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# Antimicrobial stewardship in companion animal practice: an implementation trial in 135 general practice veterinary clinics

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**Background:** Antimicrobial stewardship programmes (ASPs) have been widely implemented in medical practice to improve antimicrobial prescribing and reduce selection for multidrug-resistant pathogens.

**Objectives:** To implement different antimicrobial stewardship intervention packages in 135 veterinary practices and assess their impact on antimicrobial prescribing.

**Methods:** In October 2018, general veterinary clinics were assigned to one of three levels of ASP, education only (CON), intermediate (AMS1) or intensive (AMS2). De-identified prescribing data (1 October 2016 to 31 October 2020), sourced from VetCompass Australia, were analysed and a Poisson regression model fitted to identify the effect of the interventions on the incidence rates of antimicrobial prescribing.

**Results:** The overall incidence rate (IR) of antimicrobial prescribing for dogs and cats prior to the intervention was 3.7/100 consultations, which declined by 36% (2.4/100) in the implementation period, and by 50% (1.9/100) during the post-implementation period. Compared with CON, in AMS2 there was a 4% and 6% reduction in the overall IR of antimicrobial prescribing, and a 24% and 24% reduction in IR of high importance antimicrobial prescribing, attributable to the intervention in the implementation and post-implementation periods, respectively. A greater mean difference in the IR of antimicrobial prescribing was seen in high-prescribing clinics.

**Conclusions:** These AMS interventions had a positive impact in a large group of general veterinary practices, resulting in a decline in overall antimicrobial use and a shift towards use of antimicrobials rated as low importance, with the greatest impact in high-prescribing clinics.

## Introduction

Antimicrobial resistance (AMR) is a major threat to public health globally. In 2016, a review on AMR, commissioned by the UK government, found that approximately 700 000 people die each year because of MDR infections. This review predicted that by 2050 the global mortality rate could exceed 10 million people each year.<sup>1</sup> Direct, or indirect, contact with animals can result in human acquisition of MDR pathogens of animal origin.<sup>2–5</sup> Antimicrobials are an essential part of current and future veterinary medicine, and their use is justified to ensure optimal animal welfare and to ensure supplies of safe food for the community, but the misuse of antimicrobials in human or animal health cannot be justified.

Comprehensive antimicrobial stewardship programmes (ASPs) have been widely implemented in medical practice over the past decade to improve antimicrobial prescribing and reduce the selection pressure for the development of multidrug-resistant (MDR) pathogens. Most global<sup>6,7</sup> and national action plans<sup>8,9</sup> have called for implementation of ASPs in veterinary practices. Despite these calls, implementation of comprehensive ASPs in veterinary practices is uncommon. Medical ASPs have used restrictive interventions, which reduce the freedom of prescribers to select some antimicrobials, and persuasive interventions aimed at behaviour change. Persuasive interventions are focused on addressing predisposing factors (practitioner education), reinforcing factors (audit and feedback) and enabling factors (decision support).

Many ASPs have elements of both restriction and persuasion, but neither of these has been found to be more successful than the other over the long term.<sup>10</sup> Recently there have been reports of implementation of hospital-style ASPs in veterinary practice on a small scale,<sup>11</sup> but large-scale implementation, and assessment of that implementation, have not been reported. Implementing restriction in veterinary medicine would require new legislation, which is not currently being considered in Australia. Therefore, persuasive interventions will have to form the basis of veterinary antimicrobial stewardship (AMS) in the medium term. In addition, we believe that a comprehensive programme integrating many elements is likely to be more successful than restriction alone.

Studies of antimicrobial use patterns by Australian veterinarians have found that they predominantly use antimicrobials rated as medium importance<sup>12–15</sup> by the Australian Scientific and Technical Advisory Group on AMR (ASTAG).<sup>16</sup> In addition, inappropriate use of antimicrobials was common.<sup>13,14</sup> The enablers of and barriers to AMS in veterinary practices have also been investigated recently in this population. Veterinarians were generally supportive of additional AMS measures and recognized the threat that AMR posed both to patients and to the wider community.<sup>17</sup> The components that veterinarians believed were required for successful ASP implementation were determined to be: training in AMS and infection prevention; guidelines for antimicrobial use; resources, including client educational material; and access to cost-effective culture and susceptibility testing.<sup>17</sup> There is strong evidence in the literature that planned interventions can change prescribing practices and control infection outcomes in human hospitals,<sup>18–21</sup> and, while the challenges in general veterinary practice have been shown to be different to those in human medicine, we predict that the outcomes can be similar.

The aim of this project was to assess the effectiveness of implementation of a comprehensive antimicrobial stewardship package, compared with education alone, in a large number of veterinary clinics. This was measured by the changes in clinic rates of total antimicrobial prescribing and high-importance antimicrobial prescribing. A secondary aim was to evaluate strategies for increasing the uptake of the stewardship package, to maximize implementation.

