ORIGINAL RESEARCH

VetRecord

Cross-sectional survey of sources of information accompanying veterinary product advertisements in two professional print publications

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Abstract

Background: Veterinarians should be able to easily access scientific evidence about medical products and devices to incorporate into their clinical decision making. While the characteristics and quality of supporting information accompanying device and pharmaceutical advertisements have been studied in human medicine, little is known about this topic in veterinary medicine. The aim of this study was to characterise the supporting information provided by manufacturers of prescribed products, tests or devices in promotional material found in two commonly read UK-based veterinary publications.

Methods: Advertisements contained in issues of two veterinary periodicals published between July 2017 and July 2018 were analysed for advertisement and product characteristics and for items of accompanying information. Literature searches were conducted to assess the availability of peer-reviewed sources of information on advertised products.

Results: A minority (16%) of the 451 analysed advertisements were accompanied by references to peer-reviewed literature, despite the availability of scientific literature for many of the products advertised.

Limitation: This study sampled two professional publications over a narrow time period.

Conclusions: There may be insufficient evidence being provided to veterinary professionals via marketing features; this may limit the accessibility of scientific information for clinical decision making around advertised products.

INTRODUCTION

Evidence-based veterinary medicine (EVM) has been defined as 'the use of current best evidence in making clinical decisions combined with clinical expertise', with due consideration of patient and owner circumstances.^{1,2} Evidence-based medicine is suggested to improve human patient care and may help clinicians to better communicate clinical uncertainty to clients considering healthcare options.³ EVM requires skills in obtaining evidence and appraisal, both of which are explicitly considered minimum competencies for new graduates by the Royal College of Veterinary Surgeons.⁴ Although it is likely that veterinarians use a variety of sources of information (SOIs) to meet EVM needs, the majority of clinicians

in a 2016 study cited both academic biomedical journals and trade publications as frequently used SOIs for clinical decision making.⁵ Many of these publications contain advertisements by veterinary pharmaceutical, diagnostic test, device and nutritional/supplement manufacturers. In human medicine, medical journal advertisements are a common SOI for physicians, and it is suggested that accompanying information should be of high quality to allow for appraisal and use in clinical decision making.⁶ Manufacturers of human medicines engage in extensive marketing to prescribers using a number of approaches, one of which is journal advertising.⁷ This marketing can influence the prescribing patterns of physicians, as reviewed by Spurling et al.⁸ Indeed, one study suggested that advertising may have a greater effect on physicians'

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prescribing than exposure to scientific evidence from medical journals.⁹

The quality of supporting information accompanying advertisements directed at physicians has been examined by a number of researchers. A systematic review of pharmaceutical advertisements in medical journals (which covered the period 1950–2006) reported that a significant fraction of the advertisements lacked any references (a median of 35% across eight studies): advertisements containing references frequently cited journal articles (median of 73% of advertisements across eight studies) but non-peerreviewed sources (meeting abstracts, books, monographs) or 'data on file' were also fairly common.⁶ The quality of information accompanying medical product advertising is suggested to be better where there is direct governmental regulation of pharmaceutical marketing (as compared to regulation by stakeholders or industry).^{8,10,11} However, even in the USA, a country with relatively stringent regulation, nearly half of the advertisements in a convenience sample of biomedical journals lacked verifiable literature references.¹²

Despite the research on pharmaceutical advertising directed at physicians, there is a paucity of information regarding the quality and influence of marketing in veterinary medicine. The aim of this project was to characterise advertisements, as well as the information accompanying those advertisements, for drugs, products, tests or devices prescribed or recommended by veterinarians in two commonly read veterinary publications in the UK across a 12-month period. A secondary aim was to determine whether peer-reviewed or regulatory efficacy (or diagnostic accuracy) information was publicly available for these products at the time of advertising.

MATERIALS AND METHODS

Sampling and data collection

Features within advertisements from all issues of a UKbased peer-reviewed veterinary biomedical journal (Veterinary Record) and a trade periodical (Veterinary Times) appearing between July 2017 and July 2018 were examined by two authors (N.B. and S.F.). Both publications are pan species and aimed at a British veterinary professional audience, and both were published weekly at the time of data collection. Advertisements for products/services that could be applied to clinical decision making for diagnosis or treatment or that could be passed on to a client (e.g., deworming preparations) were eligible for inclusion. Advertisements for products or services not directly applicable to clinical decision making for individual patients and for which empirical evidence would not be sought or normally required were excluded from analysis (e.g., animal insurance and identification, professional development, external consultant, business or career services).

