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Time trends, seasonal differences and determinants of systemic antimicrobial use in companion animal clinics (2012-2015)

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ABSTRACT

Any antimicrobial use (AMU) in humans and animals selects for antimicrobial resistance (AMR) and responsible AMU should therefore be promoted both in human and veterinary medicine. Insight into current AMU in companion animal clinics is necessary to be able to optimise antimicrobial (AM) prescribing behaviour. The objective of this study was to describe systemic AMU in 44 Dutch companion animal clinics over a 3-year time period (2012–2015), using retrospectively collected data. The number of Defined Daily Doses for Animals (DDDAs) per month and per clinic were calculated from prescription data for total, 1st, 2nd and 3rd choice AMU (classification according to Dutch policy on veterinary AMU). Time trends, seasonality and the influence of potential determinants (e.g., the number of dogs, cats and rabbits per clinic and other clinic characteristics) were explored using statistical modelling. Overall, the findings show that total AMU decreased over time and a shift in used classes of antimicrobials towards more 1st choice AMs was visible. Mean total AMU decreased from 1.82 DDDA/year in 2012–2013 to 1.56 DDDA/year in 2014-2015. Aminopenicillins, with and without clavulanic acid, accounted for the largest group of antimicrobials used; 38.7% (2012–2013), 40.2% (2013–2014) and 39.3% (2014–2015) of total AMU, respectively. Strong seasonal differences in AMU were found, with highest AMU in July-August and lowest in February-March. The distribution of different animal species per clinic appeared to affect AMU as well. In clinics with a larger proportion of dogs, 2nd choice AMU was significantly higher, whereas in clinics with a larger proportion of rabbits, 2nd choice AMU was significantly lower. Despite the decrease of AMU during the study period, there is still room for improvement left, especially with regard to the antimicrobial classes prescribed. According to Dutch classification of veterinary AMU, 1st choice AMs should be used as empirical therapy. A decrease in 2nd (might select for ESBL-producing bacteria) and 3rd choice AMU (i.e. fluoroquinolones and 3rd generation cephalosporins) should be aimed for.

1. Introduction

Antimicrobial use (AMU) in humans and animals promotes the selection and dissemination of antimicrobial resistance (AMR), as well as the emergence of new resistant bacteria (Spellberg et al., 2013; EMA, 2013; McEwen and Collignon, 2018). The increase of AMR has been recognised as a global concern and risk for public health. Responsible AMU is therefore needed and should be promoted both in human and veterinary medicine (Grave et al., 2014; WHO, 2015; Collignon et al., 2016). In human medicine, guidelines and antimicrobial stewardship programmes (ASPs) are developed and implemented to promote responsible AMU (MacDougall and Polk, 2005; Allerberger and Mittermayer, 2008; Allerberger et al., 2008; Owens, 2008; Schuts et al., 2016). In veterinary medicine, just recently (inter)national guidelines to promote responsible AMU in companion animals have been developed (AMCRA, 2019; BSAVA, 2019; DSAVA (Jessen et al., 2019); ISCAID, 2019; WVAB). From 2008 onwards, AMU in Dutch food producing animals received increasing attention; action plans and

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regulations to reduce AMU were implemented, resulting in a decrease in AMU of almost 68% between 2007 and 2017 (NethMap/MARAN, 2018; SDa (the Netherlands Veterinary Medicines Institute), 2018). One of the keys to success of the Dutch reduction policy was to get complete and reliable data on AMU in food producing animals (Speksnijder et al., 2015). This transparency in AMU enabled the possibility to set reduction targets and to monitor attainment of these targets. Benchmarking of farmers was established as well, which contributed to social pressure and an increased awareness among farmers. Antimicrobial use in companion animals is not continuously monitored so far, and although AMU in companion animals is expected to be low compared to food producing animals, the antimicrobial (AM) classes used in companion animals appear to be less preferable. A survey on prescription data of 68 companion animal clinics in the Netherlands during 2009–2011, showed that use of 3rd generation cephalosporins and fluoroquinolones (i.e. highest priority critically important antimicrobials for human medicine according to the World Health Organisation (WHO)) accounted for 18% of total AMU, based upon the number of Defined Daily Doses for Animals (DDDAs) (Van Geijlswijk et al., 2013; WHO, 2017). Insight into current AM prescribing behaviour and AMU patterns in Dutch companion animal clinics is pivotal to enable development, implementation and evaluation of an antimicrobial stewardship programme (ASP) to optimise AMU. The aim of this study was to describe systemic AMU in 44 Dutch companion animal clinics over a 3-year time period (from July 2012 to June 2015) and to explore time trends, seasonality and influencing determinants. Systemic AMU was evaluated in a standardised way using the number of DDDAs.