## Methods

### Veterinary clinics

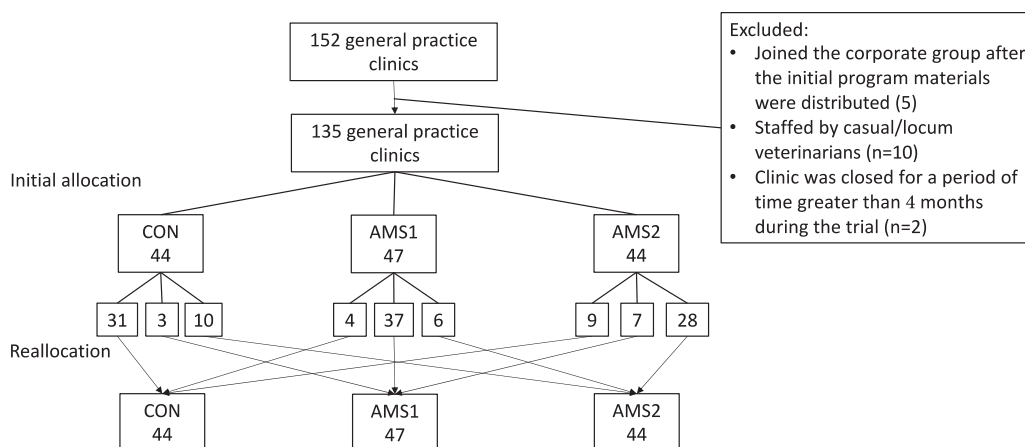
A corporate group of veterinary clinics was enrolled in the ASP trial in 2018. The corporate group included specialist, emergency and general practice veterinary clinics, but only general practice clinics were considered for the study ( $n = 152$ ) because of the relatively small number of specialist and emergency clinics in the group and the potential for different antimicrobial use patterns in these practices to bias the findings. Clinics were excluded if they joined the corporate group after the initial programme materials were distributed in October 2018 ( $n = 5$ ), if they were staffed only by casual/locum veterinarians ( $n = 10$ ), or if the clinic was closed for a period of time greater than 4 months during the trial ( $n = 2$ ) (Figure 1). There were three levels of veterinary leadership in the corporation. Firstly, a veterinary director was present in each clinic. One of six regional clinical directors oversaw a cohort of clinics and these regional directors reported to a single chief veterinary officer for the corporate group.

### Study period

Clinical records of consultations from all participating clinics were examined and all consultations with antimicrobial prescribing were identified.<sup>22</sup> The clinics were enrolled in October 2018. Clinical records from the 2 year period prior to the trial were also examined. Antimicrobial prescribing in the pre-trial period (1 October 2016 to 30 September 2018) was compared with prescribing during the implementation period (1 October 2018 to 31 July 2019) and the post-implementation period (1 August 2019 to 31 October 2020).

### Intervention

The interventions were co-designed by the research team, the chief veterinary officer and the regional clinical directors responsible for the ASP. Three arms of the trial were designed: a control group that received education only (CON), an intermediate ASP (AMS1) and an intensive ASP (AMS2) (Figure 2). At the beginning of the implementation period (October 2018) a prescribing guideline poster<sup>23</sup> was sent to all clinics in the corporate group, with space for annotation of clinic-specific prescribing policies incorporated into the poster. The education programme consisted of eight webinars, presented by national and international specialists recruited by the research team, on antimicrobial therapy in veterinary medicine (gastrointestinal disease, dental disease, peri-operative

