Survey-based pilot study into the chosen therapy and prophylaxis used by UK primary care veterinary surgeons against canine angiostrongylosis

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Canine Angiostrongylosis (CA), a gastropod-borne parasitic infection caused by the metastrongyloid nematode *Angiostrongylus vasorum*, is an important cause of significant morbidity to domestic dogs across the UK as well as in other European countries. This study aimed to ascertain the frequency at which particular drugs were used by primary care practitioners in the UK for therapy against and prophylaxis for CA. Primary care veterinary clinicians were surveyed using an online questionnaire and face-to-face or telephone interviews. Eighty-six veterinary surgeons responded. The majority of practices (n = 52) included lungworm in their standard anthelmintic protocols; moxidectin was the most common drug used for prophylaxis (n = 71). Fenbendazole was the most frequently selected drug, by 45% of vets, for treatment of confirmed cases of CA despite it being unlicensed for this purpose in the UK and the absence of a clear treatment protocol. The results of this pilot study provide an initial insight into the approach taken by primary care practitioners in their approach to CA. This provides an important starting point for future studies investigating the decision-making for CA amongst UK veterinary surgeons, particularly to clarify whether in a larger cohort an unlicensed drug remains the treatment of choice. The absence of a clear protocol for fenbendazole means that treatment of dogs affected by CA may be suboptimal, increasing the risk of morbidity and mortality.

**Keywords:**

*Angiostrongylus vasorum*; Angiostrongylosis; Dogs; Moxidectin; Milbemycin oxime; Fenbendazole
List of abbreviations:

Bronchoalveolar lavage (BAL), canine angiostrongylosis (CA), enzyme-linked immunosorbent assay (ELISA), polymerase chain reaction (PCR), royal college of veterinary surgeons (RCVS), small animal practice (SAP)
1. Introduction

Canine angiostrongylosis (CA) is a parasitic disease caused by the cardiorespiratory nematode *Angiostrongylus vasorum* (Superfamily: Metastrongyloidea). Dogs become infected after ingesting the third larval stage (L3), usually within an intermediate gastropod host or a paratenic host, such as the common frog (*Rana temporaria*) (Bolt et al., 1993) and chicken (*Gallus gallus domesticus*) (Mozzer and Lima, 2015). In addition, experimental infection of *Biomphalaria glabrata* demonstrated that infected snails shed L3 into the environment, which could create a potential free-living reservoir of infection (Barçante et al., 2003). Rising numbers of confirmed cases of CA have thrown *A. vasorum* into the spotlight globally, driving research into its epidemiology, diagnosis and risk factors (Bwangamoi, 1972; Helm et al., 2010; Kistler et al., 2014; Penagos-Tabares et al., 2018). It is well-established that *A. vasorum* has spread from its original hot spot in South West (Simpson and Neal, 1982) and South East England (Chapman et al., 2004) and is now found throughout the UK. Cases have been reported as far north as Scotland (Helm et al., 2009); this expanding parasite’s territory has probably expanded faster than our knowledge of its pathogenicity and epidemiology. The full spectrum of the factors related to increasing prevalence of *A. vasorum* in dogs in Great Britain remains unexplained. However, a study conducted in the fox populations showed that the increased prevalence and geographic spread of *A. vasorum* in this reservoir host may have contributed to the increased risk of infection in dogs (Taylor et al., 2015).

CA presents with variable clinical signs and in some cases the infection may be entirely sub-clinical. The most common presenting signs relate to the respiratory tract and include dyspnoea and coughing. Other clinical signs include pulmonary hypertension, primary and secondary disorders of haemostasis (with associated haemorrhage) and neurological signs, including seizures. This is a disease with a myriad of possible presentations and therefore
remains a diagnostic challenge for veterinarians (Chapman et al., 2004; Koch and Willesen, 2009). The lack of a clear pathognomonic profile and the non-specific clinical signs may delay anthelmintic treatment while another suspected cause is investigated, resulting in more severe pathology. This is particularly the case for dogs presenting with coagulopathies or neurological signs in the absence of obvious respiratory signs. A major concern with CA is that it may remain largely asymptomatic and can manifest as sudden death (Bourque et al., 2002; Brennan et al., 2004).

