A randomised controlled trial to reduce highest priority critically important antimicrobial prescription in companion animals

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Abstract

Robust evidence supporting antimicrobial stewardship schemes in companion animals is limited, despite frequent highest priority critically important antimicrobial (HPCIA) prescription. In this randomised controlled trial, electronic prescription data were utilised (August 2018–January 2019) to evenly assign 60 above average HPCIA-prescribing practices into a control group (CG) and two intervention groups. In March 2019, the light intervention group (LIG) and heavy intervention group (HIG) were notified of their above average status, and were provided with educational material (LIG, HIG), in-depth benchmarking (HIG), and follow-up meetings (HIG). Post-intervention, in the HIG a 30% and 42% significant reduction in canine (0.5% of consultations, 95% confidence interval, 0.4–0.6) and feline (4.4%, 3.4–5.5) HPCIA-prescribing consultations was observed, and maintained for three and six months, respectively, compared to the CG (dogs: 0.7% (0.5–0.8); cats: 7.6% (6.1-9.0)). The LIG was not associated with significant variation. This evidence is now informing development of a national stewardship scheme.

Introduction

Companion animals are increasingly being recognised as an important contributor to the development,[1,2] carriage[3] and transmission of antimicrobial resistant (AMR) bacteria both between animals and to/from humans, due, at least in part, to the close proximity in which companion animals reside with humans.[4,5] Recent population studies facilitated by the expanding availability of companion animal electronic health records (EHRs)[6,7] have identified encouraging trends in antimicrobial prescription, the primary driver of AMR,[1,2,4,8,9] including reducing antimicrobial frequency, both in general[6] and for some clinical presentations.[10–12] However, antimicrobials still remain amongst the most commonly prescribed pharmaceutical agents in companion animals.[13]

Of particular concern, cefovecin, a 3rd generation cephalosporin considered a 'highest priority critically important antimicrobial' (HPCIA) by the World Health Organisation,[14] remains the most commonly prescribed antimicrobial in cats;[6,7] such prescriptions frequently lacking clearly recorded clinical reasoning to justify their prescription.[15] HPCIAs are recommended to ideally be reserved for human use alone,[14] with current companion animal prescribing guidance suggesting HPCIAs should only be prescribed when there is clear evidence of resistance to first-line antimicrobials.[16] As cefovecin is frequently prescribed in the absence of such evidence,[15] this raises significant questions as to how appropriate such frequent prescription is in cats.

Along with more qualitative studies,[17–20] EHRs[15,21,22] have also identified key motivators for antimicrobial prescription, revealing a complex interplay between animal, owner, clinical presentation, individual veterinary surgeon, and the overarching culture of the veterinary practice in which they are employed. On a population-level, considerable inter-practice variation in antimicrobial prescription frequency, including the HPCIAs, has been identified,[6] with those practices with higher levels of professional accreditation being relatively less frequent prescribers of systemically-administered antimicrobials to dogs, compared to their non-accredited peers.[22]

Much of the work to mitigate the companion animal contribution to AMR has focused on improving antimicrobial prescription, under the banner of antimicrobial stewardship, largely through the production of evidence-based antimicrobial prescribing guidance[16] and practice benchmarking.[23] Although these are to be welcomed, robust evidence supporting their impact on companion animal antimicrobial prescribing practices is absent. In this regard, there is much to learn from medical practice, where robustly evidenced antimicrobial stewardship schemes have been established for some time.[24–30] Of particular interest, use of prescribing benchmarks within a social norms framework has shown some potential in prompting general practitioner-reflection and behavioural change.[26]

In this study, we undertook a first population-level randomised controlled trial to assess the impact of integrated EHR-driven antimicrobial prescription benchmarking and in-practice educational support on HPCIA prescription frequency, and antimicrobial prescription frequency in general. Participants were recruited from a cohort of above average HPCIA-prescribing practices within a single veterinary practice group (CVS Group Ltd.), with the hypothesis that such interventions would effectively reduce HPCIA prescription frequency post-intervention.

Materials And Methods

Data collection

This trial used data collected by the Small Animal Veterinary Surveillance Network (SAVSNET) project, which harnesses voluntarily provided electronic health records (EHR) from booked consultations in a sentinel network of UK veterinary practices. Each EHR includes information pertaining to the animal and owner, the clinical narrative, and products dispensed during such consultations. Antimicrobial prescription was identified via reference to products dispensed, and classified into systemic (oral or injectable) or topical (topical, aural, ocular) authorised administration routes using a semi-automated rule-based text-mining method, as previously described.[6] Fluoroquinolones, macrolides and 3rd generation cephalosporins were considered HPCIAs.[14] Every consultation was further classified by the attending veterinary professional into one of ten main presenting complaints (MPCs), indicating the main reason the animal was presented to the veterinary practice.[6]

Additionally, CVS Group Ltd. provided data relating to staff numbers per practice (in full-time equivalents, FTE), and the number of cytological or bacterial culture and susceptibility tests ordered by practices included in this trial. SAVSNET holds ethical approval to collect EHR data from the University of Liverpool (ethical approval reference: RETH000964); additional approval was granted to encompass interventions and data collection specific to this trial from the Universities' Veterinary Research Ethics Committee (ethical approval reference: VREC745).

Study practice selection

This three-armed randomised controlled trial (RCT) initially utilised EHRs voluntarily supplied by 157 UK veterinary practices (385 sites/branches) belonging to CVS Group Ltd., that had been participating in SAVSNET between 1 August 2018 and 15 January 2019. Pre-intervention, practice-level median HPCIA prescription as a percentage of total canine (*n* = 409,279) and feline (*n* = 164,827) consultations were 0.5% [range 0.0-2.3] and 5.3% [range 0.0-13.9], respectively. Practices were eligible for study inclusion if they were associated with above median total HPCIA (including systemic and topical formulations) prescription frequency in both dogs and cats (*n* practices = 42), or either species (*n* practices = 26).

The primary outcome was HPCIA prescription frequency post-intervention, compared to the CG. A sample size estimation indicated that to detect a 10% relative decrease in the primary outcome (standard deviation = 10%, power = 80% and α = 0.05), 17 practices would be required in each group. Hence, to allow for some loss during the study, of the 68 practices initially qualifying for selection, 60 practices were randomly and evenly allocated into three intervention groups: the control group (CG, *n* practices = 20, sites = 40), low group (LIG, *n* practices = 20, sites = 57) or high group (HIG, *n* practices = 20, sites = 51), utilising the 'complete random allocation' function available through the 'randomizr' R package (Fig. 1).[33] Practice allocation was completed by DS.

Intervention

For the LIG and HIG, the trial consisted of two phases: (1) an initial notification of above median HPCIA prescription frequency status, followed by (2) a voluntary reflection and education programme, with intensity varying by intervention group.

On 28 March 2019, LIG practices received a posted letter and email stating their above median HPCIA-prescribing status (supplementary material 1). They also received a copy of the practice group's antimicrobial prescribing policy (based on current prescribing guidance),[16] a reminder and interpretive guidance for an online anonymised antimicrobial prescription benchmarking portal already freely available to all SAVSNET-participating practices (supplementary material 2),[23] and access to AMR educational videos (can be viewed here: https://savsnetvet.liverpool.ac.uk/savsnetamr/iv?id=61). Practices could opt-out of or access these as many times as they wished.

On 28 and 29 March 2019, HIG practices also received a posted letter and email stating their above median HPCIA-prescribing frequency status. This letter included all LIG materials, and further included an in-depth benchmarking report (supplementary material 3) and explanatory video (can be viewed here: https://savsnetvet.liverpool.ac.uk/savsnetamr/iv?id=62). Practices were further invited to participate in a reflection and education programme, consisting firstly of an in-person initial review with a 'hub clinical lead' (a member of the senior clinical team of CVS Group Ltd), and a separate practice-wide meeting to discuss findings. Hub clinical leads checked in with practices on a monthly basis throughout the trial, and practices were able to hold follow-up reviews with the hub clinical lead if they wished. A final hub clinical lead review near conclusion of the study was also requested. For each of these reviews, a contributory factors question checklist was used to guide discussion (supplementary material 4).

Though individual LIG and HIG practices were aware of their involvement in a trial, they were not informed of which other practices were involved, nor interventions being performed in opposing intervention groups. The CG received no intervention beyond sustained access to the antimicrobial prescription benchmarking portal through SAVSNET, and remained unaware of their involvement in this trial. Presence and frequency of SAVSNET prescription benchmarking portal access was monitored throughout the trial for all practices included in this trial. It was not practical to blind study team members to group allocation.

Outcomes

Post-intervention monitoring was carried out between 1 April 2019 and 30 September 2019 (inclusive). The primary outcome measure was post-intervention canine or feline total HPCIA (including systemic and topical formulations) prescription frequency as a percentage of total consultations, compared to the CG. Secondary outcome measures included post-intervention total, systemic and topical antimicrobials; systemic HPCIA prescription frequency; total HPCIA prescription frequency by month; total HPCIA prescription frequency by MPC; relative antimicrobial class prescription frequency; anti-inflammatory prescription, and euthanasia frequency. Post-intervention cytological or bacterial culture and susceptibility test order numbers, and interactions with the online antimicrobial prescription benchmarking portal were also summarised.