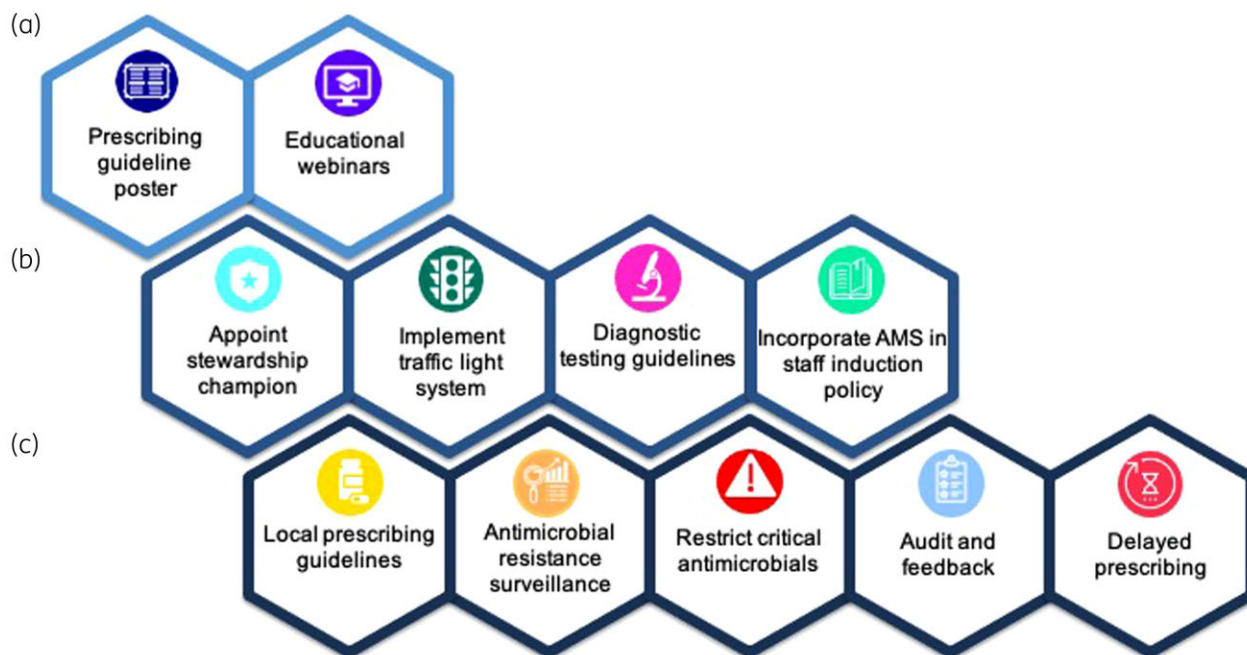


**Figure 1.** Flow diagram of clinic recruitment and allocation. CON, education only intervention; AMS1, intermediate intervention; AMS2, intensive intervention.

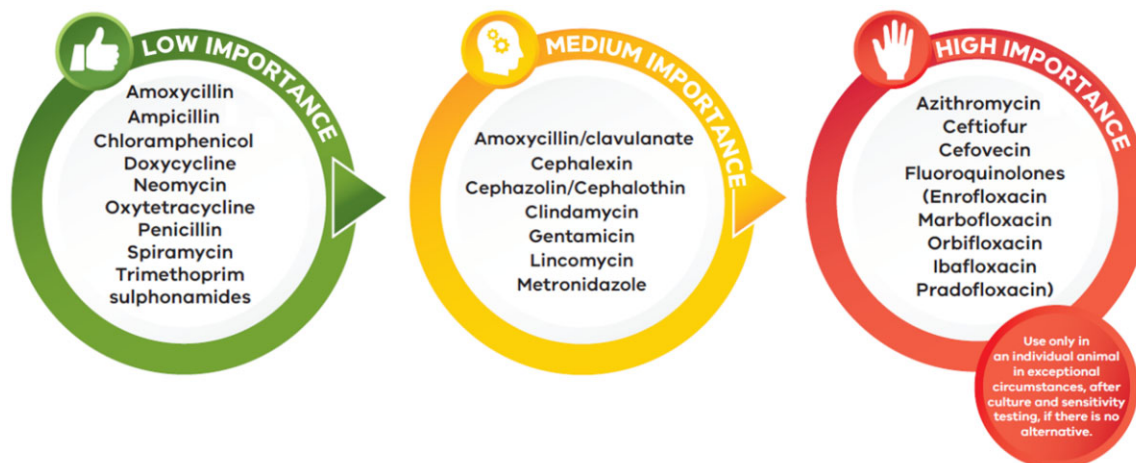
management, urinary tract syndromes, and skin disease), antimicrobial stewardship, infection control and delayed prescribing. Webinars were delivered online during the implementation period (1 October 2018 to 31 July 2019), through the corporate practice education platform, and were available for viewing online following the presentation.

AMS1 and AMS2 clinics were asked to appoint a stewardship champion to promote and lead implementation of the ASP. The champion co-ordinated implementation of a traffic light system for categorizing all the antimicrobials used in the clinic (Figure 3), based on the ASTAG<sup>16</sup> classification of antimicrobial importance for animal and human health. This required clinics in AMS1 and AMS2 to colour-code antimicrobials

according to their importance and, for AMS2 only, to restrict use of antimicrobials with a high importance rating. Diagnostic testing guidelines were provided for dermatological and urinary tract disorders, and stewardship champions were encouraged to develop other guidelines with their colleagues. Stewardship champions were also expected to conduct audit and feedback (AMS2), especially for new and recent graduates and new staff, and to track AMR isolates cultured in the clinic. A delayed prescription system was co-designed with the chief veterinary officer and a regional clinical director and implemented in AMS2. Resources for all interventions are freely available ([vetantibiotics.fvas.unimelb.edu.au](http://vetantibiotics.fvas.unimelb.edu.au)). Clinics were mailed and e-mailed copies of the AMS programme to which



**Figure 2.** Interventions included in each arm of the antimicrobial stewardship trial in general practice veterinary clinics. CON, education only intervention; AMS1, intermediate intervention; AMS2, intensive intervention. The CON programme ( $n=44$ ) included only the first level of interventions (a), the AMS1 programme ( $n=47$ ) included all interventions from the first two levels (a and b) and the AMS2 programme ( $n=44$ ) included all the interventions (a, b and c).



**Figure 3.** Categorization of antimicrobials for the traffic light colour-coding system implemented in AMS1 and AMS2.

they were allocated at the beginning of the implementation period (October 2018). The lead regional clinical director promoted the programmes at team leader meetings in May 2019. Regional clinical directors were then expected to support programme implementation within their cohort of clinics. During the implementation (1 October 2018 to 31 July 2019) and post-implementation periods (1 August 2019 to 31 October 2020), the research team was available to support the regional clinical directors and also answer questions directly from the individual clinics. Members of the research team attended the various state team leader meetings held throughout September 2019 to support the leadership teams in the implementation of the programme. Two members of the research team also attended the corporate group's annual conference in October 2019 to answer the questions of individual veterinarians, nurses and practice managers and promote the programme to the attendees.