2. Materials and methods

2.1. Study design

A retrospective survey was performed in Dutch companion animal clinics, in which AMU was evaluated using AM prescription data from 2012–2015. These clinics were part of a larger (intervention) study on AMU in Dutch companion animal clinics. Information collected from each of the participating clinics included general clinic characteristics, data on the clinic population and antimicrobial veterinary medicinal product (AVMP) prescription data on a monthly basis.

2.2. Selection of participating clinics

Companion animal clinics were approached for participation using the database of the Royal Dutch Veterinary Association (KNMvD). The total number of clinics treating companion animals was estimated to be 1204 in 2014 (HAS, 2015). Convenience sampling was used to select clinics based on previous shown interest to participate in a study on AMU in companion animal clinics and on geographic location. In 2016, clinics were invited to participate by e-mail, followed by a phone call to answer questions and to arrange a visit to collect requested data. Clinic visits were planned within a month after first contact with the clinic. Clinics were eligible for inclusion if the Practice Management System (PMS) was able to provide information on monthly antimicrobial prescription data specified for companion animals. Both clinics treating companion animals only and so-called "mixed" clinics able to specify prescription data for companion and non-companion animals were included in the study. Before enrolment in the study, all clinics received written and oral information on the purpose of the study. Each clinic signed an informed consent granting permission to use their patient data for research purposes after anonymisation.

2.3. Data collection and management

Each clinic filled out a short questionnaire on clinic characteristics and demographics at the beginning of the study. Information on the number of dogs, cats and rabbits attending the clinic at least once in a specified 3-year period, were retrieved from the PMS. AMU data were retrieved retrospectively by extracting AM prescription data per month from July 2012-June 2015.

2.4. Calculation of AMU

The European Surveillance of Veterinary Antimicrobial Consumption group (ESVAC) has defined the Defined Daily Dose for animals (DDD_{VET}) as "the assumed average dose per kg animal per species per day" (EMA, 2015, 2016). The method used in present study to calculate the number of Defined Daily Doses for Animals (DDDAs) per clinic is explained and discussed in detail in a previous study (Hopman et al., 2019). In summary, to calculate the number of DDDAs per clinic, two variables are needed (Bos et al., 2013). First, the total animal mass in kilogram that can be treated for one day with the amount of AMs prescribed. Second, the total weight (in kg) of the clinic animal population at risk to be treated with the AVMPs. By dividing the two variables for all individual AVMPs prescribed and consequently adding up the outcomes, the total number of DDDAs was obtained. This sum of all prescribed AVMPs per month describes the mean AMU of all dogs, cats and rabbits of the concerning clinic ($DDDA_{CLINIC}$) which enables comparison of AMU between clinics and over time. A $DDDA_{CLINIC}$ of 0.5 per month implies that the average animal (dog, cat and rabbit) in the clinic was exposed to antimicrobials for half a day per month.

For each clinic, total $DDDA_{CLINIC}$ was calculated per month from 1 July 2012 till 30 June 2015 and specified per antimicrobial class, according to Dutch policy on veterinary AMU (Table 1) (WVAB, 2018 (Dutch Working Party on Veterinary Antibiotic Policy) www.wvab.nl)

In the present study, only systemic (i.e. oral or parenteral) AMU was described, antimicrobials applied topically were excluded from further analyses.

2.5. Data analysis

Potential determinants of AMU (all the clinic characteristics retrieved from the questionnaire and the number of dogs, cats and rabbits per clinic, as shown in Table 2) were evaluated in a multivariable regression model with log-transformed AMU data (either total, 1^{st}, 2^{nd}, or 3^{rd} choice AMU) as the outcome variable. All determinants were entered in the model to explore the possible influence of determinants of AMU in their context. To reduce collinearity between variables, the

Table 1
Classification of veterinary AMU according to Dutch policy on veterinary AMU.