In the UK, a number of macrocyclic lactone-based products are licensed to treat angiostrongylosis, containing moxidectin in a topical form (along with imidacloprid) or milbemycin oxime in tablet form. The treatment efficacy for a single dose of the formulation of imidaclorpid/moxidectin was found to be 85.2%. There was no significant difference between this and the 91.3% efficacy of fenbendazole administered daily for 20 days. The former of these treatment being licensed for use against AV in dogs, whereas the latter is not. Of those dogs still shedding larvae which received a further dose of imidacloprid/moxidectin, all were then found to be Baermann negative (Willesen et al., 2007).

Besides being licensed for treatment of adult worms imidacloprid/moxidectin is licensed for monthly use for the prevention of angiostrongylosis and prevention of patent infection, with 100% efficacy against L4 larvae and immature adults (L5) of A. vasorum (Schnyder M. et al., 2009). In regards to milbemycin oxime, commonly available in combination with praziquantel, a two-dose protocol achieved a clinical improvement, but without clearance of larval shedding and treatment was therefore extended to a protocol of using 4 weekly treatments to reduce the level of infection, achieving negative faecal Baermann results in 14 out of 16 dogs (Conboy, 2004). Monthly use of milbemycin oxime is licensed for prevention of angiostrongylosis by reduction in the level of infection by immature adult (L5) and adult parasite stages, with a recent study showing a worm count reduction efficacy of 94.9%
(Lebon et al., 2016). Whilst there are additional publications testifying the efficacy of fenbendazole in naturally occurring CA infections (Brennan et al., 2004; Chapman et al., 2004; Manning, 2007), in the absence of licensing, optimal dose, frequency and duration remain unclear. The risks of using unlicensed products are highlighted by levamisole, which was historically advocated for the treatment of CA due to its potency and rapid onset of action. However despite efficacy against CA, this is no longer recommended due to the occurrence of significant side-effects including anaphylaxis in levamisole-treated patients, thought to result at least in part from the rapid increase in circulating worm antigen (Søland and Bolt, 1996).

The efficacies of many of these drugs have been studied experimentally and in a number of clinical studies, and they have been licensed as a result. It is at present however unknown which products primary care veterinary surgeons in the UK are choosing to treat CA. It is suspected anecdotally that fenbendazole, whilst unlicensed remains the first-choice anthelminthic treatment for most primary care vets. In addition to this, it also remains unknown as to their choice of prophylaxis. A review of the therapeutic choices made by veterinary surgeons around CA treatment and prophylaxis across the UK is therefore important. In addition, the reasons behind these choices and the ‘perceived’ efficacy of this choice made by primary care clinicians are also of value. Whilst the latter point is difficult to prove retrospectively, the vet’s opinion is important as this will influence their future therapeutic choices. Perhaps a more important rationale for this study in the UK is the importance of prescribing veterinary medication according to the cascade. Therefore, the aims of this pilot survey were to identify which anthelmintic drugs were being used for therapy and prophylaxis of CA by UK primary care veterinary surgeons. An additional aim was to review the reported clinical signs in the confirmed cases of CA along with the method by which the disease was confirmed. Finally, the clinical outcome of cases diagnosed with
CA and the perspective of the veterinary surgeons on the efficacy of drugs used in the
treatment was also examined.

2. Material and methods

2.1. Ethics statement

The Institutional ethical review committee approved this study. Responses to the survey were
totally voluntary and all data obtained was anonymised and stored securely.