### Allocation

Initially, clinics were allocated to one of the three arms of the intervention trial using a random number generator in Microsoft Excel. Clinic allocation was then reviewed by the regional clinical directors. Allocation was altered based on clinic human resources, the existing level of interest in the clinic and other factors (staff turnover, number of casuals/locums, clinic management structures) that may have affected the ability of the clinic to implement the allocated programme (Figure 1).

### Evaluation

For all participating clinics, de-identified data (1 January 2016 to 31 October 2020) were sourced from VetCompass Australia (Version 0.5).<sup>24</sup> Antimicrobials were categorized based on the antimicrobial importance ratings of the ASTAG, which classifies the antimicrobials as low, medium or high importance (Figure 3).<sup>16</sup> Inventory items, which map to all prescriptions and consultation texts, were extracted from the records. A previously described method was used to label antimicrobials within the inventory items and map them to their active ingredients and ASTAG importance rating.<sup>15</sup> As many consultation records were blank, with no inventory items associated with them, the consultation table was inner-joined to the table with the inventory items associated with them. At least one inventory item and one clinical note combined for a single consultation was required for inclusion in the study. All topical antimicrobials and other routes of antimicrobial therapy (e.g. intrasynovial, intraperitoneal) were excluded from analysis.

### Data analysis

Descriptive statistics were computed, with percentages reported as a proportion of consultations in the data set that received antimicrobial therapy or as a proportion of total consultations. High-prescribing clinics were defined as those in the top 25% of antimicrobial prescribers in the pre-trial period.

A multilevel Poisson regression model was used to identify factors that were associated with the incidence rate (IR) of antimicrobial therapy (exposure to antimicrobials) in the study population. The fixed explanatory variables assessed in the model included the AMS programme level, the trial period, the species of animal treated, the season, the 12 month period prior to the implementation period, and the impact of the COVID-19 pandemic. The random effect variables were regional clinical director and clinic. Exposure variables were total consultations. Unconditional associations between each of the hypothesized explanatory variables and the outcome of interest were computed using an incidence rate ratio (IRR). Explanatory variables with unconditional associations significant at  $P < 0.20$  (two-sided) were selected for multivariable modelling. For the multivariable model, the outcome of interest was parameterized as a function of the explanatory variables with unconditional associations significant at  $P < 0.20$ , as described above.

Explanatory variables that were not significant were then removed from the model one at a time, beginning with the least significant, until the estimated regression coefficients for all explanatory variables retained were significant at an alpha level of  $< 0.05$ . Explanatory variables that were excluded at the initial screening stage were tested for inclusion in the final model and were retained in the model if their inclusion changed any of the estimated regression coefficients by more than 20%. Plausible two-way interactions were tested, and significance was set at an alpha level of 0.05. Two-way ANOVA was performed to evaluate the effect of the intervention on prescribing rates in high-prescribing clinics compared with low-prescribing clinics. Data were tested for normality using the Shapiro-Wilks test. Homogeneity of variances across the six groups was tested using Levene's test. The impact of the COVID-19 pandemic was evaluated as a confounding factor in the Poisson model by marking prescribing events during the pandemic in clinics involved in the trial (between 15 March 2020 to 31 October 2020). Data analysis was performed using functions within Stata v14.

### Ethics

This research was approved by the University of Melbourne Faculty of Veterinary and Agricultural Sciences Human Ethics Advisory Group under Approval No. 1851029.1.

### Results

Veterinary clinics ( $n = 135$ ) were enrolled in the study in October 2018. The number of veterinarians in each clinic varied between clinics and within clinics over the trial periods, with most having between one and three full-time equivalent veterinarians (range 1–9). Over the total study period (1 October 2016 to 31 October 2020), there were 8 394 568 consultations and 240 700 systemic antimicrobial treatments dispensed across the 135 participating clinics (Table 1). Eight antimicrobials accounted for 94% of all antimicrobials dispensed: amoxicillin/clavulanate ( $n = 95 625$ , 40%), cefalexin ( $n = 32 734$ , 14%), metronidazole ( $n = 25 261$ , 10%), cefovecin ( $n = 24 461$ , 10%), doxycycline ( $n = 21 290$ , 8.8%), enrofloxacin ( $n = 12 190$ , 5.1%), cefazolin ( $n = 8251$ , 3.4%) and amoxicillin ( $n = 5971$ , 2.5%).

In the pre-trial period (1 October 2016 to 30 September 2018), the overall IR of antimicrobial prescribing to dogs and cats was 3.7 per 100 consultations. AMS1 and AMS2 clinics had a lower rate of prescribing compared with CON (Table 2). The IR of antimicrobial prescribing for cats was 9% lower than that for dogs (IRR 0.91, 95% CI 0.90–0.92,  $P < 0.001$ ). The IR of prescribing decreased by 14% in the period from 1 October 2016 to 30 September 2018 compared to the period from 1 October 2016 to 30 September 2017 (IRR 0.86, 95% CI 0.86–0.87,  $P < 0.001$ ) (Figure 4). The IR of antimicrobial prescribing varied considerably between clinics, from 1.29 to 8.9 per 100 consultations (mean of 3.6 per 100 consultations, SD 1.22), but 89% of clinics ( $n = 125$ ) prescribed an antimicrobial in fewer than 5 per 100 consultations.