Classification	Reasoning	Main classes of AMs
1^{st} choice	Empirical therapy; Do not select for (to current knowledge), nor are specifically meant for treatment of ESBL-producing micro-organisms.	Tetracyclines, nitroimidazoles, narrow-spectrum penicillins, trimethoprim, sulfonamides and phenicols.
2^{nd} choice	All AMs not classified as 1^{st} or 3^{rd} choice AMs; Use of these AMs might select for ESBL-producing bacteria or is specifically indicated in case of an ESBL-infection.	Aminopenicillins (with/without beta-lactamase inhibitors), 1^{st} generation cephalosporins, aminoglycosides and colistin.
3^{rd} choice	Highest Priority Critically Important AMs for human medicine according to WHO; By Dutch law restricted to use only in individual animals and after culture and susceptibility testing.	Fluoroquinolones, 3^{rd} and 4^{th} generation cephalosporins.

Table 2
Characteristics of 44 participating Dutch companion animal clinics.

Characteristic (number of clinics = 44)	Mean (range)
Number of dogs	2151 (14 - 5353)
Number of cats	1910 (350 - 5113)
Number of rabbits	271 (0 - 797)
Total number of veterinarians	3 (1 - 10)
Number of veterinarians treating companion animals	2.7 (1 - 8)
Number of affiliated practices	1.25 (1 - 3)
Mean number of years experience per clinic	16.2 (5.8 - 34)
Characteristic (number of clinics = 44)	**Distribution (% of total)**
Companion animals only versus mixed-animal clinics	40 (90.9%) / 4 (9.1%)
Urban, rural or urban-rural	29 (65.9%) / 14 (31.8%) / 1 (2.3%)
Conventional medicine only versus also offering non-conventional medicine options	39 (88.6%) / 5 (11.4%)
Veterinarians only graduated in the Netherlands versus other countries of graduation	31 (70.5%) / 13 (29.5%)
Only female, only male or mixed gender clinic	19 (43.2%) / 6 (13.6%) / 19 (43.2%)
Serving shelters or kennels versus not serving shelters or kennels	11 (25%) / 33 (75%)
Serving breeders versus not serving any breeders	29 (65.9%) / 15 (34.1%)
PMS* type used 1 / 2 / 3 / 4 (in which 4='remaining group')	26 (59.1%) / 6 (13.6%) / 5 (11.4%) / 7 (15.9%)

* PMS type 1, 2 and 3 represent three different Practice Managements Systems, PMS type 4 represents a group of 'other' systems, all only used in a few clinics.

Table 3
Mean AMU in numbers of DDDA/year (total, 1st, 2nd and 3rd choice antimicrobials) in the participating clinics in the 3 consecutive years (July 2012-June 2013, July 2013-June 2014 and July 2014-June 2015).

Classification of antimicrobials	2012/2013	2013/2014	2014/2015
First choice (% of total)	0.62 (33.8%)	0.67 (40.3%)	0.7 (44.6%)
Second choice (% of total)	0.88 (48.5%)	0.81 (48.9%)	0.74 (47.2%)
Third choice (% of total)	0.32 (17.7%)	0.18 (10.8%)	0.13 (8.1%)
Total DDDA per year (SD)	1.82 (1.0)	1.65 (0.98)	1.56 (1.0)