2.2. Data collection

Data were collected for this study using a combination of an online questionnaire (Table 1),
and telephone or face-to-face interviews, all targeting small animal veterinary surgeons in
primary care practice. The online survey contained 4 sections, beginning with a demographic
question asking for the number of years the clinician had been working in small animal
practice (SAP). This was followed by questions on the drugs used to prevent CA (clinicians
could indicate more than one), and whether the practice’s standard worming prophylaxis was
licensed for lungworm prevention. The final section was focused on treatment of CA, asking
the clinician for the drug they used and their efficacy rating for this drug. For ease of
comparison, drugs were listed according to their classification and not trade name for ease of
understanding. Clinicians were allowed to indicate more than one drug. The survey provided
an optional ‘other’ field which contained drugs less frequently mentioned (ivermectin and
selamectin). The online questionnaire was piloted by using other primary care veterinary
surgeons and changes were implemented where required. The questionnaire was available for
completion by veterinary surgeons during the pilot project period: between 11/10/2016 and
28/10/2016 via a specific URL provided to 287 primary care practices throughout England.
Additional interviews were conducted to supplement the online questionnaire, using the same questions and additionally requesting the standard worming protocol of the practice, then determining if the product was licensed in the UK to prevent CA. Eleven interviews were conducted in-person and 28 (of 59 practices contacted) consented to a telephone interview. Direct interviews were conducted across Greater Manchester, Lancashire, Leicestershire, Nottinghamshire and Norfolk. This produced a distribution of 326 practices (287 via email, 28 via telephone and 11 via direct interview).

2.3. Data analysis
Responses to the online survey and interview locations were plotted on a map of England in order to assess geographical coverage. Data from all response types was collected, categorized and analysed using Excel 2016 (Microsoft Corporation©) and SPSS Version 23 2005 (IBM®). Maps were created using the mapping feature of Excel 2016 (Microsoft Corporation©).

3. Results

3.1. Participants and distribution
Eighty-six responses were obtained from the 326 practices contacted representing a 26% response rate. The online questionnaire provided 47 responses (representing 14% of total distribution), 28 were from the telephone interviews (8.6% of total) and 11 from face-to-face interviews (3.4% of total). In order to assess how demographics of the participants influenced their responses, the number of years’ post-qualification that the veterinary surgeons had been in SAP was collated into a histogram (Fig. 1). The spread of all responses by county is shown in Fig. 2A. Greater London provided the greatest number of responses (13), followed by
Bristol (5) and then Cornwall, Norfolk, Nottinghamshire and Warwickshire (all of which provided 4). An additional map was created, displaying the number of confirmed cases of CA varying by county (Fig. 2B). Of the 86 responding practices, 19 (22%) stated that one or more confirmed cases of CA had been examined at that practice within the previous year. When the respondents were asked for the exact number of cases examined, the total came to 41 across all practices. The maximum number of cases examined at any one practice was 10 with a median of 2 cases per practice (IQR 1-2).

3.2. Frequency of clinical signs

A variety of clinical signs were reported by the study participants, those associated with the haematologic, respiratory and neurological systems were the most commonly reported (Table 2). One case was excluded from this analysis due to the fact CA was only discovered at referral and the primary care clinician completing the survey was unaware of the presenting clinical signs. Three respondents (handling 14 serologically confirmed cases of CA between them) observed subclinical cases and another three (6 confirmed cases in total) witnessed the sudden death of infected dogs. Signs relating to the gastrointestinal system were noted infrequently (one case reporting vomiting and one diarrhoea).

3.3 Diagnostic testing

Clinicians were asked to select the method(s) they had used to confirm a suspected case of CA from the options of: coproscopic examination (sub-options: Baermann, faecal smear), cytological diagnosis by bronchoalveolar lavage (BAL), in-house serological assay (Angio Detect™), external laboratory ELISA and other (Fig. 3). Two clinicians reported that they were unaware of the diagnostic test used for diagnosis. Over 50% of the veterinary surgeons
reported using the Angio Detect™ (IDEXX Laboratories, Wetherby, West Yorkshire, UK) to confirm their diagnosis of CA whilst none sent serum samples to an external laboratory for ELISA diagnosis. Of the 13 clinicians who used the Angio Detect™ test, three did so in conjunction with another testing modality. One respondent used a combination of BAL and PCR.

