete than data collected with the other methods (Kuipers et al., 2015). The different software systems used were not mutually compatible, making the data extraction difficult and complex. Hence, this emphasises the need of a standardised system to quantify and assess the antimicrobial consumption at practice and farm level.

4.5. Future perspectives and implications

The results of this study show that the collection of antimicrobial data with the garbage bin could be an appropriate tool to record antimicrobials administered by farmers. This method could detect use of preparations which were not prescribed by contractual veterinarians as well as preparations which are not approved in Switzerland for the indication mastitis.

In contrast, the recording of AMU by the farmer in a treatment journal seems to considerably underestimate usage. There were huge discrepancies in data completeness between the participating farms. Therefore, this method cannot be recommended for collecting data on AMP or AMU for benchmarking or monitoring purposes.

Finally, the results of this study further emphasise the need of implementing a standardised system to record antimicrobial treatments at individual animal and farm level. In Switzerland, one step towards this need was completed in 2019 with the implementation of the Information System Antimicrobials in Veterinary Medicine (IS ABV). Within this system, veterinary practices and clinics have to record data on AMP for individual and group therapies in a standardised format into a central database. The database contains information on animal species, age class and production type, number of treated animals, antimicrobial drug, dosage and diagnosis or indication for treatment. This allows for calculation of standardised measures of treatment intensity such as prescribed daily dose or defined daily dose (DDDvet) (European Surveillance of Veterinary Antimicrobial Consumption (ESVAC), 2016). Therefore, treatment intensity can be compared among different animal species and age classes (Federal Food Safety and Veterinary Office, 2020).

5. Conclusion

The results of this study demonstrate a significant lack of data consistency between three different collection methods. No single collection method was able to capture the integrity of data on AMU in the participating farms. As a standardised monitoring system with centralized data analysis, the newly launched Information System Antimicrobials in Veterinary Medicine (IS ABV) can provide a better understanding of AMP at farm and veterinary practice level in Switzerland. Data quality is a critical aspect of such a system, because it is unlikely that one single recording method is going to represent the total quantity of antimicrobial usage.

Declaration of Competing Interest

The authors report no declarations of interest.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.prevetmed.2020.105221.

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