number of veterinarians (highly correlated with the total number of dogs, cats and rabbits treated, Pearson's $r = 0.75$) and the proportion of cats (highly correlated with the proportion of dogs, Pearson's $r = 0.75$) were excluded from further analyses. P-values ≤ 0.05 were considered as statistically significant and P-values between 0.05 and 0.10 were considered borderline statistically significant and represent a trend or tendency. General time trends were modelled using natural regression splines with a single interior knot placed at the median time point (January 2014), while seasonal effects were modelled using a combination of four (two pairs of) harmonic (sine/cosine) functions. To allow for between-clinic heterogeneity in time and seasonal trends and to account for the autocorrelation of observations within a clinic over time, the statistical model included clinic-specific intercepts and trend coefficients as random effects and an auto-regressive (AR1) correlation structure for the residuals. The natural spline bases were centred at the interior knot location to allow interpretation of the fixed effects as the ratio of geometric means (GMR) of estimated AMU at this timepoint. Model fit for simpler models (e.g., models that did not include an auto-regressive structure) proved inferior to that of the selected model. Despite small numerical differences, results were qualitatively similar. A model allowing for clinic-specific residual variances failed to converge when used with the full determinant model, but point estimates and standard errors compared well with the selected model for smaller submodels.

SAS (SAS 9.4, SAS Institute, Inc. Cary, NC, USA) was used to organise the data and R (version 3.5) was used to perform the statistical analyses, using the nlme package (version 3.1) to fit the mixed effects models and to graphically present the data.

3. Results

3.1. Participating clinics

In total, 54 clinics were contacted to participate. Six clinics were not willing to participate and four clinics did not have a suitable PMS to provide monthly prescription data. Finally, 44 clinics were included in the study. Table 2 shows characteristics of the participating clinics.

Eight clinics were not able to provide prescription data from July 2012 onwards (e.g., because the clinic had just opened or switched to another PMS), for these clinics data were provided from the earliest moment possible.

3.2. Defined daily doses for animals

3.2.1. Mean AMU per year

Mean total AMU decreased from 1.82 to 1.56 DDDA/year in the participating clinics (Table 3). Aminopenicillins (amoxicillin with and without clavulanic acid) accounted for the largest group of used AMs in the three consecutive periods, 38.7%, 40.2% and 39.3% of total AMU, respectively. Tetracyclines accounted for 8%, 11.2% and 12.6% of total AMU in these three years. Cefovecin (3rd generation cephalosporin) was the second most used substance in 2012/2013 (9.5%). However, the use of cefovecin decreased 3-fold when comparing the first year with the last year (from 0.17 DDDA/year to 0.05 DDDA/year). Likewise, the use of fluoroquinolones showed a decrease from 2012 to 2015 (0.15 DDDA/year to 0.07 DDDA/year).

3.2.2. Time trends and seasonality

Results from our statistical model indicated that total, 1st, 2nd and 3rd choice AMU changed significantly over time ($P < 0.001$), in which total, 2nd and 3rd choice AMU decreased, whereas 1st choice AMU increased. AMU showed a strong seasonal pattern with a peak in July-August and a lowest value in February-March (see Fig. 1 for total AMU). This seasonal pattern was statistically significant ($P < 0.001$) for total, 1st and 2nd choice AMU.

3.2.3. Determinants of AMU

Results of the multivariable regression analysis are shown in Table 4. Total AMU tended to be higher in clinics with a larger proportion of dogs (GMR 1.22, 95% CI 0.99–1.50 per 10% increase in the proportion of dogs), which was significant for 2nd choice AMU (GMR 1st choice AMU 1.24, 95% CI 0.94–1.65, GMR 2nd choice AMU 1.26, 95% CI 1.06–1.51, GMR 3rd choice AMU 1.01, 95% 0.66–1.54, respectively,

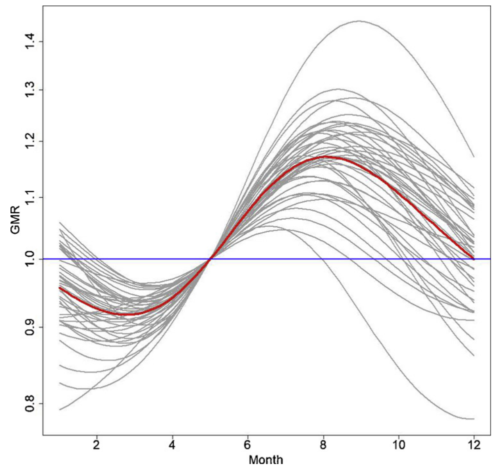

Fig. 1. Seasonality in total AMU in participating companion animal clinics during July 2012-June 2015. Seasonal effects are expressed as Geometric Mean Ratios (GMRs), comparing the geometric mean AMU in each month to that of the average across the year. Seasonal effects were modelled using harmonic functions and estimated using a mixed effect model that allowed for between-clinic heterogeneity. The mean of the random effects distribution ("average" seasonal effect) is shown in red, clinic specific (empirical bayes) estimates are shown in grey. On the horizontal axis, numbers 1–12 are used for January-December (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