3.4. Treatment of CA

The treatment choices for confirmed cases of CA by those clinicians surveyed are presented in Fig. 4A. There were 51 responses to this question, 17 of which related to treatment given in a confirmed case with 34 relating to which drug the clinician would select, were they to encounter a case of CA. In the 17 confirmed cases, 45.5% of clinicians selected fenbendazole, which was the most popular drug used. Moxidectin and milbemycin oxime were each selected by 27.3% of responding clinicians. No other drugs were recommended as treatment for CA. In contrast, when asked which drug the clinician would use in a hypothetical case of CA, the most frequent response was moxidectin (41%), followed by fenbendazole (28%) and milbemycin oxime (23%).

There were a variety of treatment protocols for CA reported by the responding clinicians. The most consistent was monthly moxidectin, with 19/22 (86%) of respondents advising this was given to treat CA. Four respondents using milbemycin oxime to treat cases of CA advised that this should be given weekly for 4 weeks, one respondent prescribed this weekly for 2 weeks and one recommended a single dose to be sufficient for treatment. The remaining 9 respondents selecting milbemycin oxime to treat CA did not specify the frequency or duration of treatment. The dosing schedule reported by 43% of the respondents for fenbendazole was once daily. However, there was considerable discrepancy in duration of therapy. One clinician reported 3 days, one recommended 5 days, three recommended 7 days,
two recommended 10 days and two recommended 14 days. Unfortunately, 12 clinicians using fenbendazole therapy failed to provide a therapeutic frequency or duration. We asked the 19 clinicians reporting confirmed cases of CA to describe response to therapy. Interestingly, only 4 clinicians reported that they re-tested dogs after therapeutic intervention, corresponding to 6 of the 41 (15%) infected dogs. Of these six re-tested dogs, all produced negative results using the in-house serological assay (Angio Detect™).

3.5. Prevention of CA

When asked the clinicians if their practice’s standard prophylactic de-worming protocol included lungworm prevention, 52 agreed and 28 disagreed. Six respondents reported using more than one standard protocol, depending on the dog’s ‘risk of infection’. Surveyed clinicians provided information on which drugs were most frequently used as prophylaxis against CA. Fig. 4B displays the frequency of drugs being selected as prevention for CA. Those respondents that included lungworm prevention in their standard protocol were then asked which product was chosen to achieve this (more than one product could be selected). Products containing moxidectin and milbemycin oxime were the most commonly prescribed preventatives, with 71 clinicians selecting moxidectin and 56 selecting milbemycin oxime. One respondent selected fenbendazole as their prophylactic treatment of choice and two selected selamectin.

4. Discussion

This pilot study was conducted to begin to understand more about how anthelmintics are used for treatment of and prophylaxis against CA by primary care clinicians in the UK. The survey responses provided a reasonable spread across the UK and there was a reasonable response rate of 26%. Despite the reasonable response rate, the absolute number of responses was low
which represents a limitation. This is likely to reflect the short period of data collection, which was necessitated due to the timescale over which this pilot study was conducted. There was a predominance of responses from those vets with fewer years in small animal practice. It is difficult to know whether this reflects that newer graduates are more likely to respond to questionnaires perhaps because they did not anticipate compensation or monetary incentives for the time spent completing the survey or because newer and updated knowledge about diseases and treatments have become available in recent years. Also, young veterinarians, aged between 26-35, represent a third of veterinary surgeons in the UK according to the 2014 RCVS survey (Buzzeo et al., 2014); thus it is feasible to expect younger vets to represent a large proportion of the respondents. The highest correlation between the number of responses and the frequency of detection of clinical cases has been detected in Greater London, which is in agreement with others (Kirk et al., 2014). This correlation might be due to previous knowledge and experience in CA therapeutics in clinics in this geographic area, which had prolonged history of receiving cases of CA than those in the low endemic areas. However, the small sample size limits the generalization of our finding and does not allow a robust correlation between the participant responses to the questionnaire and the spatial distribution and intensity of clinical *A. vasorum* cases seen in dogs in England to be made. How this correlation may differ with age of the clinicians remains to be determined.

Under the veterinary prescribing cascade in the UK, clinicians must first use a drug that is licensed to treat the condition in question (in this case CA) in the patient’s species (in this case dogs) before moving onto alternatives in justifiable circumstances (VMD, 2015). Therefore, a clinician’s first choice of treatment for CA should theoretically contain either moxidectin or milbemycin oxime. The results obtained here suggest that the majority of clinicians are using fenbendazole to treat CA, which is off license and does not follow the cascade. The reasons behind this were not interrogated in this pilot study, but a subsequent
study is planned to understand more about what drives decision-making for treatment of CA.