Statistical analyses

The statistical programme 'R' was used for all analyses. Descriptive proportions and 95% confidence intervals were adjusted for clustering within practices (bootstrap method, *n* = 5,000 samples).[34] Mixed effects panel regression models, modelling practice as the random effect, were used for making intervention group comparisons, utilising the R package 'plm'.[35] For each of the outcome measures described, practice-level pre-intervention (August 2018 – March 2019) and post-intervention (April – September 2019) values were compared with intervention group (modelled as interacting variables). For total HPCIA prescription frequency, intervention group was also compared across all pre- and post-intervention months. The CG was

used as the reference category for all analyses. Analyses were performed on an intention-to-treat basis, as EHR data were available for all practices, regardless of participation opt-out status. Number of practices within each group interacting with SAVSNET's antimicrobial prescription benchmarking portal were compared pre- and post-intervention via a two-sided Fisher's Exact Test. The trial was completed according to CONSORT guidelines,[36] and statistical significance was defined as $P < 0.05$ throughout.

Results

Following above median total HPCIA prescription frequency notification (28–29 March 2019), practices were given the option to voluntarily participate in a further reflection and education programme; no LIG practices opted out, whereas two HIG practices opted out (Fig. 1). All 18 consenting HIG practices participated in an initial review with a hub clinical lead (15 held in April, two in May and one in June 2019), and 16 held a separate practice meeting (held April-June 2019). Of these, 15 requested a hub clinical lead follow-up review (held April-July 2019), seven requested a further hub clinical lead follow-up review (held May-July 2019), and 16 held a final hub clinical lead review (held August-October 2019). Baseline characteristics were broadly comparative across groups in terms of demographics (Table 1) and antimicrobial prescription (Tables 2 and 3).

Antimicrobial prescription frequency

Pre-intervention, 0.71% (95% confidence interval, CI, 0.57–0.86, *n* consultations = 88,298), 0.72% (CI 0.60–0.83, *n* consultations = 107,223), and 0.68% (CI 0.47–0.90, *n* consultations = 63,366) of canine consultations were associated with total HPCIA prescription in the CG, LG and HG, respectively (Table 2). In cats, 7.44% CG (CI 6.27–8.61, *n* consultations = 33,613), 7.03% LG (CI 6.32–7.74, *n* consultations = 39,803), and 8.03% HG (CI 7.16–8.90, *n* consultations = 25,661) consultations were associated with total HPCIA prescription (Table 3). The 'respiratory', 'kidney disease' and 'pruritus' MPCs in dogs, and 'respiratory' and 'trauma' MPCs in cats were associated with increased total HPCIA prescription frequency, relative to other MPCs.

Post-intervention, HG canine total HPCIA prescription frequency significantly reduced by 30% (0.46%, CI 0.35–0.58, $P = 0.02$, *n* consultations = 48,543), but no significant change was observed in the LG (0.78%, CI 0.60–0.95, $P = 0.47$, *n* consultations = 81,056), compared to the CG (0.66%, CI 0.48–0.84, *n* consultations = 64,357) (Table 2; full model results Supplementary tables, Table 1). For cats, a significant 41% decrease was observed in the HG (4.44%, CI 3.42–5.46, $P < 0.01$, *n* consultations = 19,290), though no significant LG change was seen (6.31%, CI 5.34–7.28, $P = 0.09$, *n* consultations = 28,066), compared to the CG (7.56%, CI 6.14–8.98, *n* consultations = 23,704) (Table 3; full model results Supplementary tables, Table 2). Fifteen and twenty HG practices recorded post-intervention total HPCIA prescription frequency decreases in dogs (Fig. 2A) and cats (Fig. 3A), respectively. In the LG, ten practices were associated with post-intervention reductions in both species, whereas in the CG, nine and eight practices were associated with post-intervention reductions in dogs and cats respectively.

Regarding HIG month-by-month variation, significant reductions in total HPCIA prescription frequency were observed for three and six post-intervention months in dogs (Table 4; Fig. 2B; full model results Supplementary tables, Table 3) and cats (Table 4; Fig. 3B; full model results Supplementary tables, Table 4), respectively, with a particularly steep decline being observed between March and April 2019 in cats. The LIG was associated with a significant reduction in cats in June 2019 only, compared to the CG.

On consideration of HIG canine total HPCIA prescription frequency by MPC, the 'tumour' and 'other healthy' MPCs were associated with significant reductions (Table 2; full model results Supplementary tables, Table 5), whereas cats were associated with significant reductions in six MPCS (Table 3; full model results Supplementary tables, Table 6). In the LIG for dogs, no MPCS showed significant reductions, although the 'vaccination' MPC was associated with a significant increase. In cats in the LIG, only the 'tumour' MPC showed a significant reduction.

Considering antimicrobial prescription more broadly, the HIG was also associated with a 21% significant decrease in the percentage of both dog (Table 2; full model results Supplementary tables, Table 1) and cat (Table 3; full model results Supplementary tables, Table 2) consultations prescribed a systemic antimicrobial, compared to the CG, respectively. Significant reductions in total antimicrobial prescription frequency were also observed in both species. In terms of other pharmaceutical agents, we found no significant post-intervention group variation in anti-inflammatory prescription nor frequency of euthanasia in either species (dogs, Table 2, Supplementary tables, table 7; cats, Table 3, Supplementary tables, table 7).

Antimicrobial prescription choice

A summary of antimicrobial prescription choice variation as a percentage of total antimicrobial prescriptions by class, and for beta-lactams by sub-class, is available in Table 5 (dogs; full model results Supplementary tables, Table 8) and Table 6 (cats; full model results Supplementary tables, Table 9), and as a percentage of total consultations in Supplementary Tables 10 (dogs) and 11 (cats). Though no comparisons were significant, there was some evidence of post-intervention increases in clavulanic acid potentiated amoxicillin prescription in cats in the HIG, overtaking 3rd generation cephalosporins as the most prescribed antimicrobial.

Bacterial diagnostic test frequency

Pre-intervention there were 3,932 cytological test orders, representing 1.09% of CG (CI 0.67–1.51), 1.03% LIG (CI 0.47–1.58) and 1.18% HIG (CI 0.54–1.83) consultations. Of 3,405 post-intervention cytological test orders, 1.16% of CG (CI 0.66–1.66), 1.23% LIG (CI 0.47-2.00) and 1.49% HIG (CI 0.87–2.11) post-intervention consultations were associated with an order. However, no significant variation was observed, compared to the CG (LIG $P = 0.52$; HIG $P = 0.71$).

Pre-intervention, there were 4,517 bacterial culture and susceptibility test orders, representing 1.16% of CG (CI 0.77–1.55), 1.01% LIG (CI 0.64–1.39) and 1.76% HIG (CI 1.05–2.47) consultations. Of 3,448 post-intervention bacterial culture and susceptibility test orders, 1.11% of CG (CI 0.76–1.47), 1.11% LIG (CI 0.70–1.53) and 1.76% HIG (CI 1.16–2.36) post-intervention consultations were associated with an order. However, no significant variation was observed, compared to the CG (LIG $P = 1.00$; HIG $P = 0.16$). Full regression model results for both comparisons are available in Supplementary tables, Table 7.

Use of antimicrobial prescription benchmarking portal

Prior to the intervention (1st February and 27th March 2019 inclusive), there was no significant variation between practices logging into their antimicrobial benchmarking portal: CG ($n = 0$), LIG ($n = 3$) and HIG ($n = 3$) (Fisher's Exact Test, $P = 0.23$). Post-intervention (1st April – 30th September 2019 inclusive) however, significant variation was observed between practices logging into the portal within the CG ($n = 3$), LIG ($n = 8$) and HIG ($n = 15$), respectively (Fisher's Exact Test, $P < 0.001$). The two HIG practices that declined further participation did not interact with their portal pre- or post-intervention. A pronounced increase in LIG and HIG practice engagement with the portal was observed in April 2019, declining towards the end of the trial (Fig. 4).

Discussion

Here we describe the first use of EHR data from veterinary practices to initiate and sustain voluntary antimicrobial prescribing behavioural change in veterinary prescribing. In so doing, we have outlined a data-led and educational support framework by which HPCIA prescription frequency can be significantly reduced, while preserving care quality and clinical autonomy. These insights are now being used to inform a national antimicrobial stewardship scheme, led by RCVS Knowledge (https://knowledge.rcvs.org.uk/home/), firmly demonstrating a profession-wide commitment to responsible usage of antimicrobials.

A primary component of behaviour change is to effectively draw attention to an issue, [37] and departure from 'social norms' has been previously demonstrated as a motivator for antimicrobial prescription behaviour change.[26] In the absence of evidence, individuals tend to over-estimate perceived negative traits in their peers, thus serving as justification for their own behaviour (e.g. alcohol consumption frequency).[38] A similar tendency regarding antimicrobial prescription amongst veterinary surgeons has been previously observed,[17] leading us to hypothesise that lack of knowledge of relative frequencies of antimicrobial prescription might in itself serve as a driver for more frequent prescription. Hence, by incorporating an intervention based on social norm messaging of high HPCIA prescription frequency, we ensured that these prescribers were aware of their unusual status.