The process of coding data from the advertisements (see Supporting Information 1) was piloted on issues published within a single month (July 2017) by two authors working independently (S.F. and N.B.). Discrepancies were discussed and resolved by the two authors. The wider research team (S.F., N.B., L.M. and M.B.) discussed and resolved any remaining discrepancies, and a final extraction and coding system was developed as a result. In the main study, data were independently entered into a Microsoft Excel (2010 Microsoft Corporation) spreadsheet that had been created after the pilot study by two authors (S.F. and N.B.). Any coding disagreements were resolved by discussion with two other reviewers (M.B. and L.M.). The extracted and categorised data included (but were not limited to) publication and issue, advertisement type and page spread, product name, business entity, target species, method of administration, action of the product and reference information provided by the advertiser (see Supporting Information 1 for details of the categorisation systems used). In cases where an advertisement generally promoted a sponsor's range of therapeutics for species and/or indication, this was categorised as a named product line rather than a named product. The references were considered to be peer reviewed if the cited article was from a publication listed on Ulrich's Web.¹³ Peer-reviewed references (PRRs) were not assessed on whether they supported any diagnostic or therapeutic claims made in advertisements.

Data analysis

The data were cleaned and analysed by C.W. using Stata IC 16.1 (CW-StataCorp). Reference and product categories were further collapsed for some portions of the analysis (see 'code' categories in Supporting Information 1). The data were primarily analysed descriptively (e.g., frequency counts, percentages, central tendencies and percentiles). Univariate analysis was carried out using chi-squared or Fisher's exact tests, depending on the expected cell count. Probability values are presented when statistically significant at a level of $\alpha = 0.05$ when corrected for multiple comparisons using the Bonferroni correction.¹⁴

Literature and regulatory approval document searches

If extracted information adequately captured the specific product trade name or diagnostic test, species and indication to allow for specific identification of the active pharmaceutical ingredient/formulation, diagnostic assay, manufacturer and clinical indication(s), the product names were searched. In an attempt to replicate the process that practitioners might go through to find published scientific information, PubMed was searched using keywords and medical subject heading identifiers for product, assay and/or active pharmaceutical ingredient and species. Screening for randomised controlled trials and clinical trials was performed using PubMed search filters. For diagnostic tests, a publication was considered a relevant diagnostic accuracy study if performed for the claimed indication and if results included sensitivity and specificity data or data relevant to those parameters in categorising diseased versus non-diseased animals. If no relevant publications were identified using PubMed, subsequent searches of CAB Abstracts and Google Scholar were similarly performed. The retrieved publications were examined by one author with epidemiological expertise (C.W.) to verify that they conformed to a controlled trial or diagnostic accuracy study design and reported data that could be used to evaluate clinical effectiveness (or diagnostic accuracy claims for diagnostic testing). The concordance of published results with advertisers' claims was not assessed.

Product regulatory status within the UK was verified by a single author (C.W.) by searching the Veterinary Medicines Directorate (VMD) and European Medicines Agency (EMA) veterinary medicine databases. Advertised products that were distributed by the same manufacturer in the USA using an identical formulation to that marketed in the UK were identified using the US Food and Drug Administration (FDA) and UK VMD online databases. Freedom of information (FOI) new animal drug application (NADA) summaries for each of these identified drugs were downloaded from the FDA Animal Drugs website using NADA numbers. These were examined for the presence of detailed safety and effectiveness data submitted for drug approval. The search was limited to application summaries freely available online.

RESULTS

One hundred and five issues of the two publications published between July 2017 and July 2018 were assessed: 50 issues of the biomedical journal and 55 issues of the trade publication. In these issues, 451 advertisements met the inclusion criteria for analysis. The majority of these (428/451; 95%) were traditional advertisements; 22 were advertorials (advertisements imitating editorial content as described)¹⁵; one advertisement was inadvertently not coded as either but was subsequently identified from other characteristics as a traditional advertisement for analysis purposes.