It is possible that the first-line use of fenbendazole is as a result of its long-standing presence in the market place, suggesting veterinary surgeons feel more familiar with the outcome for CA cases. That said, the majority of our responses came from relatively recent graduates and not from clinicians that had been in the profession for a considerable time period. Moxidectin became available in April 2003, shortly followed by milbemycin oxime tablets, compared to fenbendazole which was first produced in January 1993 (VMD, 2017). This clearly warrants further investigation to provide important insight into understanding decision-making around this condition. This is important, as at least from this pilot study, the licensed products are less frequently used than the unlicensed one, despite the advice of the RCVS and the VMD.

In trying to seek some consensus as to the treatment strategies employed by the cohort of clinicians surveyed, it seems that selected fenbendazole is being used for differing periods of time. Periods ranged from 3 to 14 days. The literature would suggest that fenbendazole may be effective in treating CA with courses lasting between 5 and 21 days (Chapman et al., 2004; Willesen et al., 2007). There was no association between those vets using fenbendazole for a shorter period and ineffective therapy or relapse. Further research is necessary to clarify the most appropriate duration of therapy required to obtain maximum efficacy of fenbendazole.

Whilst all drugs, fenbendazole, moxidectin and milbemycin oxime (Conboy, 2004; Willesen et al., 2007), have been demonstrated to be efficacious, Moxidectin was found to be the most frequently prescribed drug in hypothetical cases of CA. The reasoning behind this is currently unclear but may be because it only requires a single application or that it doesn’t rely on having to tablet the dog. Milbemycin oxime was the least frequently prescribed drug (excluding ivermectin and selamectin, categorised into the field entitled “other”) in a hypothetical case. This could be due to a perceived low efficacy, the fact that it comes in tablet form, the need for multiple doses or another reason. Another study into the treatment
efficacy of milbemycin oxime to ascertain the minimum number of weeks treatment needed, would benefit clinicians.

The low number of treated cases that are re-tested at a later date could be influenced by a host of factors, such as the cost of such testing, perceived hassle or possible fatality. Whilst there are many reasons clinicians may avoid re-testing patients, it must be remembered that without this information it cannot be concluded as to whether the apparent improvement in clinical signs was associated with true resolution of infection. It is important to reiterate that the eradication of the infection means that there is no residual worm burden that could lead to recrudescence. Treatment of CA does not result in lasting immunity and as such treated dogs (even those that re-test negative) should continue to receive a monthly anthelmintic for preventative purposes (Böhm et al., 2014; Lebon et al., 2016; Schnyder et al., 2009).

This study found that, moxidectin and milbemycin oxime were the most frequently prescribed preventative drugs, reflecting their general popularity in primary practice. Alternatively, this may represent an attempt to include lungworm prevention in the standard de-worming protocol of a practice, without the need to use an additional drug. In this small survey, moxidectin was more frequently prescribed than milbemycin oxime. Whether this is owing to its higher efficacy or simply its existing popularity in veterinary practice is unclear. The majority of clinicians responded yes when asked if their practice’s standard de-worming protocol included lungworm prophylaxis. Whilst important that 65% of the surveyed practices are including prophylaxis for CA, this means that 35% of practices do not. This may relate to a perceived lower prevalence in their area, however it is now widely accepted that *A. vasorum* is spreading throughout the UK implying that no area can be guaranteed as lungworm-free (Kirk et al., 2014). Some clinicians may wish to adopt a risk-based approach to CA prevention in areas where the parasite is not endemic. Assessing the relative risk is one way that this could be carried out. The risk factors include: age (dogs less than 18 months old
were most likely to test positive), no CA prophylaxis for the past 3 months and possibly season (dogs were more likely to test positive in winter and spring) (Morgan et al., 2010). It must be mentioned here that the online respondents were directly asked if their standard de-worming protocol included lungworm prevention and not to provide details of this protocol. This creates the possibility that these clinicians may in fact not be using effective CA prophylaxis however given the nature of the study, the protocol could not be determined from the responses.