In the LIG and HIG, use of the SAVSNET antimicrobial benchmarking portal significantly increased post-notification, with increases being most apparent in the two months following notification, suggesting these notifications prompted enhanced portal engagement. However, while post-intervention 75% of HIG practices interacted with the portal, only 40% of LIG practices did so. Further, while engagement waned to at or below pre-intervention levels within two months of notification in the LIG, interest exceeded pre-intervention levels for four months post-notification in the HIG. It is probable that either the additional in-depth benchmarking report provided to practices in the HIG, or post-notification offer of assistance from the hub clinical leads might have enhanced initial interest compared to the LIG. Though the relative contributions of each was not able to be elucidated here, individuals are more likely to re-evaluate existing behaviours if modifying behaviour might bring reward, or not doing so might bring punishment.[37] Although the supportive, optional nature of the trial was emphasised throughout, requested hub clinical lead intercession might have nevertheless introduced a perception of potential reward or punishment linked with engagement with the trial. It is also possible that the letter and email sent to LIG practices was not disseminated beyond clinical directors in some cases, whereas practice-wide meetings held in HIG practices ensured engagement of all staff.

There was concern that notification of relatively high HPCIA prescription alone could prompt practice policy changes not reflective of latest clinical evidence, such changes being potentially detrimental to animal welfare or employee wellbeing. Structured reflection and education programmes have been shown to be effective at achieving sustained improvements in anti-infective prescription habits in the medical field,[25] and in this trial we compared both a light (LIG) and heavy (HIG) reflection and educational intervention. While significant and sustained reductions in HPCIA prescription frequency were seen in both species in the HIG, no significant decreases were observed in the LIG. Across the veterinary sector impressive reductions have been achieved over the past five years, especially in pigs and poultry,[39,40] utilising a variety of statutory[41] and voluntary[42] improvement measures. Though over this time reductions in antimicrobial prescription frequency in companion animals have been noted,[6,10,12] HPCIA use has remained an issue, particularly in cats.[6,7,15] Unlike other veterinary sectors, no statutory policies have been introduced to prompt improvements in antimicrobial prescription in companion animals. It is unknown what impact such enforced measures might have on animal welfare, and thus we consider findings presented here to be an encouraging sign that practitioners might be willing to voluntarily engage with improvement efforts, potentially negating need for firmer regulatory approaches.

This study further demonstrated the relative ease by which EHRs can be utilised to both identify participants and monitor key outcomes in near real-time. Such efficiency advantages have been previously outlined in medical research, enabling rapid scaling of interventions to instigate national quality improvement.[26] Only comparatively recently have EHRs become available for research and surveillance in the veterinary sector,[43] and as such

we believe this work serves as an exciting demonstration of what could be achieved using EHR data-led approaches, expanding beyond practitioner-focused interventions to those encompassing owners, or pragmatic efficacy assessment of surgical and pharmaceutical interventions in routine practice, for example.

Though the intervention package provided in this trial represented a comprehensive approach to encouraging evidence-based behaviour change, it did limit our ability to determine which individual components might have been of greatest impact. Interestingly, though both LIG and HIG practices received a high feline HPCIA prescription frequency notification at the beginning of the trial, no significant reductions were subsequently noted in LIG practices. However, all HIG practices, including both HIG practices that refused engagement with the reflection and education programme, reported decreases post-notification. Though variation in scale of reduction was evident, circumstantially, these findings might suggest that hub clinical lead involvement was a motivational factor in prompting behavioural change. In either case, the aforementioned refusals do indicate a limiting factor in intervention scalability to a wider audience. Further, this trial benefited from utilising existing quality improvement management structures within a single large practice group for the HIG. Thus, there remains a question as to whether this intervention would be feasible amongst other practices, including those that are relatively infrequent HPCIA prescribers, over a longer period of time than the six months observed here.

More broadly, several and two MPCs in cats and dogs respectively in the HIG were associated with significant HPCIA prescription frequency reductions, a number of which (e.g. respiratory, trauma) were previously associated with frequent HPCIA prescription,[6,21] despite often lacking clear clinical justification for their prescription.[21] These findings suggest a generalised culture change not necessarily being restricted to reflection on individual disease presentations. This result is supported by significant reductions in systemic and overall antimicrobial prescription frequency in both species. In HIG dogs, these wider reductions were greater than that contributed by HPCIA reductions alone, suggesting that the trial had a wider impact on discouraging antimicrobial prescription more generally. However, in HIG cats the opposite was seen; HPCIA reductions were greater than overall decreases, suggesting a tendency of some practitioners to move from prescribing a HPCIA to prescribing another non-HPCIA antimicrobial, instead of avoiding prescription altogether.

Whilst no prescription choice comparisons were significantly different, 3rd generation cephalosporin feline prescription does appear to have decreased to a degree in the HIG, while clavulanic acid potentiated amoxicillin prescription increased, suggesting a preferred alternative to 3rd generation cephalosporins. Clavulanic acid potentiated amoxicillin is an authorised, widely used antimicrobial in veterinary practice.[6] However, like 3rd generation cephalosporins, use of clavulanic acid potentiated amoxicillin has also been associated with resistance development,[44] and is only infrequently prescribed in medical practice.[45] Thus, future stewardship efforts will need to expand scope beyond HPCIAs to also consider how to promote responsible use of all antimicrobials, and indeed other medicines too.

For instance, we have previously reported a tendency for antimicrobials and anti-inflammatories to be prescribed at the same time, despite perhaps limited clinical evidence to suggest necessity for both pharmaceutical agents.[13] However, we have also noted a recent reversing trend for respiratory disease whereby antimicrobial prescription frequency has decreased whilst anti-inflammatory prescription frequency has increased.[10] These findings perhaps reflect increasing recognition of frequent non-infectious mediators for respiratory disease,[46] or increased attention to prescribing guidance.[16] It was interesting to note that no significant variation in anti-inflammatory prescription was observed here, perhaps demonstrating more generalised ‘de-coupling’ of anti-inflammatory and antimicrobial prescription. Though measuring frequency of use represents a relatively simple method for demonstrating change, reduced use is not necessarily representative of more responsible use. Hence, it is probable that more nuanced methods for ascertaining whether a pharmaceutical agent has been prescribed appropriately will be needed. As part of these developments, we would advocate increased attention on use of other pharmaceutical agents that might form effective alternatives to antimicrobial prescription, whilst also satisfying the recognised need of a practitioner to provide a clear demonstration of action via provision of a therapeutic product, to the client.[17]

Though prescribers retained full autonomy to prescribe what they considered best for the animal under their care, we incorporated euthanasia frequency as a relatively crude measure of any increase in adverse health effects associated with change in prescription decision-making prompted by this trial. While no significant increases were observed in either intervention group, compared to the CG, we recognise that this method lacks sensitivity, not taking into account a range of potential sub-optimal outcomes that might compromise animal welfare. Though effectively and efficiently quantifying such adverse effects from EHRs at the scale required for this trial presents a significant challenge,[47] we recommend further development of text-mining and statistical methodologies to explore such nuances, both for this and subsequent trials.

Use of bacterial infection-associated diagnostic tests was not significantly affected in this trial. Low frequency of use of such tests has been identified as a barrier to effective stewardship,[48] likely reflecting low confidence in their ability to provide timely, useful clinical insights.[49] Indeed, across all groups, test orders were low, indicating a preference for empirical antimicrobial prescription throughout the trial. Used correctly, these tests do play an important role in correctly managing a patient;[50] however, there is clearly more work needed to convince practitioners – and owners – of the benefits of regularly pursuing these diagnostic routes. That said, during this trial a lack of equipment and training for cytological examinations within practices was identified, which resulted in wide-scale equipment and training provision (unpublished observations). Thus, there is hope that significant impact will be generated beyond the confines of this trial.

Conclusions

In this trial we outlined a data-led benchmarking, reflection and education antimicrobial stewardship framework that successfully reduced HPCIA, systemic and overall antimicrobial prescription frequency in dogs and cats in practices belonging to a single large practice group. However, whilst initially encouraging, further work is required to understand the relative impact of different antimicrobials on conferring clinically meaningful resistance, and how to incentivise increased use of diagnostic testing in preference to empirical antimicrobial prescription. This work provides the first robust evidence base for future antimicrobial stewardship interventions in companion animal practice, and findings are now being used to inform development of a national stewardship scheme, in collaboration with RCVS Knowledge and CVS Group (UK) Limited.

Declarations

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Conflict of interest statement

The authors declare no conflicts of interest.

Author contributions

DAS and GLP conceived of and devised the trial design and prepared trial materials, including intervention letters, educational videos and benchmarking reports. DAS collated and prepared data, conducted analysis and wrote the manuscript, with supervision from GLP. PJMN and ADR supported trial design, and provided oversight of manuscript drafts. BB initially recruited all trial practices onto the SAVSNET project, and provided communications support between SAVSNET and trial practices throughout. SS provided database support, created online platforms for educational videos to be viewed, and devised the practice antimicrobial benchmarking portal monitoring capability. AR assisted trial design, acted as a liaison between SAVSNET and CVS Group Ltd., and trained HCLs in how to correctly implement devised interventions.

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Tables

Table One: Practice, canine and feline pre-intervention (August 2018 – March 2019 (inclusive)) baseline characteristics. Practice characteristics summarised as of March 2019.