From the 451 advertisements, more than 100 identifiable named products or product lines were identified and categorised according to 18 different clinical indications (Table 1 and Supporting Information 2). A handful of advertised marketed product lines, rather than individual products, are usually aimed at one species and indication (e.g., cattle anti-infectives two different product lines, cattle vaccines—two different product lines, cattle reproduction—one product line, small animal therapeutic diets—five different product lines, small animal intoxication—one product line). The majority (343/451, 76%) of advertisements targeted small companion animal species (primarily dogs and cats), while a smaller proportion (72/451, 16%) were aimed at production animals (primarily cattle); the small number of remaining advertisements targeted equine practice or multiple species. Just over one-third (164/451, 36.4%) of the advertisements were for products intended to prevent or treat endoand ectoparasites. Nutraceutical/probiotic (foods or supplements with a putative health benefit) was the second most common product category (36/451, 8%). Although cardiovascular products were advertised nearly as often as nutraceuticals (35/451, 7.7%), almost all of these advertisements marketed a single approved veterinary drug (34/35, 97%). There were no significant differences between product categories advertised in the two publications, with the exception of advertisements for nutraceuticals/probiotics, which appeared only in the trade magazine (chi-squared p <0.001). Advertisements for veterinary diets were found solely in the trade publication, but this difference did not reach statistical significance. For a number of therapeutic product classes (emetic, endocrine and antacid), there were no advertisements that contained PRRs.

The median number of advertisements per product was 2 (interquartile range 1-4), but 10 products had 10 or more advertisements and accounted for 43% (195/451) of all advertisements, with a single cardiovascular product found in 34 advertisements. The majority of the products for which there were 10 or more advertisements were for antiparasitics (6/10,60%), of which three products had 20 or more advertisements. Antiparasitics were also the most frequent product found in advertorials (11/22, 50%), followed by cardiovascular drugs (7/22, 32%). Most advertorials were found in the trade magazine (18/22, 82%). Most of the advertisements were at least full-page or cover presentations (364/451; 81%). A wide range of manufacturers (n = 35) were identified; however, marketing from just eight of these companies comprised 71% of all advertisements analysed and five firms accounted for more than half of all advertisements (Figure 1).

Overall, only a small proportion of advertisements (71/451; 16%) were accompanied by a PRR (Table 2 and Figure 2). Advertisements with a PRR were significantly (chi-squared p = 0.008) more prevalent in the academic journal (28/120; 23%) than in the trade periodical (43/331; 13%). There was no significant difference in the prevalence of advertorials between the two publications (4/120 academic; 18/331 trade, chi-squared p = 0.359), but advertorials were significantly more likely to contain a PRR (17/22 advertorials vs. 54/429 traditional advertisements, chi-squared p < 0.001). Two trade-named drugs accounted for the majority of advertisements with PRR (cardiac drug 30/71; antiemetic drug 10/71). The remaining 30 advertisements with PRR represented 15 additional products. There were no significant associations between targeted species or method of administration and the presence of a PRR. In general, there was no

manufacturers, publication type	and target species				- J ((- - - - -		
	Total number of	Number of products or product lines in	Number of companies	Biomedical	Trade veterinary	Small comnanion	Food/fibre		Mixed
Product category	advertisements	category	identified	journal	magazine	animal	animal	Equine	species
Antiparasitic	164	18	6	55	109	146	16	2	0
Nutraceutical/ probiotic	36	14	9	0	36	36	0	0	0
Cardiovascular	35	2	1	12	23	35	0	0	0
Dermatologic/ steroid	28	13	9	2	21	28	0	0	0
Vaccine	25	6	4	4	21	0	25	0	0
NSAID	22	6	6	8	14	10	1	1	10
Antimicrobial	19	≥4	2	8	11	0	19	0	0
Sedative/ anaesthetic	18	9	4	1	17	16	0	7	0
Emetic	17	1	1	4	13	17	0	0	0
Diagnostic test	16	4	3	33	13	10	0	0	9
Antiemetic	16	2	2	7	6	16	0	0	0
Diet	15	7	5	0	15	15	0	0	0
Reproduction/ lactation	10	8	4	8	2	0	10	0	0
Wound closure/ coaptation	6	ę	Э	1	œ	ŝ	0	0	9
Endocrine	9	3	2	0	9	6	0	0	0
Antacid	4	2	2	0	4	0	0	4	0
Other (ophthalmic/oral care/euthanasia)	9	4	ς	0	9	IJ	0	0	1
Unclassifiable	5	2	2	2	33	0	1	0	4
Total	451	108		120	331	343	72	6	27

TABLE 1 Advertisements (by product category) extracted from two British veterinary publications between July 2017 and July 2018, displayed by number of marketed products or product lines and

FIGURE 1 Proportion of advertisements attributable to individual commercial entities found in a study extracting data from advertisements in two veterinary periodicals



association between company sponsor and the presence of PRR, with the exception of the cardiac and antiemetic drug advertisements.