per 10% increase in the proportion of dogs). A negative association was found between total AMU and the proportion of rabbits, which was significant for 2^{nd} choice AMU (GMR for total AMU 0.00, 95% CI 0.00–17.79, GMR for 2^{nd} choice AMU 0.00, 95% CI 0.00-0.04, respectively, per 1% increase in the proportion of rabbits). Total AMU in mixed-animal clinics appeared lower compared to companion animal only clinics, but this was only significant for 2^{nd} choice AMU (GMR for total AMU 0.60, 95% CI 0.31–1.16, GMR for 2^{nd} choice AMU 0.54, 95% CI 0.31-0.95). All other determinants showed no or only borderline associations with AMU (Table 4).

4. Discussion

This study describes systemic AMU in companion animals over the period 2012–2015 in Dutch companion animal clinics, based upon monthly prescription data and using the number of DDDAs as a measure to quantify systemic AMU. Overall, the findings show that AMU-patterns are changing over time with a decrease in total AMU and a shift in the used classes of antimicrobials towards more 1^{st} choice AMs. Strong seasonal differences in AMU were found and the distribution of different animal species appeared to affect AMU.

Only a limited number of studies describe AMU in companion animals and all studies use different measurements to quantify AMU. Incautious comparison of AMU in different studies might lead to wrong conclusions. We chose to use the number of Defined Daily Doses for Animals as a measure to quantify AMU. This measure is already established for Dutch food producing animals and takes dosing differences between AMs and between animal species into account. Using the number of DDDAs and $DDDA_{CLINIC}$, and its strengths and limitations, are discussed in detail in a previous study (Hopman et al., 2019).

Whether the participating 44 clinics are representative for the whole country is difficult to assess. The number of clinics is limited and estimated to be approximately 4% of the total number of companion animal clinics in the Netherlands. Participation was based on voluntariness and interest to participate in a larger study on AMU in companion animals. Large differences in AMU between clinics indicate that participating clinics seem to be diverse. Moreover, the decreasing trend shown in the current study resembles findings of another Dutch study on yearly procurement data of 100 companion animal clinics (Hopman et al., 2019).

The observed decrease in the use of cefovecin and fluoroquinolones (i.e. 3^{rd} choice AMs) in present study can most probably be attributed to a combination of increased awareness on AMR and implementation of policies to reduce AMU in the Netherlands, e.g., the mandatory susceptibility testing for veterinary use of these 3^{rd} choice AMs (Staatscourant, 2013). In other countries, e.g., Denmark and Sweden, similar policies have been implemented, which resulted in comparable decreasing trends in the use of critical AMs like fluoroquinolones and 3^{rd} and 4^{th} generation cephalosporins (SWEDRES/SVARM, 2016; DANMAP, 2018).

The reduction in total, 2^{nd} and 3^{rd} choice AMU is a promising development, however, the use of aminopenicillins, that might select for ESBL-producing bacteria, is still relatively high and 3^{rd} choice AMU (i.e. AMs considered as highest priority critically important AMs for human medicine by WHO (WHO, 2017)) still accounts for 8% of total AMU. In

Table 4
Effect estimates for potential determinants of AMU from a multivariable regression model, for total, 1^{st}, 2^{nd} and 3^{rd} choice AMU (log-transformed data). Time trends were modelled using natural regression splines, seasonal effects were modelled using a combination of four harmonic functions. The statistical model included clinic-specific intercepts and trend coefficients as random effects and an auto-regressive (AR1) correlation structure for the residuals.