Variable	Control group	Light intervention group	Heavy intervention group
PRACTICE CHARACTERISTICS			
Median vet FTE [a] / practice [range]	3.8 [1.1 – 17.4]	4.1 [1.0 – 13.4]	5.0 [1.1 – 11.5]
% of total FTE locum cover	6.5	5.0	6.8
CANINE			
Median n consultations / practice [range]	2,657.5 [460.0 – 23,889.0]	3,814.5 [1,004.0 – 13,476.0]	3,127.0 [443.0 – 9,145.0]
Median n unique animals / practice [range]	1,442.5 [335.0 – 14,436.0]	2,104.0 [626.0 – 6,613.0]	1,745.5 [310.0 – 4,785.0]
Main presenting complaint - % of total consultations (95% confidence interval, CI)			
Vaccination	32.5 (29.5-35.4)	29.4 (26.9-31.9)	33.5 (29.9-37.0)
Other healthy	21.8 (17.7-26.0)	27.7 (23.6-31.7)	21.7 (18.7-24.7)
Post-operative check	9.8 (6.8-12.8)	8.4 (7.0-9.8)	7.1 (6.1-8.2)
Gastroenteric	3.0 (2.4-3.7)	3.2 (2.7-3.7)	3.1 (2.5-3.7)
Respiratory	1.0 (0.7-1.2)	0.9 (0.8-1.0)	1.0 (0.7-1.2)
Pruritus	4.8 (3.8-5.9)	4.7 (3.7-5.6)	4.7 (3.9-5.6)
Trauma	4.2 (3.3-5.0)	4.4 (3.7-5.0)	4.4 (3.5-5.3)
Tumour	1.4 (1.1-1.7)	1.5 (1.2-1.7)	1.7 (1.3-2.0)
Kidney disease	0.3 (0.2-0.3)	0.3 (0.2-0.4)	0.3 (0.2-0.4)
Other unwell	21.3 (18.1-24.5)	19.6 (16.6-22.7)	22.4 (20.0-24.7)
Animal characteristics – % of total consultations (95% CI)			
Sex: Male	51.2 (50.4-51.9)	51.0 (49.9-52.1)	52.5 (51.3-53.8)
Neutered	67.4 (65.4-69.4)	66.4 (62.2-70.6)	67.9 (65.1-70.8)
Insured	34.9 (21.9-48.0)	31.6 (22.2-41.0)	25.2 (15.7-34.8)
Vaccinated	79.8 (78.1-81.6)	79.7 (77.6-81.8)	81.9 (79.4-84.3)
Median age [range]	5.8 [0.0 – 20.7]	5.9 [0.0 – 24.7]	6.2 [0.0 – 24.0]
FELINE			
Median n consultations / practice [range]	868.0 [231.0 – 8,608.0]	1,609.0 [424.0 – 6,365.0]	1,062.0 [457.0 – 2,626.0]
Median n unique animals / practice [range]	577.0 [161.0 – 5,996.0]	1,031.0 [340.0 – 3,922.0]	740.0 [373.0 – 1,895.0]
Main presenting complaint - % of total consultations (95% CI)			
Vaccination	36.7 (33.0-40.5)	33.9 (31.7-36.2)	37.7 (33.9-41.4)
Other healthy	20.4 (16.6-24.2)	27.8 (23.7-31.9)	21.7 (18.3-25.1)
Post-operative check	7.9 (5.1-10.7)	6.6 (5.4-7.9)	5.8 (5.0-6.6)
Gastroenteric	2.3 (1.6-3.0)	2.2 (1.8-2.5)	2.2 (1.7-2.7)
Respiratory	1.4 (1.0-1.9)	1.2 (0.8-1.6)	1.4 (1.1-1.8)
Pruritus	2.5 (1.8-3.2)	2.0 (1.6-2.5)	2.3 (1.9-2.7)
Trauma	4.6 (3.5-5.7)	4.6 (3.7-5.5)	4.2 (3.6-4.8)
Tumour	0.7 (0.5-0.9)	0.9 (0.6-1.2)	0.9 (0.7-1.2)
Kidney disease	0.8 (0.5-1.0)	0.7 (0.6-0.9)	1.1 (0.7-1.4)

Other unwell	22.6 (19.3-25.9)	20.1 (17.6-22.6)	22.7 (20.4-25.1)
Animal characteristics – % of total consultations (95% CI)			
Sex: Male	48.5 (47.5-49.5)	49.0 (47.8-50.1)	49.6 (48.5-50.7)
Neutered	81.6 (79.0-84.3)	83.0 (80.9-85.0)	80.0 (77.1-82.9)
Insured	24.9 (11.1-38.6)	21.7 (14.2-29.2)	17.3 (12.1-22.5)
Vaccinated	68.9 (65.6-72.2)	71.5 (68.1-74.9)	72.0 (69.2-74.7)
Median age [range]	6.7 [0.0 – 26.7]	7.3 [0.0 – 27.0]	7.3 [0.0 – 26.8]

[a] Full-time equivalent (40 hours), inclusive of locum veterinary surgeon FTE.

Table Two: Canine antimicrobial and anti-inflammatory prescription, and euthanasia as a percentage of total canine consultations by intervention group, split into pre-intervention (August 2018 – March 2019) and post-intervention (April – September 2019) phases. Antimicrobial prescription considered in total, by authorised administration route, and by priority classification; the latter also being summarised by main presenting complaint. Also included are *P*-value outputs of a series of mixed effects panel regression models, modelling prescription category against intervention group, pre- and post-intervention. Full regression model outputs are available in upplementary material, Tables One (Antimicrobial prescription), Five (HPCIA prescription by main presenting complaint) and Seven (other prescriptions).

CANINE	Control group		Light intervention group			Heavy intervention group		
Variable	Pre-intervention	Post-intervention	Pre-intervention	Post-intervention	*P*	Pre-intervention	Post-intervention	*P*
PRIMARY OUTCOME								
HPCIA [a]	0.71 (0.57-0.86)	0.66 (0.48-0.84)	0.72 (0.60-0.83)	0.78 (0.60-0.95)	0.467	**0.68 (0.47-0.90)**	**0.46 (0.35-0.58)**	**0.015**
Antimicrobial prescription – % of total consultations (95% confidence interval, CI)								
Total	17.44 (16.23-18.65)	17.57 (16.04-19.10)	17.44 (16.40-18.48)	17.46 (16.45-18.47)	0.143	**17.28 (16.20-18.36)**	**15.40 (13.83-16.96)**	**<0.001**
Systemic	10.49 (9.56-11.42)	10.59 (9.46-11.71)	10.32 (9.43-11.22)	10.09 (9.17-11.00)	0.110	**10.25 (9.33-11.16)**	**8.35 (7.33-9.37)**	**<0.001**
Topical	7.58 (6.95-8.22)	7.62 (6.83-8.40)	7.79 (7.39-8.18)	7.93 (7.58-8.29)	0.652	7.61 (7.11-8.11)	7.50 (6.70-8.30)	0.175
Systemic HPCIA	0.40 (0.29-0.52)	0.32 (0.22-0.43)	0.39 (0.34-0.44)	0.36 (0.29-0.42)	0.404	0.51 (0.35-0.67)	0.20 (0.12-0.29)	0.051
HPCIA prescription by main presenting complaint - % of relevant consultations (95% CI)								
Vaccination	0.10 (0.06-0.14)	0.13 (0.07-0.19)	**0.15 (0.10-0.19)**	**0.22 (0.11-0.33)**	**0.026**	0.12 (0.04-0.20)	0.03 (0.00-0.05)	0.055
Other healthy	0.70 (0.45-0.95)	0.74 (0.39-1.10)	0.47 (0.30-0.63)	0.72 (0.50-0.95)	0.278	**0.43 (0.27-0.59)**	**0.28 (0.14-0.41)**	**0.006**
Post-operative check	0.75 (0.15-1.36)	0.59 (0.21-0.96)	0.62 (0.38-0.87)	0.54 (0.36-0.72)	0.301	0.53 (0.26-0.81)	0.35 (0.13-0.56)	0.532
Gastroenteric	0.60 (0.25-0.95)	0.12 (0.00-0.28)	0.59 (0.30-0.88)	0.41 (0.15-0.67)	0.307	1.52 (0.37-2.67)	0.44 (0.00-0.91)	0.615
Respiratory	2.05 (0.67-3.43)	1.24 (0.00-2.86)	1.88 (0.99-2.78)	0.78 (0.18-1.39)	0.602	2.34 (0.87-3.80)	0.44 (0.00-1.25)	0.373
Pruritus	1.69 (0.87-2.51)	1.35 (0.75-1.94)	2.39 (1.57-3.22)	2.22 (1.47-2.97)	0.575	1.30 (0.57-2.04)	1.17 (0.76-1.58)	0.932
Trauma	0.55 (0.25-0.86)	0.28 (0.07-0.49)	0.49 (0.24-0.74)	0.61 (0.23-0.99)	0.469	0.61 (0.36-0.87)	0.54 (0.21-0.88)	0.278
Tumour	0.71 (0.38-1.04)	0.65 (0.05-1.25)	0.62 (0.11-1.14)	0.40 (0.00-0.80)	0.051	**0.87 (0.25-1.48)**	**0.10 (0.00-0.29)**	**0.033**
Kidney disease	2.06 (0.16-3.97)	1.37 (0.00-3.28)	1.22 (0.00-2.59)	2.25 (0.40-4.09)	0.937	4.65 (1.46-7.83)	2.24 (0.58-3.91)	0.971
Other unwell	1.39 (1.11-1.68)	1.36 (1.08-1.64)	1.58 (1.08-2.08)	1.52 (1.02-2.03)	0.586	1.44 (0.88-2.00)	1.13 (0.85-1.41)	0.108
Other prescriptions - % of total consultations (95% CI)								
Anti-inflammatory	20.26 (18.99-21.54)	20.94 (19.75-22.13)	19.91 (18.86-20.95)	20.03 (18.96-21.10)	0.900	21.41 (19.90-22.92)	21.41 (19.79-23.03)	0.649
Euthanasia	0.99 (0.80-1.18)	1.04 (0.82-1.27)	1.09 (0.90-1.29)	1.11 (0.91-1.32)	0.768	1.07 (0.95-1.19)	1.15 (1.02-1.29)	0.502