The overall IR of antimicrobial prescribing decreased during the implementation and post-implementation periods. The IR of antimicrobial prescribing during the implementation phase was 2.4 per 100 consultations, a decrease of 36% from the pre-trial period. This reduced further in the post-implementation phase to 1.9 per 100 consultations, a decrease of 50% from the pre-trial period (Table 1). During both the implementation and post-implementation phases of the trial, and after adjusting for the effect of the COVID-19 pandemic, species, season, and

**Table 1.** Overall antimicrobial prescribing

Period <sup>a</sup>	Consultations		IR <sup>b</sup>	Adjusted IRR <sup>c</sup> (95% CI)	P value
	Antimicrobial	All			
Pre-trial	152877	4179535	3.7	Ref	-
Implementation	40424	1714557	2.4	0.64 (0.63–0.66)	<0.001
Post-implementation	47399	2500476	1.9	0.50 (0.49–0.51)	<0.001
Total	240700	8394568	2.9	NA	NA

IR, incidence rate; IRR, incidence rate ratio.

<sup>a</sup>Pre-trial period: 1 October 2016 to 30 September 2018; Implementation period: 1 October 2018 to 31 July 2019; Post-implementation: 1 August 2019 to 31 October 2020.

<sup>b</sup>Per 100 consultations.

<sup>c</sup>Adjusted for fixed effects (intervention level, COVID-19 pandemic, species, season) and random effects (regional clinical director, clinic).

**Table 2.** Antimicrobial prescribing in the pre-trial period

Intervention	No. clinics	Consultations		IRR <sup>a</sup>	95% CI	P value
		Antimicrobial	All			
CON	44	48640	1345572	Ref	-	-
AMS1	47	51768	1351551	0.80	0.70–0.93	0.003
AMS2	44	44393	1315806	0.78	0.67–0.90	0.001

CON, education-only intervention; AMS1, intermediate intervention; AMS2, intensive intervention; IRR, incidence rate ratio.

<sup>a</sup>Adjusted for fixed effects (COVID-19 pandemic, species, season) and random effects (regional clinical director, clinic). Full models are provided in the [Supplementary data](#) (Table S1).

random effects of regional clinical director and clinic, the change in antimicrobial prescribing attributable to the AMS2 intervention was a 4% and 6% reduction compared with CON (AMS2 # implementation IRR 0.96, 95% CI 0.94–0.99,  $P=0.011$ ; AMS2 # post-implementation IRR 0.94, 95% CI 0.91–0.96,  $P<0.001$ ) (Table S1, available as [Supplementary data](#) at JAC-AMR Online). The adjusted rate of antimicrobial prescribing in clinics enrolled in AMS1 did not differ from that of clinics enrolled in CON in either the implementation or post-implementation phases (Table S1).