A secondary aim of this survey was to look at the range of clinical signs associated with CA, encountered in primary care practice. Morgan et al. (2010) found the 3 most common clinical signs to be coughing, dyspnoea and lethargy respectively. This pilot study identified coughing, haemorrhage and depression as the most frequently reported signs. These are therefore very similar in as much as the interpretation of lethargy and depression could be considered variations on the same presenting sign associated with the neurological system. An important highlight from this study is that CA may be an incidental finding and therefore particular presenting clinical signs may not be associated with the infection per se, but the result of an unconnected comorbidity. Although respiratory signs and coagulopathy are well-accepted presenting signs association with CA, vomiting/diarrhoea have been less frequently reported to be significant findings in previous studies (Chapman et al., 2004; Koch and Willesen, 2009; van Doorn et al., 2009). The single episodes of vomiting and diarrhoea occurring in this pilot study are unlikely to be directly related to CA. As expected, the preferred diagnostic approach to confirm a suspected case of CA was the Angio Detect™ test. Whilst the specific reasons for this were not surveyed, it is perhaps due to its simplicity, reliability and rapidity of results (Liu et al., 2017). Despite a specificity of 100%, it must be remembered that with a sensitivity of 84.6% (lower than the commercially available CA ELISA 94.9%) it is less suited as a screening test (Schnyder et al., 2014). Therefore given the
potential for a false negative result with Angio Detect™, it is important that additional
diagnostics are employed to effectively rule out CA when it is a major differential.

5. Conclusion

Responding clinicians indicated that they would be likely to use moxidectin to treat a
hypothetical case of CA, however contrary to this, the most commonly prescribed drug in
confirmed cases of CA was actually fenbendazole. It is therefore unclear as to what
influences UK veterinary surgeon’s choice of drug for CA, particularly when fenbendazole is
unlicensed. From this small pilot study and in line with the literature on CA regarding the
optimal duration and dose of fenbendazole, there appeared to be no consensus amongst the
vets as to the optimal duration and dose of therapy for fenbendazole. This study highlights the
need for larger and more detailed studies in to the choices that veterinary surgeons in the UK
are making in relation to CA. Once these have been completed the reasons for particular
therapeutic choices can be better understood.

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Fig. 1. A histogram displaying the frequency of responses from different brackets of years in SAP. The slight left skew in the curve indicates that more survey responses were obtained from clinicians who had spent less time working in SAP, whereas those with more years in SAP were less represented.
Fig. 2. Mapping the distribution of the survey respondents and clinical cases of CA in England. (A) Geographical distribution of responses to the survey by county. A relatively even coverage of England was achieved with Greater London providing the highest number of total responses. Shading intensity reflects the number of responses – darker reflects more responses. (B) Geographical distribution of CA cases reported by the responding clinicians. Confirmed cases were reported in Bristol (3), Buckinghamshire (1), Cumbria (1), Essex (1), Greater London (9), Greater Manchester (4), Kent (2), Merseyside (4), Nottinghamshire (3), Surrey (2) and Warwickshire (12).
Fig. 3. The method(s) used by primary care clinicians to diagnose CA. The numbers at the outer edge of the chart represent the percentage of clinicians using that diagnostic test. Coproscopic examination consisted of: Baermann test, faecal smear or unspecified, and clinicians could select more than one. The most frequently used test was Angio Detect™ while none of the surveyed clinicians used the external ELISA.
Fig. 4. (A) The percentage of clinicians selecting the drugs to treat both confirmed and hypothetical cases of CA. Although the most frequently selected drug in a hypothetical case was moxidectin, fenbendazole was the most commonly used drug in confirmed cases. Other responses include selamectin (selected by 2 clinicians) and ivermectin (selected by 1 clinician). (B) The most frequently used drugs for the prevention of CA. Moxidectin was the most commonly advised preventative drug, with milbemycin oxime second. Two clinicians recommended selamectin and only one advised fenbendazole.
Table 1