[a] Highest priority critically important antimicrobial

Table Three: Feline antimicrobial and anti-inflammatory prescription, and euthanasia as a percentage of total feline consultations by intervention group, split into pre-intervention (August 2018 – March 2019) and post-intervention (April – September 2019) phases. Antimicrobial prescription considered in total, by authorised administration route, and by priority classification; the latter also being summarised by main presenting complaint. Also included are *P*-value outputs of a series of mixed effects panel regression models, modelling prescription category against intervention group, pre- and post-intervention. Full regression model outputs are available in supplementary material, Tables Two (Antimicrobial prescription), Six (HPCIA prescription by main presenting complaint) and Seven (other prescriptions).

FELINE	Control group		Light intervention group			Heavy intervention group		
Variable	Pre-intervention	Post-intervention	Pre-intervention	Post-intervention	*P*	Pre-intervention	Post-intervention	*P*
PRIMARY OUTCOME								
HPCIA [a]	7.44 (6.27-8.61)	7.56 (6.14-8.98)	7.03 (6.32-7.74)	6.40 (5.42-7.38)	0.090	**8.03 (7.16-8.90)**	**4.44 (3.42-5.46)**	**<0.001**
Antimicrobial prescription – % of total consultations (95% confidence interval, CI)								
Total	16.68 (15.19-18.17)	16.79 (15.48-18.09)	14.97 (13.46-16.49)	14.99 (13.66-16.33)	0.129	**15.26 (14.34-16.18)**	**14.01 (12.59-15.43)**	**0.001**
Systemic	14.08 (12.60-15.55)	13.98 (12.73-15.23)	12.43 (11.13-13.74)	12.25 (10.97-13.53)	0.134	**12.75 (11.91-13.58)**	**11.26 (9.98-12.55)**	**0.001**
Topical	3.03 (2.70-3.35)	3.34 (2.99-3.70)	2.98 (2.64-3.33)	3.14 (2.89-3.40)	0.236	2.95 (2.62-3.28)	3.08 (2.80-3.37)	0.083
Systemic HPCIA	7.35 (6.12-8.58)	7.49 (6.06-8.91)	6.93 (6.23-7.63)	6.31 (5.34-7.28)	0.079	**7.95 (7.08-8.82)**	**4.35 (3.31-5.40)**	**<0.001**
HPCIA prescription by main presenting complaint - % of relevant consultations (95% CI)								
Vaccination	0.76 (0.34-1.19)	1.06 (0.41-1.71)	1.02 (0.51-1.52)	1.15 (0.54-1.76)	0.900	**1.35 (0.35-2.36)**	**0.46 (0.32-0.61)**	**0.049**
Other healthy	5.17 (3.42-6.93)	6.22 (4.03-8.42)	5.65 (4.49-6.82)	5.12 (3.84-6.40)	0.336	**5.92 (4.29-7.55)**	**3.68 (2.12-5.25)**	**0.005**
Post-operative check	5.81 (1.88-9.75)	5.36 (0.49-10.23)	3.50 (2.06-4.94)	3.68 (2.62-4.74)	0.539	4.54 (3.05-6.03)	2.95 (1.25-4.65)	0.740
Gastroenteric	4.86 (3.19-6.53)	4.78 (1.60-7.96)	4.45 (2.34-6.56)	3.97 (1.56-6.37)	0.945	6.44 (4.00-8.88)	2.44 (0.92-3.96)	0.239
Respiratory	27.35 (20.07-34.63)	25.00 (13.08-36.93)	24.99 (19.21-30.77)	18.86 (13.85-23.86)	0.689	32.19 (24.15-40.23)	14.75 (8.54-20.97)	0.074
Pruritus	15.71 (11.25-20.17)	16.11 (10.33-21.89)	17.76 (13.63-21.90)	14.53 (11.22-17.83)	0.273	**19.70 (14.05-25.35)**	**10.48 (6.15-14.80)**	**0.042**
Trauma	28.86 (22.65-35.08)	27.22 (21.96-32.48)	27.39 (24.18-30.60)	23.20 (17.85-28.55)	0.174	**29.19 (24.71-33.66)**	**14.01 (9.19-18.84)**	**0.001**
Tumour	13.20 (10.09-16.32)	15.63 (11.11-20.15)	**12.03 (9.25-14.82)**	**8.20 (4.99-11.41)**	**0.003**	**13.24 (8.80-17.68)**	**7.38 (4.45-10.31)**	**<0.001**
Kidney disease	15.28 (7.27-23.28)	15.89 (7.03-24.76)	13.02 (8.34-17.69)	9.73 (5.78-13.69)	0.766	15.69 (11.67-19.71)	8.80 (4.58-13.01)	0.267
Other unwell	14.13 (11.79-16.47)	13.17 (11.21-15.12)	13.25 (11.49-15.01)	11.89 (10.05-13.72)	0.687	**14.99 (13.01-16.97)**	**8.43 (6.24-10.62)**	**0.008**
Other prescriptions - % of total consultations (95% CI)								
Anti-inflammatory	19.03 (17.12-20.93)	19.50 (18.00-21.00)	17.50 (16.23-18.76)	18.02 (16.81-19.23)	0.435	18.67 (17.06-20.28)	18.77 (17.27-20.28)	0.460
Euthanasia	2.14 (1.64-2.65)	2.20 (1.70-2.70)	2.29 (1.99-2.58)	2.32 (1.96-2.69)	0.988	2.13 (1.89-2.38)	2.38 (1.96-2.79)	0.662

[a] Highest priority critically important antimicrobial

Table Four: Canine and feline HPCIA prescription as a percentage of total consultations, summarised by month between August 2018 and September 2019. Also included is an incident rate ratio between the control group and intervention groups, and *P*-value outputs of mixed effects panel regression, modelling intervention group against month. Full regression model outputs are available in supplementary material, Table Three (dogs) and Four (cats).