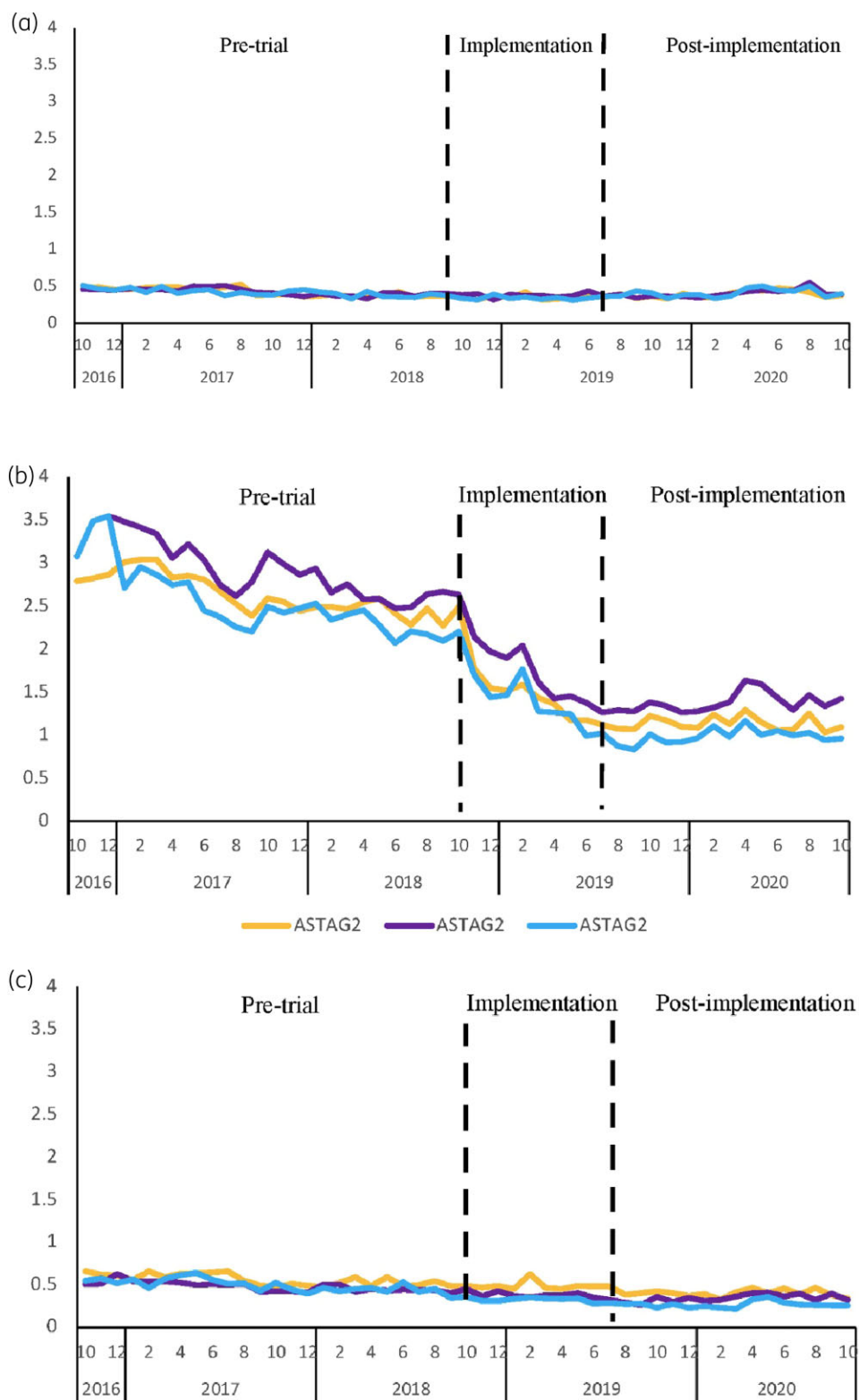
The proportion of prescriptions for medium-importance antimicrobials (out of total antimicrobial prescriptions) decreased during the implementation and post-implementation periods in all groups, with a corresponding increase in the prescribing of low-importance antimicrobials (Table 3). After adjusting for fixed effects of COVID-19 impact, species and season and random effects of regional clinical director and clinic, the effect of the intervention (intervention # trial period) differed between AMS1 and AMS2 (Table 3, Tables S2 to S4). In AMS1 the change attributable to the intervention in the implementation period was a 17% increase in the IR of prescribing of low importance antimicrobials, with no change in prescribing of medium- and high-importance antimicrobials, whereas in AMS2 there was no change to prescribing of low- and medium-importance antimicrobials, but a 24% reduction in prescribing of high-importance antimicrobials attributable to the intervention. Similarly, in the post-implementation period, in AMS1 there was a 10% increase in the IR of prescribing

of low-importance antimicrobials and a 5% increase in prescribing of medium-importance antimicrobials, but no change in prescribing of high-importance antimicrobials attributable to the intervention. In AMS2, in the post-implementation period, the change in IR attributable to the intervention in low-importance antimicrobial prescribing was an increase of 12%, and for medium- and high-importance antimicrobials there was a decrease of 6% and 24%, respectively (Table 3, Tables S2 to S4).

The effects of the AMS interventions on the pre-existing prescribing practices of clinics were examined to determine the effects in high-prescribing clinics. High-prescribing clinics were defined as those clinics in the top 25% of antimicrobial prescribers overall in the pre-trial period. Tests for normality and homogeneity of variances showed that the assumptions of the two-way ANOVA were met. There was a significant interaction between the level of intervention and the change in IR of prescribing of high-prescribing clinics compared with all other clinics [ $F(2,127) = 4.01, P=0.02$ ]. Irrespective of the level of intervention there was a significant effect in reducing the IR of antimicrobial prescribing in high-prescribing clinics compared with all other clinics (Table 4).

## Discussion

This quantitative evaluation of a large-scale implementation trial in veterinary practice demonstrated that a bundle of AMS



**Figure 4.** Unadjusted incidence rate (per 100 consultations) of antimicrobial prescribing in CON (yellow), AMS1 (purple) and AMS2 (blue) for (a) low-, (b) medium- and (c) high-rated antimicrobials according to the Australian Scientific and Technical Advisory Group on AMR in the pre-trial and trial periods (1/1/2016 to 31/10/2020). CON, education only intervention; AMS1, intermediate intervention; AMS2, intensive intervention.