	Total AMU		First choice[1]		Second choice[1]		Third choice[1]	
Clinic characteristic	GMR	95% CI	GMR	95% CI	GMR	95% CI	GMR	95% CI
Proportion of dogs (per 10% increase)	1.22	**0.99-1.50**[**]	1.24	0.94-1.65	1.26	**1.06-1.51**[*]	1.01	0.66-1.54
Proportion of rabbits (per 1% increase)	0.00	0.00-17.79	0.91	0.00-62.9 × 10^3	0.00	**0.00-0.04**[*]	0.64	0.00 - 10.4 × 10^6
Total number of animals	0.98	0.88-1.10	0.93	0.80-1.08	1.09	**0.99-1.20**[**]	0.94	0.75-1.18
Number of affiliated practices	1.09	0.78-1.52	0.96	0.61-1.51	1.05	0.79-1.39	1.18	0.60-2.34
Mean experience per clinic (number of years)	0.91	0.67-1.24	0.95	0.63-1.43	1.04	0.80-1.34	0.79	0.43-1.47
Mixed-animal clinics versus companion animals only	0.60	0.31-1.16	0.73	0.30-1.78	0.54	**0.31-0.95**[*]	0.57	0.15-2.16
Urban versus rural or urban-rural	1.28	0.82-2.00	1.09	0.60-2.01	1.15	0.79-1.68	1.88	0.76-4.64
Conventional medicine only versus also offering non-conventional medicine options	0.79	0.45-1.41	0.62	0.29-1.35	0.85	0.52-1.37	0.66	0.20-2.12
Veterinarians only graduated in the Netherlands versus other countries of graduation	0.96	0.64-1.45	0.90	0.52-1.58	1.08	0.76-1.52	1.79	0.77-4.17
Only female (versus only male or mixed gender clinic)	1.14	0.70-1.86	0.98	0.51-1.91	1.46	**0.97-2.19**[**]	0.99	0.37-2.66
Not serving shelters or kennels versus serving shelters or kennels	0.89	0.61-1.31	1.07	0.64-1.81	0.89	0.64-1.24	0.75	0.34-1.65
Not serving any breeders versus serving breeders	1.04	0.64-1.69	0.60	0.31-1.16	1.20	0.79-1.82	0.85	0.32-2.31
PMS 2 versus PMS 1, 3 or 4	0.82	0.50-1.33	0.86	0.45-1.66	0.66	**0.44-0.99**[**]	0.83	0.31-2.24

[1] According to Dutch policy on veterinary AMU (Table 1).
* P-value ≤ 0.05.
** 0.05 < P-value ≤ 0.10.

other countries similar data are shown for the use of these antimicrobial classes (Mateus et al., 2011; Buckland et al., 2016; Singleton et al., 2017; Hardefeldt et al., 2018). This warrants the need for guidelines or actions to further restrict the use of these AMs in animals. A possible explanation for the relatively high use of aminopenicillins could be the fact that aminopenicillins have a wide range of indications, dogs and cats tolerate them quite well, many authorised formulations are available for both dogs and cats in the Netherlands and, probably likewise important, companion animal veterinarians are used to these AMs, as was shown in a previous qualitative study (Hopman et al., 2018).

In the present study, seasonal differences in AMU were found with the highest total use in July-August and the lowest use in February-March. A similar seasonal pattern was described for AMU in dogs and cats in Australia (Hardefeldt et al., 2018). In dogs AMU was higher in spring and summer compared to AMU in winter months, and was discussed on as attributable to peaks in seasonal diseases, such as allergic dermatitis, seen in warmer months (Hardefeldt et al., 2018). In human medicine, seasonality was also shown for AMU, with higher systemic AMU in winter months (Goossens et al., 2005; Suda et al., 2014; Van der Velden et al., 2016; ECDC, 2018). Higher use of AMs in humans in winter coincides with the occurrence of flu epidemics. In companion animals, the higher use of 2nd choice AMs (mainly aminopenicillins and 1st generation cephalosporins) in summer months might be explained by more (bite)wounds and dermatological problems during warmer months. Cephalosporins (1st generation) are often used for dermatologic problems in dogs (Summers et al., 2014). Aminopenicillins have a wide range of indications, an important indication for the use of these AMs in cats could be wound infections, which might be more prevalent during summer when cats are roaming outside and fight more than in winter. Singleton et al. (2017) confirm that the main complaints resulting in AM prescribing are pruritus in dogs and trauma in cats, which could fit with the seasonal increase of 2nd choice AMU. The peak in 1st choice AMU is partially caused by a peak in tetracyclines of which the most common one is doxycycline. Doxycycline is mainly indicated for respiratory infections (Lappin et al., 2017), suggesting that respiratory problems might be more present in late summer/autumn period. This may be caused by the holiday season when pets are housed in kennels more often increasing the risk for respiratory infections, like kennel cough. An increased risk on vector borne diseases, like borreliosis and anaplasmosis, most often treated with doxycycline, might be another explanation for this peak in 1st choice AMs. However, more detailed studies are needed to explore these suggestions.