Month	Control group	Light intervention group			Heavy intervention group		
	HPCIA [a] % (CI) [b]	HPCIA % (CI)	IRR [c] (CI)	*P*	HPCIA % (CI)	IRR[b] (CI)	*P*
CANINE							
August, 2018 (pre-intervention)	0.73 (0.48-0.98)	0.79 (0.62-0.95)	1.10 (0.84-1.45)	0.369	0.62 (0.37-0.88)	0.86 (0.61-1.20)	0.623
September, 2018	0.71 (0.48-0.94)	0.77 (0.62-0.92)	1.12 (0.83-1.49)	0.452	0.65 (0.41-0.90)	0.92 (0.65-1.31)	0.741
October, 2018	0.78 (0.53-1.02)	0.64 (0.51-0.76)	0.83 (0.63-1.11)	0.174	0.56 (0.34-0.78)	0.73 (0.52-1.02)	0.122
November, 2018	0.67 (0.54-0.81)	0.66 (0.49-0.83)	0.98 (0.72-1.33)	1.000	0.79 (0.53-1.05)	1.16 (0.84-1.61)	0.780
December, 2018	1.00 (0.70-1.30)	0.93 (0.69-1.16)	0.95 (0.71-1.26)	0.639	0.83 (0.51-1.15)	0.83 (0.58-1.18)	0.513
January, 2019	0.62 (0.41-0.84)	0.84 (0.64-1.05)	1.36 (1.01-1.83)	0.501	0.68 (0.32-1.03)	1.08 (0.75-1.54)	0.129
February, 2019	0.75 (0.52-0.99)	0.55 (0.38-0.72)	0.72 (0.52-1.00)	0.164	**0.82 (0.45-1.18)**	**1.06 (0.75-1.49)**	**0.043**
March, 2019	0.49 (0.29-0.70)	0.56 (0.42-0.70)	1.18 (0.82-1.68)	0.986	0.59 (0.39-0.80)	1.22 (0.82-1.83)	0.418
April, 2019 (post-intervention)	0.60 (0.35-0.85)	0.76 (0.52-1.00)	1.31 (0.96-1.80)	0.909	0.49 (0.33-0.64)	0.84 (0.56-1.28)	0.222
May, 2019	0.88 (0.62-1.14)	0.78 (0.54-1.03)	0.91 (0.69-1.20)	0.338	**0.46 (0.26-0.66)**	**0.53 (0.37-0.78)**	**0.022**
June, 2019	0.63 (0.37-0.89)	0.71 (0.52-0.90)	1.16 (0.84-1.60)	0.437	0.49 (0.27-0.72)	0.80 (0.54-1.19)	0.220
July, 2019	0.43 (0.26-0.60)	0.69 (0.48-0.89)	1.64 (1.17-2.29)	0.536	0.56 (0.36-0.77)	1.33 (0.91-1.96)	0.399
August, 2019	0.79 (0.54-1.04)	0.95 (0.74-1.16)	1.24 (0.94-1.63)	0.568	**0.37 (0.18-0.56)**	**0.48 (0.32-0.73)**	**0.005**
September, 2019	0.66 (0.42-0.90)	0.77 (0.52-1.01)	1.24 (0.94-1.63)	0.382	**0.38 (0.23-0.53)**	**0.59 (0.38-0.92)**	**0.042**
FELINE							
August, 2018 (pre-intervention)	8.49 (7.42-9.57)	7.90 (7.16-8.63)	0.94 (0.82-1.07)	0.337	8.47 (7.41-9.53)	1.01 (0.87-1.17)	0.878
September, 2018	7.60 (5.95-9.25)	7.40 (6.45-8.35)	0.98 (0.85-1.14)	0.799	8.70 (7.31-10.09)	1.15 (0.99-1.35)	0.308
October, 2018	6.81 (5.55-8.07)	7.54 (6.24-8.83)	1.12 (0.97-1.29)	0.857	8.03 (6.73-9.33)	1.19 (1.02-1.39)	0.770
November, 2018	7.01 (5.93-8.08)	6.78 (5.66-7.90)	0.98 (0.84-1.14)	0.574	7.14 (5.95-8.32)	1.03 (0.87-1.22)	0.394
December, 2018	7.77 (5.65-9.89)	7.63 (6.21-9.06)	1.00 (0.85-1.18)	0.626	8.31 (6.88-9.73)	1.08 (0.90-1.31)	0.397
January, 2019	6.83 (5.22-8.44)	5.44 (4.51-6.37)	0.81 (0.69-0.96)	0.312	7.74 (6.73-8.76)	1.15 (0.97-1.37)	0.874
February, 2019	7.86 (6.10-9.62)	7.03 (6.09-7.98)	0.91 (0.78-1.07)	0.060	7.65 (6.47-8.82)	0.98 (0.83-1.17)	0.166
March, 2019	7.42 (6.10-8.75)	6.37 (5.58-7.15)	0.86 (0.73-1.02)	0.557	8.29 (6.93-9.64)	1.13 (0.95-1.34)	0.572
April, 2019 (post-intervention)	8.10 (6.50-9.69)	6.71 (5.53-7.89)	0.84 (0.71-0.98)	0.325	**4.88 (3.84-5.92)**	**0.61 (0.50-0.75)**	**0.001**
May, 2019	7.68 (6.36-9.00)	5.98 (4.76-7.20)	0.78 (0.66-0.92)	0.195	**4.77 (3.32-6.22)**	**0.63 (0.52-0.76)**	**0.001**
June, 2019	8.35 (6.00-	**6.69 (5.43-**	**0.82 (0.70-**	**0.033**	**3.97 (2.82-5.13)**	**0.49 (0.40-**	**<0.001**

	10.70)	**7.94)**	**0.96)**			**0.60)**	
July, 2019	6.86 (5.29-8.43)	6.34 (5.43-7.25)	0.94 (0.81-1.10)	0.788	**4.05 (2.99-5.11)**	**0.60 (0.49-0.73)**	**0.005**
August, 2019	7.49 (6.03-8.95)	6.47 (5.52-7.42)	0.87 (0.75-1.02)	0.110	**4.28 (2.72-5.83)**	**0.58 (0.48-0.71)**	**<0.001**
September, 2019	6.95 (5.61-8.30)	6.19 (4.79-7.60)	0.89 (0.75-1.06)	0.740	**4.84 (3.15-6.52)**	**0.71 (0.58-0.87)**	**0.006**

[a] Highest priority critically important antimicrobial

[b] 95% Confidence interval

[c] Incidence Rate Ratio

Table Five: Canine antimicrobial prescription choice as a percentage of total antimicrobial prescriptions, presented by class and for beta-lactams, by sub-class, and by intervention group split into pre- and post-intervention time periods. Also included are *P*-value outputs of a series of mixed effects panel regression models, modelling antimicrobial class or sub-class against intervention group, pre- and post-intervention. Full regression model outputs are available in Supplementary material, Table Eight.

CANINE Antimicrobial class	Control group % (95% CI) [a]		Light intervention group % (95% CI)			Heavy intervention group % (95% CI)		
	Pre-intervention	Post-intervention	Pre-intervention	Post-intervention	*P*	Pre-intervention	Post-intervention	*P*
Aminoglycoside	10.94 (9.00-12.88)	5.76 (4.38-7.14)	10.60 (8.08-13.13)	6.32 (4.45-8.19)	0.581	9.81 (7.71-11.90)	6.41 (3.41-9.42)	0.720
Amphenicol	7.14 (4.88-9.39)	8.08 (5.98-10.19)	5.38 (3.44-7.31)	7.21 (5.20-9.23)	0.726	6.60 (4.21-8.99)	7.79 (4.84-10.74)	0.301
Beta-lactam	41.71 (37.35-46.07)	44.42 (40.68-48.17)	43.48 (40.85-46.11)	45.34 (42.01-48.67)	0.354	41.87 (39.20-44.53)	41.81 (38.81-44.81)	0.251
Amoxicillin	*5.27 (0.58-9.97)*	*3.84 (0.10-7.59)*	*4.58 (2.21-6.94)*	*4.29 (1.87-6.71)*	*0.656*	*6.83 (1.49-12.18)*	*5.76 (1.72-9.80)*	*0.944*
Clavulanic acid potentiated amoxicillin	*73.80 (69.84-77.76)*	*73.82 (68.95-78.68)*	*73.31 (68.49-78.14)*	*76.76 (70.80-82.72)*	*0.264*	*74.46 (69.46-79.46)*	*78.27 (72.09-84.44)*	*0.285*
1st generation cephalosporin	*18.85 (14.87-22.83)*	*20.99 (16.57-25.40)*	*20.43 (15.65-25.22)*	*17.37 (12.39-22.34)*	*0.817*	*16.13 (13.14-19.11)*	*15.10 (11.39-18.80)*	*0.165*
2nd generation cephalosporin	*0.10 (0.00-0.19)*	*0.07 (0.00-0.15)*	*0.06 (0.00-0.13)*	*0.07 (0.00-0.15)*	*0.860*	*0.29 (0.03-0.54)*	*0.03 (0.00-0.08)*	*0.598*
3rd generation cephalosporin [b]	*1.71 (1.13-2.30)*	*1.14 (0.71-1.58)*	*1.31 (0.83-1.80)*	*1.28 (0.79-1.78)*	*0.374*	*2.24 (1.61-2.86)*	*0.84 (0.37-1.31)*	*0.298*
Penicillin	-	-	-	*0.01 (0.00-0.04)*	*0.298*	*0.02 (0.00-0.05)*	-	*0.120*
Other beta-lactams	*0.38 (0.00-0.92)*	*0.08 (0.00-0.20)*	*0.30 (0.00-0.62)*	*0.16 (0.00-0.38)*	*0.633*	*0.09 (0.00-0.26)*	-	*0.812*
Fluoroquinolone [b]	2.75 (2.17-3.33)	2.98 (2.25-3.70)	2.97 (2.32-3.62)	3.43 (2.53-4.32)	0.213	2.50 (1.51-3.49)	2.43 (1.83-3.03)	0.245
Fusidic acid	18.03 (16.35-19.71)	13.45 (11.82-15.08)	19.40 (18.24-20.56)	15.09 (13.00-17.18)	0.338	19.97 (18.74-21.19)	18.70 (16.40-21.01)	0.878
Lincosamide	3.96 (2.76-5.17)	4.11 (2.84-5.38)	2.73 (2.06-3.40)	2.22 (1.53-2.90)	0.371	3.55 (2.32-4.78)	3.00 (2.19-3.82)	0.161
Macrolide [b]	0.03 (0.01-0.06)	0.03 (0.00-0.06)	0.04 (0.01-0.08)	0.04 (0.01-0.06)	0.579	0.03 (0.00-0.06)	0.01 (0.00-0.03)	0.405
Nitroimidazole	6.83 (4.96-8.70)	7.63 (5.87-9.40)	5.52 (3.73-7.31)	6.23 (4.50-7.97)	0.913	6.21 (4.27-8.15)	6.25 (3.89-8.60)	0.201
Nitroimidazole-macrolide	0.20 (0.05-0.34)	0.19 (0.05-0.34)	0.29 (0.06-0.51)	0.35 (0.09-0.61)	0.376	0.44 (0.00-1.10)	0.24 (0.00-0.54)	0.868
Other antimicrobials	7.12 (5.29-8.95)	12.40 (10.54-14.26)	8.86 (6.71-11.00)	13.13 (10.99-15.26)	0.229	8.25 (7.12-9.38)	12.44 (10.71-14.17)	0.246
Sulphonamide	0.05 (0.00-0.11)	-	0.02 (0.00-0.05)	-	1.000	0.06 (0.00-0.13)	0.04 (0.00-0.07)	0.508
Tetracycline	1.25 (0.81-1.70)	1.01 (0.37-1.65)	0.71 (0.46-0.95)	0.62 (0.39-0.85)	0.617	0.69 (0.38-1.00)	0.85 (0.41-1.29)	0.374

[a] 95% Confidence interval

[b] Highest Priority Critically Important Antimicrobial

Table Six: Feline antimicrobial prescription choice as a percentage of total antimicrobial prescriptions, presented by class and for beta-lactams, by sub-class, and by intervention group split into pre- and post-intervention time periods. Also included are *P*-value outputs of a series of mixed effects panel regression models, modelling antimicrobial class or sub-class against intervention group, pre- and post-intervention. Full regression model outputs are available in Supplementary material, Table Nine.