**Table 3.** Prescribing of antimicrobials according to their importance as defined by the Australian Scientific and Technical Advisory Group on Antimicrobial Resistance (ASTAG)

ASTAG importance/intervention	Pre-trial IR <sup>a</sup> (% AM)	Implementation IRR <sup>b</sup> (95% CI), <i>P</i> value (IR <sup>a</sup> [%AM])	Post-implementation IRR <sup>b</sup> (95% CI), <i>P</i> value (IR <sup>a</sup> [%AM])
Low			
CON (Ref)	0.422 (12)	(0.354 [15])	(0.391 [20])
AMS1	0.424 (11)	1.17 (1.09–1.27), <0.001 (0.378 [15])	1.10 (1.03–1.17), 0.002 (0.396 [19])
AMS2	0.415 (12)	1.03 (0.96–1.11), 0.428 (0.341 [15])	1.12 (1.05–1.19), <0.001 (0.406 [25])
Medium			
CON (Ref)	2.63 (73)	(1.51 [64])	(1.13 [59])
AMS1	2.93 (76)	1.00 (0.97–1.04), 0.832 (1.77 [70])	1.05 (1.02–1.09), 0.001 (1.38 [65])
AMS2	2.47 (73)	1.01 (0.97–1.05), 0.611 (1.42. [68])	0.94 (0.91–0.97), <0.001 (0.981 [59])
High			
CON (Ref)	0.600 (15)	(0.480 [20])	(0.397 [21])
AMS1	0.478 (12)	0.98 (0.92–1.05), 0.603 (0.383 [15])	1.01 (0.95–1.07), 0.816 (0.344 [16])
AMS2	0.492 (15)	0.76 (0.71–0.82), <0.001 (0.323 [16])	0.76 (0.71–0.81), <0.001 (0.267 [16])

IR, incidence rate; %AM, proportion of antimicrobial prescriptions out of total antimicrobial prescriptions; IRR, incidence rate ratio.

<sup>a</sup>Unadjusted rate per 100 consultations.

<sup>b</sup>Change attributable to intervention (intervention # trial period). Interaction term adjusted for the fixed effects of species, season, intervention group and time and the random effects of regional clinical director and clinic, the full models available in the [Supplementary data](#) (Tables S2 to S4).

**Table 4.** Effect of intervention on antimicrobial prescribing in high prescribing clinics (top 25% of IR of antimicrobial prescriptions)

Intervention	High prescribing clinics IR <sup>a</sup>				All other clinics IR <sup>a</sup>				<i>P</i> value
	Pre-trial	Trial <sup>b</sup>	Mean difference	95% CI	Pre-trial	Trial <sup>b</sup>	Mean difference	95% CI	
CON	6.5	2.3	4.2	2.4–6.1	4.1	1.8	2.3	0.7–3.9	<0.001
AMS1	7.3	2.5	4.8	1.7–7.8	3.7	1.7	2.0	0.1–3.9	<0.001
AMS2	5.9	2.4	3.5	2.0–5.0	3.7	1.6	2.1	0.3–3.9	<0.001

<sup>a</sup>Per 100 consultations

<sup>b</sup>Trial incorporates implementation and post-implementation periods.

interventions in antimicrobial prescribing can have an impact in general veterinary practice. Compared with the pre-trial period (3.7 per 100 consultations), the use of antimicrobials declined in the implementation period (to 2.4 per 100 consultations) and post-implementation period (to 1.9 per 100 consultations) and the clinics in AMS2 had a greater reduction in overall antimicrobial use compared with clinics in CON. Although antimicrobial use had declined during the 2 year pre-trial period, (13% between the two 12 month periods), this was accelerated and sustained during the implementation (36%) and post-implementation (50%) periods. There was a high level of commitment to the project from corporate leadership, and planning discussions with regional clinical directors (starting in July 2018) may have resulted in early promotion of AMS and improved antimicrobial use, even before the implementation phase started.

A previous study of AMS in companion animal practice in The Netherlands also resulted in an overall reduction in antimicrobial use,<sup>11</sup> similar in magnitude to that seen in our study. In that study, as in the trial described here, there were absolute

decreases in both first- and second-choice antimicrobial use overall, but the impact attributable to our trial was an increase in the use of low-importance antimicrobials in AMS1 in both implementation and post-implementation periods and in AMS2 in the post-implementation period. Although prescribing rates of antimicrobials with a high importance rating also decreased during the implementation and post-implementation periods in our study, the proportion of consultations in which high-importance antimicrobials were prescribed was higher in all arms of the trial, indicating that prescribers decreased use of antimicrobials with low- and medium-importance ratings more than they decreased use of those with a high-importance rating. A change in the rate of prescribing of high-importance antimicrobials that was attributable to the intervention was only seen in AMS2, in which there was a 24% reduction compared with CON in both implementation period and post-implementation periods (Table 3). The interventions had an impact on the use of high-importance antimicrobials in AMS2 by reducing the adjusted rate of prescribing and maintaining the overall proportion of consultations in

which antimicrobials were prescribed in comparison to the increase seen in CON. In AMS1, the change attributable to the intervention was an increase in the rate of prescribing of low-importance antimicrobials with no change in the rate of high-importance prescribing (Table 3). This contrasts with the trial in The Netherlands, in which the adjusted proportion of third-line antimicrobial use reduced (although not significantly). The interventions also differed markedly, being less labour-intensive in our study and therefore able to be implemented in a much larger number of clinics. However, the overall impact was similar, suggesting that different interventions can have similar outcomes in different populations.