Questions completed by clinicians who took part in the online survey.

| Category      | Question                                                                                                                                 |
|---------------|-------------------------------------------------------------------------------------------------------------------------------------------|
| Demographic   | – Please provide your practice’s post code                                                                                                                                                     |
|               | – How many years have you worked in SAP?                                                                                                                                                        |
| Prophylaxis   | – Which de-worming product(s) do you recommend for the prevention of *A. vasorum* infection and at what dose/frequency?                                                                     |
|               | – To your knowledge, how many times has a dog become infected with *A. vasorum* whilst using this prevention protocol?                                                                         |
|               | – Does your practice’s standard de-worming protocol include lungworm prevention?                                                                                                                  |
| Cases         | – Have you seen a confirmed case of angiostrongylosis at your practice within the last year (if yes, please indicate how many cases)?                                                            |
|               | – Which of the following symptoms were exhibited by the patient(s)? *                                                                                                |
|               | – By what method was the diagnosis of angiostrongylosis confirmed? *                                                                                                                          |
| Treatment     | – Which de-worming product(s) have you used in the past to treat a confirmed case of angiostrongylosis and at what dose/frequency?                                                                 |
|               | – How would you rate the efficacy of this treatment?                                                                                                                                              |
|               | – If the treatment was successful, after what period of time was the patient considered to be cured of infection?                                                                           |
- How many of the treated dogs were re-tested at a later date?
- Of these re-tested dogs, how many displayed a positive result?

*For these questions, clinicians could select multiple options from lists on the screen, or add their own choice.
Table 2

The frequency of clinical signs relating to CA. Clinical signs reported by responding clinicians associated with confirmed cases of CA categorised into those presenting with single or multiple clinical signs. Coughing, haemorrhage and depression were the most commonly reported signs.

| Clinical presentation | Clinical signs (number of confirmed cases) |
|-----------------------|---------------------------------------------|
| **Individual signs**  |                                             |
| Coughing              | Coughing (2)                                |
| Dyspnoea              | Dyspnoea (1)                                |
| Haemorrhage           | Haemorrhage (1)                             |
| **Total number of cases** | = 4                                        |
| **Combined signs**    |                                             |
| Coughing, exercise intolerance, haemorrhage | Coughing, exercise intolerance, haemorrhage (3) |
| Coughing, haemorrhage, sudden death     | Coughing, haemorrhage, sudden death (3)     |
| Dyspnoea, coughing, exercise intolerance | Dyspnoea, coughing, exercise intolerance (2) |
| Dyspnoea, coughing, depression, haemorrhage, sudden death | Dyspnoea, coughing, depression, haemorrhage, sudden death (2) |
| Depression, haemorrhage           | Depression, haemorrhage (2)                 |
| Coughing, depression, haemorrhage   | Coughing, depression, haemorrhage (2)       |
| Depression, haemorrhage, vomiting, neurological deficits | Depression, haemorrhage, vomiting, neurological deficits (2) |
| Coughing, haemorrhage            | Coughing, haemorrhage (1)                   |
| Dyspnoea, coughing, depression    | Dyspnoea, coughing, depression (1)          |
| Depression, exercise intolerance, diarrhoea | Depression, exercise intolerance, diarrhoea (1) |
| Dyspnoea, haemorrhage, sudden death | Dyspnoea, haemorrhage, sudden death (1)     |
| Dyspnoea, coughing, depression, exercise intolerance | Dyspnoea, coughing, depression, exercise intolerance (1) |
| Coughing, asymptomatic           | Coughing, asymptomatic (10)                 |
| Haemorrhage, asymptomatic        | Haemorrhage, asymptomatic (2)               |
| **Total number of cases**        | = 33                                       |
| **Asymptomatic**                |                                             |
| No clinical signs               | No clinical signs (2)                       |
| **Total number of cases**       | = 2                                        |
| **Unspecified***                |                                             |
| Unknown                          | Unknown (2)                                 |
| **Total number of cases**       | = 2                                        |

*One respondent (2 confirmed cases) failed to specify which clinical signs had been displayed as CA was discovered at referral.