FELINE Antimicrobial class	Control group % (95% CI) [a]		Light intervention group % (95% CI)			Heavy intervention group % (95% CI)		
	Pre-intervention	Post-intervention	Pre-intervention	Post-intervention	*P*	Pre-intervention	Post-intervention	*P*
Aminoglycoside	3.36 (2.54-4.18)	1.98 (0.98-2.99)	3.95 (2.77-5.13)	2.29 (1.45-3.14)	0.682	3.62 (2.74-4.49)	2.33 (1.51-3.14)	0.789
Amphenicol	2.50 (0.80-4.20)	3.45 (1.68-5.22)	1.91 (1.48-2.35)	1.91 (1.38-2.44)	0.355	1.92 (1.07-2.77)	2.73 (1.65-3.81)	0.307
Beta-lactam	74.53 (69.92-79.14)	74.25 (70.81-77.69)	73.08 (71.04-75.12)	74.07 (71.57-76.56)	0.810	70.63 (67.22-74.05)	71.43 (68.86-73.99)	0.303
Amoxicillin	*9.11 (1.96-16.25)*	*6.59 (1.57-11.61)*	*6.95 (2.49-11.41)*	*6.71 (2.34-11.08)*	*0.929*	*6.84 (3.70-9.99)*	*9.96 (5.46-14.46)*	*0.976*
Clavulanic acid potentiated amoxicillin	*37.80 (28.44-47.16)*	*39.48 (30.52-48.45)*	*37.07 (30.73-43.40)*	*42.50 (34.96-50.03)*	*0.703*	*29.14 (23.72-34.57)*	*51.29 (41.86-60.73)*	*0.078*
1st generation cephalosporin	*0.72 (0.43-1.00)*	*0.82 (0.36-1.29)*	*1.31 (0.33-2.29)*	*1.48 (0.49-2.47)*	*0.343*	*0.96 (0.19-1.72)*	*1.52 (0.24-2.81)*	*0.843*
2nd generation cephalosporin	*0.02 (0.00-0.06)*	*0.03 (0.00-0.09)*	*0.04 (0.00-0.13)*	*0.03 (0.00-0.09)*	*1.000*	-	*0.05 (0.00-0.13)*	*1.000*
3rd generation cephalosporin [b]	*52.45 (42.80-62.09)*	*53.23 (43.05-63.40)*	*54.57 (45.64-63.51)*	*49.53 (42.52-56.55)*	*0.971*	*63.11 (57.45-68.77)*	*37.19 (29.49-44.89)*	*0.090*
Penicillin	*0.06 (0.00-0.15)*	*0.07 (0.00-0.20)*	*0.02 (0.00-0.05)*	-	*0.373*	*0.03 (0.00-0.09)*	-	*0.373*
Other beta-lactams	-	-	-	-	-	-	-	-
Fluoroquinolone [b]	0.96 (0.56-1.36)	1.22 (0.88-1.56)	1.55 (1.10-2.01)	1.36 (0.96-1.76)	0.783	3.14 (1.00-5.29)	1.55 (0.94-2.16)	0.869
Fusidic acid	10.50 (9.00-12.01)	9.39 (7.98-10.80)	11.53 (10.36-12.70)	11.29 (9.60-12.98)	0.419	11.79 (10.68-12.91)	11.92 (10.33-13.51)	0.750
Lincosamide	3.06 (1.61-4.51)	3.16 (1.78-4.55)	3.04 (1.14-4.93)	2.81 (1.09-4.53)	0.963	2.81 (1.88-3.75)	3.38 (2.26-4.51)	0.683
Macrolide [b]	-	0.02 (0.00-0.08)	-	-	0.319	0.02 (0.00-0.07)	0.03 (0.00-0.10)	1.000
Nitroimidazole	1.11 (0.57-1.66)	1.03 (0.63-1.42)	0.59 (0.31-0.87)	0.83 (0.58-1.08)	0.755	1.44 (0.91-1.97)	1.17 (0.70-1.65)	0.640
Nitroimidazole-macrolide	0.32 (0.01-0.63)	0.34 (0.12-0.56)	0.12 (0.02-0.21)	0.08 (0.00-0.18)	0.274	0.31 (0.00-0.66)	0.17 (0.00-0.36)	0.319
Other antimicrobials	2.37 (1.60-3.13)	4.01 (3.02-5.00)	2.99 (2.45-3.53)	4.35 (3.67-5.03)	0.502	2.99 (2.39-3.59)	3.74 (2.77-4.70)	0.209
Sulphonamide	-	-	0.01 (0.00-0.04)	-	-	-	-	-
Tetracycline	1.35 (0.41-2.28)	1.15 (0.33-1.98)	1.22 (0.81-1.63)	1.02 (0.61-1.42)	0.877	1.31 (0.29-2.33)	1.52 (0.66-2.38)	0.837

[a] 95% Confidence interval

[b] Highest Priority Critically Important Antimicrobial

Figures

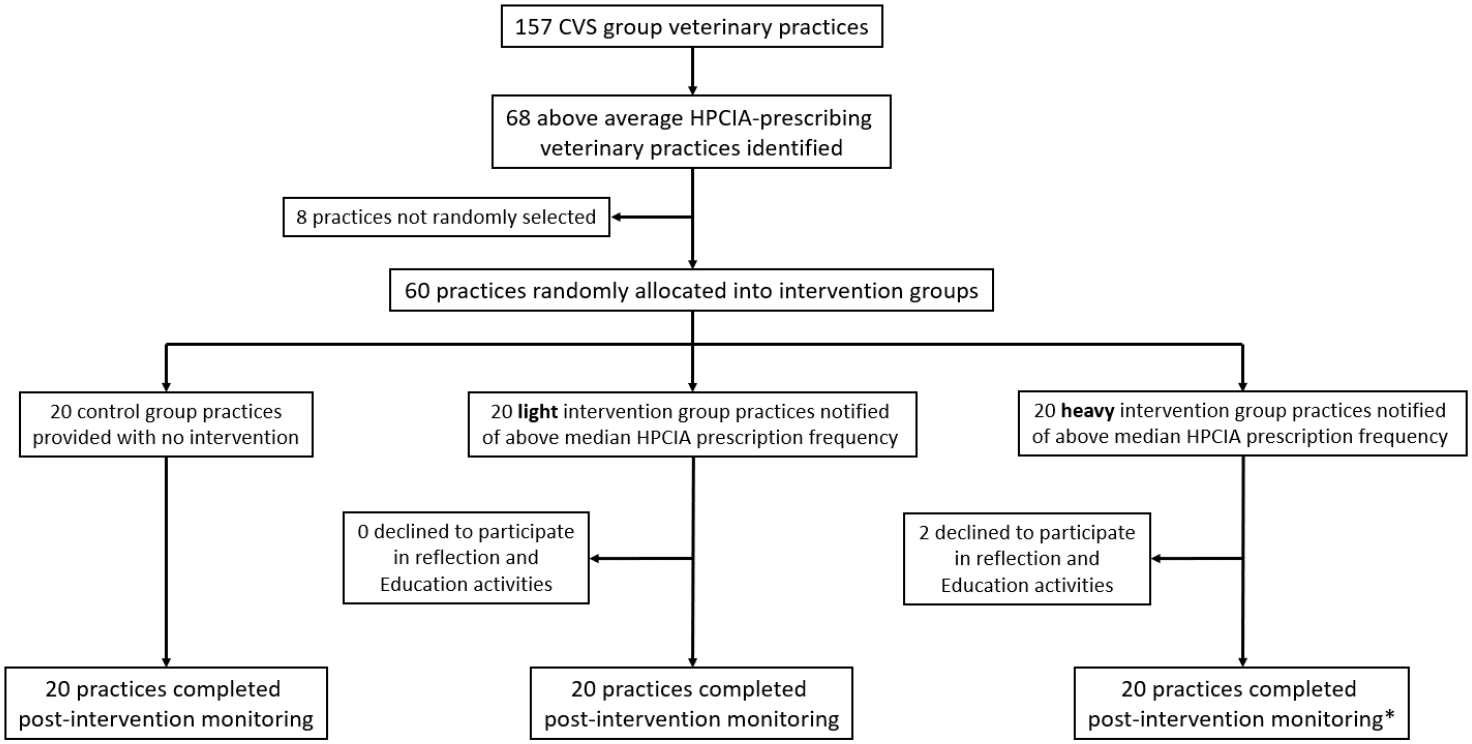

Figure 1

Schematic diagram of the process used to select above average HPCIA-prescribing veterinary practices, followed by drop-off rate following the initial benchmarking intervention.