The distribution of different animal species per clinic appeared to affect AMU. Clinics with a higher proportion of rabbits appeared to be associated with lower AMU, especially of 2nd choice AMs. This could be explained by the fact that 2nd choice AMs are mainly aminopenicillins and 1st generation cephalosporins. Oral treatment with these AMs is generally considered contra-indicated in rabbits because it may result in dysbiosis and enterotoxaemia (Broens and Van Geijlswijk, 2018). In the Netherlands, there are only a few 2nd choice AMs authorised for use in rabbits. Second choice AMU was significantly higher in clinics with a higher proportion of dogs. There are several studies indicating that dogs receive more AMs compared to cats and thus supporting current findings (Buckland et al., 2016; Hardefeldt et al., 2018). Second choice AMs appear to be used more often in dogs, whereas especially 3rd generation cephalosporins (which are defined as 3rd choice AMs) are used more frequently in cats (Buckland et al., 2016; Singleton et al., 2017; Hardefeldt et al., 2018). Six participating clinics in the present study were able to produce individual animal-specified prescription data (data not shown). These animal-specified data, also based upon actual animal weights according to the PMS (average dog weight of 21.2 kg, average cat weight of 4.3 kg), demonstrated that dogs receive in general slightly more AMs than cats (approximately 14% more over the whole 3-year period). Differences are more prominent in the choices of AMs used, with dogs receiving more 1st and 2nd choice AMs than cats (approximately 1.3 and 1.6 times, respectively) and cats receiving explicitly more 3rd choice AMs than dogs (approximately 4 times more). To be able to optimise AMU in the future, more information is needed on the differences in AMU between dogs, cats and rabbits and on which specific indications account for the highest AMU.

Most clinics and practice management systems are not equipped to extract data on individual prescription information linked to specific indications in an automatic, uniform and feasible way. However, this detailed information is needed to optimise AMU further within companion animal clinics. Therefore, companies developing practice management systems are requested to enable this within their systems.

Slight differences in AMU appeared to be present between companion animal only and mixed-animal clinics. However, only four clinics were mixed-animal clinics, therefore this could be coincidence. On the other hand, AMU in food producing animals already received attention since 2008 onwards and actions were taken at different levels (Letter to the parliament, 2008; Speksnijder et al., 2015). This might have resulted in an early, increased awareness in companion animal veterinarians in mixed-animal clinics as well.

Although systemic AMU decreased and used AM classes changed during the study period, there still is room for improvement left. According to the Netherlands Veterinary Medicines Institute (SDa), continuous monitoring of AMU in companion animals is not needed so far, only once every three years (SDa, 2019). However, the Dutch formulary on AMU in companion animals (WVAB, 2018a) advises proper diagnostics and, if necessary, prefers the use of 1st choice AMs over the use of 2nd and 3rd choice AMs. Therefore, present study and used calculation method could be used as a starting point for a follow-up study on the development, implementation and evaluation of an antimicrobial stewardship programme in Dutch companion animal clinics to optimise AMU.

In conclusion, this study showed a decrease and a change in systemic AMU towards more preferable AMs in 44 Dutch companion animal clinics (2012–2015). The influence of season and the distribution of different animal species per clinic were demonstrated using the number of DDDAs and $DDDA_{CLINIC}$ to quantify veterinary AMU.

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Submission declaration

This research study has not been previously published elsewhere. Preliminary data were presented at the ICOHAR congress (16–18 April 2019, poster presentation) and at the BSAVA congress (4–7 April 2019, oral presentation).

Ethical approval

Not required.

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