A trial in the UK focusing on the highest priority critically important antimicrobial use was successful in reducing the use of these antimicrobials when this was the sole target of the intervention.<sup>25</sup> Identifying the interventions that are likely to be effective in changing behaviour in a population is key to successful AMS interventions, and co-design with participants is encouraged to allow for adaptation to the social, economic, educational and cultural backgrounds where they will be applied.<sup>26,27</sup> Co-design has been used extensively in AMS interventions in human medicine,<sup>28–31</sup> but only in a smaller number of studies in veterinary medicine.<sup>32,33</sup> Our interventions focused on promoting guidelines, implementing a traffic-light system and delivery of educational webinars, while the trial in The Netherlands discussed above focused on small group education and self-reflection. A wide range of planned interventions have also reduced inappropriate prescribing in human hospitals.<sup>18–21</sup> Qualitative investigation of the implementability of interventions targeting antimicrobials with a high-importance rating is needed in this population because the proportional use of these drugs did not reduce. It is possible that the behavioural drivers for using these drugs are not sufficiently understood to design effective interventions. Further research is needed to explore these behavioural drivers in more detail.

In this intervention trial, the greatest impact was seen in clinics that were in the top 25% of prescribers in the pre-trial period. This was an interesting finding, as in this trial high prescribers were not targeted with social norm feedback, an intervention that has been effective in the medical sector.<sup>34,35</sup> There was also a greater difference in clinics in the CON intervention (IR mean difference of 2.3) than in the AMS1 (IR mean difference of 2.0) and AMS2 (IR mean difference of 2.1) interventions. It is possible that regional clinical directors or practice managers identified high-prescribing clinics and put more effort into implementing ASPs in these practices, and this had an impact on the implementation of the interventions. Alternatively, high-prescribing practices may be able to achieve greater reductions in use more easily than practices with low prescribing rates. This should be further investigated with future surveys and interviews of participants.

The challenge in implementing interventions aimed at behavioural change is maintaining that change over time. There is concerning evidence from some studies that change does not last. Even intervention teams that have produced positive clinical outcomes have warned that a single intervention is not likely to result in sustained change.<sup>36</sup> However, well-designed intervention bundles can have a sustained impact.<sup>37</sup> The barriers to AMS in veterinary practice have been evaluated previously and the

commitment of practice leaders has been identified as a critical factor.<sup>17</sup> The involvement of all levels of management within this corporate group is likely to have been critical in the successful implementation of the bundled interventions and their short- and medium-term sustainability. This interest of management in AMS may also explain the reduction in antimicrobial use in the pre-trial period. This should be further investigated using qualitative methods.

This trial was designed to investigate the most effective way to reduce antimicrobial use in a sustained manner. An implementation trial model was adopted, as we recognized that stewardship interventions are rarely ‘one-size-fits-all’ and that interventions need to be adapted based on cultural, socio-economic and personnel factors. The ‘buy-in’ to the strategy by practitioners was as important as any of the interventions we implemented. For this reason, we identified that some practices needed to start at a lower level of intervention in the first phase of this trial. This approach is in contrast to a randomized controlled trial and may have had an impact on the external validity of the results in this study. Appropriate antimicrobial use is measured in medical AMS,<sup>38–40</sup> but the method for measuring this outcome is yet to be developed in veterinary medicine. While appropriate antimicrobial use could not be directly evaluated, the reduction in overall antimicrobial use and the shift towards prescribing antimicrobials with a low-importance rating, from those with a medium-importance rating, was used as a proxy for this outcome. Another limitation of this study is that we do not know what interventions were fully implemented in each veterinary clinic and cannot evaluate the effectiveness of each of the individual interventions within the bundles. However, as discussed previously, a bundle of interventions has been shown to be more sustainable than individual interventions.<sup>37</sup> Hence, a study of bundled interventions is more useful in achieving the goal of improving antimicrobial use over the long-term, and minimizing the likelihood of selection of antimicrobial resistance. An evaluation survey of participants and participant interviews will help elucidate which intervention elements were most useful in veterinary clinics and, in combination with the results presented here, will guide further implementation of AMS interventions. The effect of delayed prescribing was not evaluated in this study as it was inconsistently recorded, but this is unlikely to have had a major impact on the outcomes of the study.

This corporate group of clinics may not be an ideal indicator of the likelihood of implementation success in independent general veterinary practices. The distribution of antimicrobial use across these clinics was similar to that seen in previous studies of veterinary antimicrobial use in Australia,<sup>12,15</sup> but the trial clinics were predominantly located in metropolitan regions and only attended to companion animal patients, so results may vary in a population of practices that treat horses and food animals, and/or practices in rural and regional areas. The AMS interventions trialled may also have different effects in emergency and referral clinics, which were excluded from this study.

In conclusion, we have shown a positive impact of three different AMS programmes in a large group of general veterinary practices, resulting in both a decline in overall antimicrobial use and a shift in use towards prescribing of low-importance antimicrobials, with the greatest impact seen in high-prescribing clinics. Further research is needed to evaluate the experience of veterinarians

involved in the trial and to investigate the impact that these interventions may have in practices that see horses and/or food production animals in addition to dogs and cats.

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## Transparency declarations

None to declare.

## Supplementary data

Tables S1 to S4 are available as [Supplementary data](#) at JAC-AMR Online.

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