Although many of the advertisements were for products regulated under EMA or VMD authorisation schemes, relatively few referenced authorisation or compendium information sources (70/451; 16%). A disproportionate number of these (53/70; 76%) were for antiparasitic products. Similarly, the majority of advertisements referencing grey literature (i.e., conference proceedings or non-peer-reviewed independent studies) or expert opinion sources were also for antiparasitic products. Advertisements infrequently referenced company-held data (32/451; 7%), and of those, 22 did not cite other supporting information in the form of peer-reviewed articles, grey literature or authorisation documents.

Supporting information (aside from company contact information) was absent in more than half of advertisements (227/451, 50.3%). Advertisements for nutraceuticals/probiotics (29/36, 80%) and diagnostic tests (15/16, 94%) lacked supporting information as compared to every other product class (p < 0.002). In the remaining 224 of 451 advertisements, which provided any reference other than company contact details, 494 items of accompanying information were identified. A minority of these were references to individual peer-reviewed articles (111/494, 22%). Grev literature citations were the most common item found (184/494; 37%). Authorisation and compendium resources comprised a small number of references (75/494, 15%). Expert opinion (61/494, 12%), company-held data (32/494, 6%), market research studies (25/494, 5%) and company promotional materials (webinars and case studies; 6/494, 1%) comprised the remainder of individual pieces of information.

Although most advertisements did not contain references to peer-reviewed SOI, published controlled trials or diagnostic accuracy studies were located and assessed for most products intended for therapy or diagnosis that were identified in the advertisements (Table 3 and Supporting Information 2). Additionally, detailed safety and efficacy trial data for a number of products in FDA NADAs were identified (Table 3 and Supporting Information 2). Finally, some of the published clinical trials identified during searches could be identified as trials performed for regulatory approval (FDA or EMA) by article disclosures or by cross-referencing article information to FDA approval documents or EMA public assessment reports (Table 3 and Supporting Information 2). Additionally, although this study was not aimed at appraising the quality of advertisement references, we noticed that not all PRRs found in advertisements were relevant to product claims and some advertisements that did contain PRRs omitted available articles directly relevant to the appraisal of product claims (e.g., two antiemetic products containing active pharmaceutical ingredient).

DISCUSSION

This study found that, in a sample of two British veterinary publications, a minority of advertisements for products used in veterinary clinical practice were accompanied by references to publications in peerreviewed biomedical literature. There may be a number of explanations for this finding, but regardless, it could have an impact on veterinary professionals' ability to be able to easily integrate research-based evidence into clinical practice. The frequency of advertisements accompanied by a PRR was substantially lower than that reported for physician-directed pharmaceutical advertising and represented a small fraction of the total advertised products in this sample. However, advertisements for a select handful of product categories frequently contained PRR; this is likely because of the frequency of advertisements for two specific products. Additionally, the lack of association between the presence of PRR and features such as targeted species or method of administration could be due to small sample sizes (generating type II statistical errors). Grey literature citations were the most common type of reference found in advertisements, particularly in advertisements for antiparasitics, followed by references to the summary of product characteristics (SPC) or compendium information.