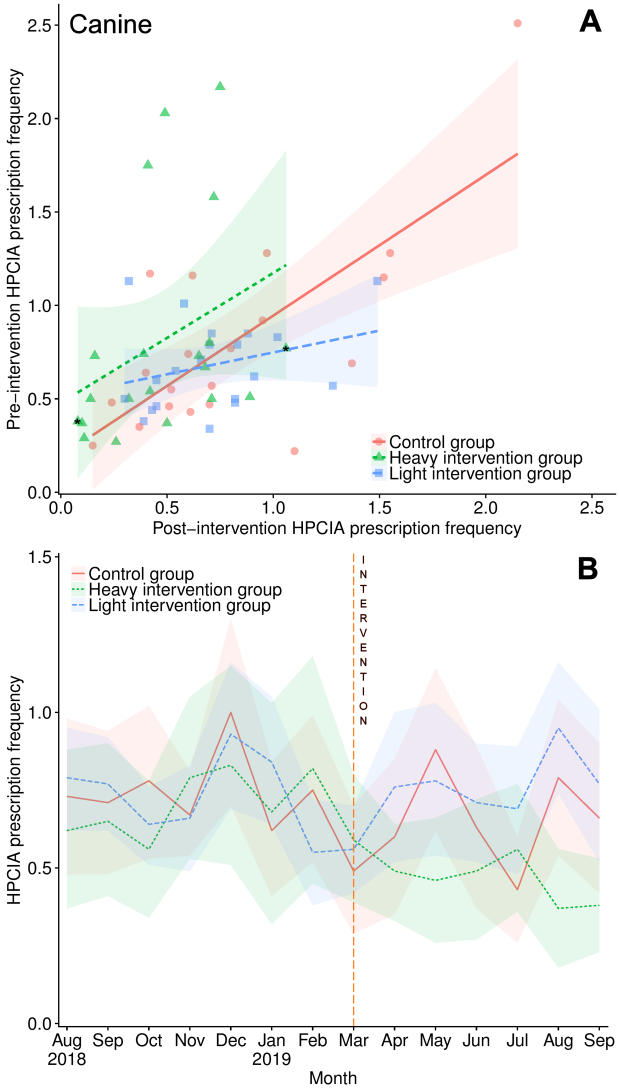

Figure 2

Canine highest priority critically important antimicrobial (HPCIA) prescription frequency as a percentage of total consultations, measured by (A) practice pre-intervention (August 2018 – March 2019 inclusive) and post-intervention (April – September 2019 inclusive), and (B) month. Lines in plot A refer to linear regression fits, modelling intervention status by practice, and asterisks refer to the two practices in the HIG which declined to participate in the post-benchmarking intervention reflection and education programme. Shaded regions refer to 95% confidence intervals.

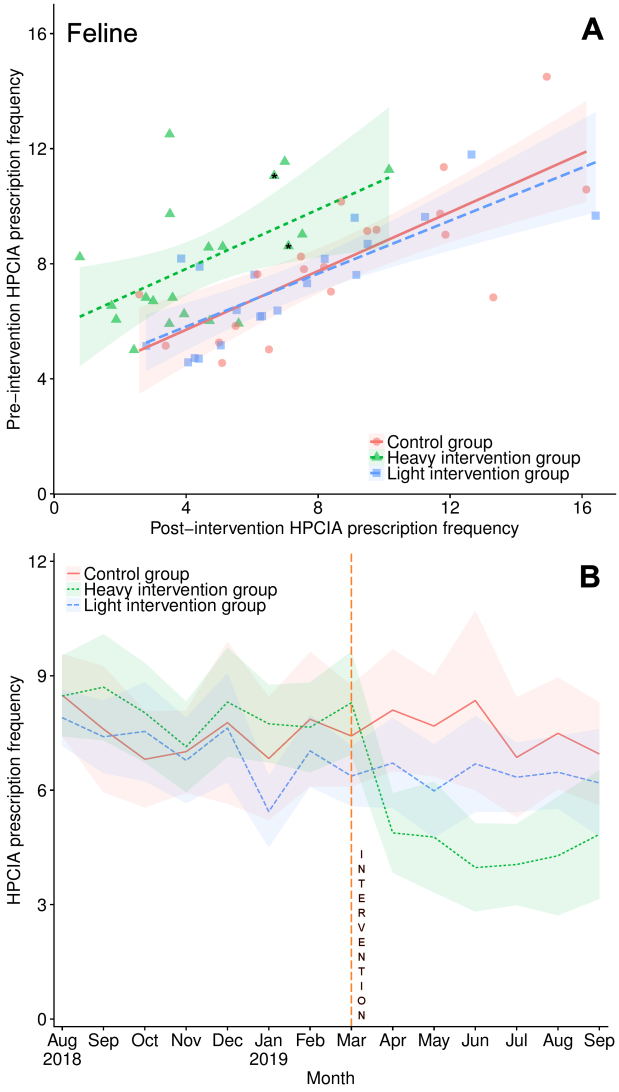

Figure 3

Feline highest priority critically important antimicrobial (HPCIA) prescription frequency as a percentage of total consultations, measured by (A) practice pre-intervention (August 2018 – March 2019 inclusive) and post-intervention (April – September 2019 inclusive), and (B) month. Lines in plot A refer to linear regression fits, modelling intervention status by practice, and asterisks refer to practices in the HIG which declined to participate in the post-benchmarking intervention reflection and education programme. Shaded regions refer to 95% confidence intervals.

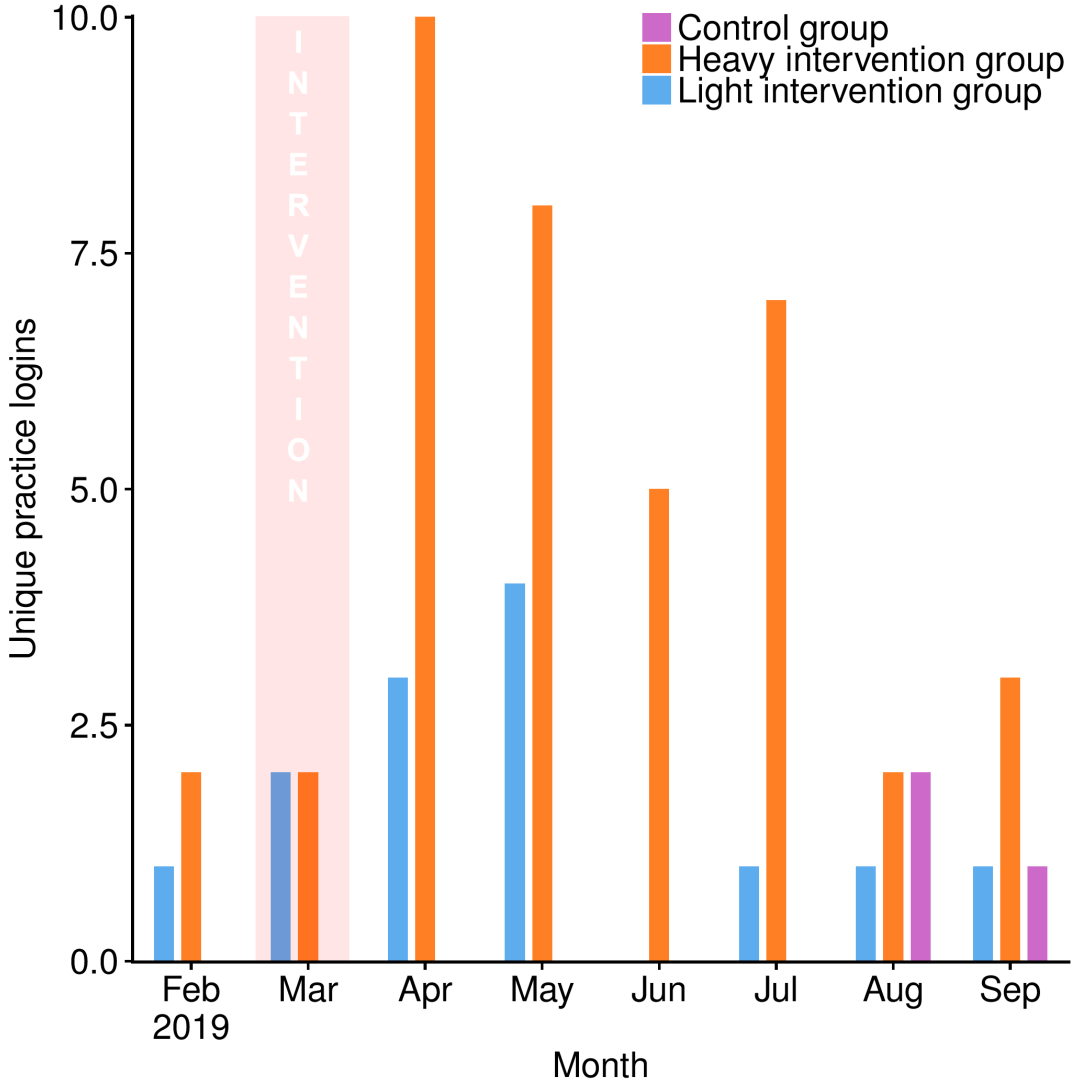

Figure 4

Number of practices logging into the SAVSNET antimicrobial prescription benchmarking portal by month (February – September 2019 inclusive) and intervention group.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Supplementarymaterial.pdf
- Supplementarytables.pdf
- CONSORTchecklist.pdf