5 of 10

Matrix becaution metalization metalizationMatrix metalization metalizationMatrix metalization metalizationMatrix metalization metalizationMatrix metalization <th></th> <th></th> <th>Number of advertisements</th> <th>Percentage of advertisements</th> <th>Number of advertisements with</th> <th>Number of</th> <th>Number of</th> <th>Number of advertise-</th> <th>Number of</th> <th>Number of</th>			Number of advertisements	Percentage of advertisements	Number of advertisements with	Number of	Number of	Number of advertise-	Number of	Number of
	Product category	Number of advertisements	wuu peer-reviewed published reference	wuu peer-reviewed published reference	no ancurat y information (including company contact details)	auver usernents providing only company contact information	auveruse- ments citing grey literature SOI	SPC or compendium SOI	auver use- ments citing expert opinion SOI	auveruse- ments citing company-held data
36 0 0 2 27 0 M 0 4 Autrecuted/prototic 3 3 3 3 3 3 3 4	Antiparasitic	164	6	5.5	66	7	55	53	23	3
Nutractifical/problotic Nutractifical/problotic Nutractifical/problotic Nutractifical/problotic Nutractifical/problotic 3 1 86 4 0 2 1 2 1 Demusiopic/steroid 3 0 2 4 4 5 8 7 2 7 Vactine 2 3 13.6 11 3 4 2 3 7 2 7 7 NSND 2 3 13.6 11 3 4 2 1 0 7 2 7 7 7 7 7 7 7 7 0 0 1 0 1 0 1 <		36	0	0	2	27	0	NA	0	4
Cardioaccular 35 31 886 4 0 2 1 2 1 Dematologic/steroid 28 6 21.4 4 5 2 1 2 1 2 1 Dematologic/steroid 28 1 3 1 3 2 1 2 1 2 1 2 1 Next 2 3 136 11 3 2 1 2 1 2 1 3 Next 1 53 17 0 2 1 1 2 1 2 1 2 1 3 Next 1 53 1 0 2 1 1 1 1 2 1 <th1< th=""> 1 1</th1<>	Nutraceutical/probioti	c								
Dermatologic/steric 28 6 21.4 4 5 8 7 2 7 2 7 7 2 7 7 2 7 7 2 7 7 7 7 7 7 7 7 7 7 7 2 7 2 7 7 2 7 7 2 7 7 2 7 7 7 2 7 7 7 7 7 7 7 7 7 7 7 7 1	Cardiovascular	35	31	88.6	4	0	2	1	2	1
Vactile 25 2 8 12 8 12 1 1 1 0 NSMD 22 3 13.6 11 3 4 2 3 0 NSMD 22 3 13.6 11 5.3 17 0 2 3 0 Number/old 19 1 5.3 17 0 2 1 1 0 0 Sedative/ansetter 18 5 27.8 6 0 0 1 0 1 0 1 0 1 0 1 0 1 0 1 0 1 0 1 0 1 0 1 0 1 0 1 0 1 0 1 1 0 1 1 1 1 1 1 1 0 1 1 1 1 1 1 1 1 1 1 1 <td>Dermatologic/steroid</td> <td>28</td> <td>6</td> <td>21.4</td> <td>4</td> <td>5</td> <td>8</td> <td>7</td> <td>2</td> <td>7</td>	Dermatologic/steroid	28	6	21.4	4	5	8	7	2	7
NSAID 22 3 13.6 11 3 4 2 3 0 Antimicrobial 19 1 5.3 17 0 2 1 0 1 0 Sedative/anaschetic 18 5 27.8 6 0 1 0 0 0 Sedative/anaschetic 17 0 0 0 1 1 0 1 0 0 Sedative/anaschetic 16 0 0 0 0 1 0 1 0 1 0 1 1 0 1	Vaccine	25	2	8	12	8	2	1	1	0
	NSAID	22	3	13.6	11	3	4	2	3	0
Sedative/manechetic 18 5 27.8 6 6 1 0 1 0 0 1 Emetic 17 0 0 0 15 3 0 12 12 Diagnosit test 16 10 62.5 0 0 1 NA 0 12 Antiemetic 15 2 13.3 7 3 2 NA 1 2 0 1 Antiemetic 16 2 13.3 7 3 2 NA 1 2 0 1 2 Antiemetic 16 2 13.3 7 3 2 NA 1 2 1 2 1 2 1 2 1 2 1 2 1 1 2 1 1 2 1 1 2 1 1 2 1 1 1 1 1 1 1 1	Antimicrobial	19	1	5.3	17	0	2	0	1	0
	Sedative/anaesthetic	18	5	27.8	6	9	0	1	0	0
	Emetic	17	0	0	0	0	5	n	0	12
	Diagnostic test	16	0	0	0	15	1	NA	0	0
	Antiemetic	16	10	62.5	0	0	0	0	2	0
Reproduction/ 10 2 20 7 1 2 0 2 0 2 0 1 lactation 9 0 0 1 5 0 NA 0 3 Wound 9 0 0 1 5 0 NA 0 3 Wound 6 0 0 1 0 1 0 3 Endocrine 6 0 0 1 0 1 0 0 0 Antacid 4 0 0 1 2 0 1 0 0 Other 6 0 0 3 2 0 1 0 <	Diet	15	2	13.3	7	3	2	NA	1	2
Wound 9 0 0 NA 0 3 closure/coaptation 6 0 1 0 4 0 3 Endocrine 6 0 1 0 1 0 4 0 Antacid 4 0 0 1 0 4 0 0 Antacid 4 0 0 1 2 0 1 0 Other 6 0 0 3 2 0 1 0 Other 6 0 0 3 2 0 1 0 Cophthalmic/oral 1 1 2 0 1 0 0 Curve/euthansia) 1 1 1 2 0 1 0 0 Inclassifiable 5 0 0 1 1 1 1 1 1 1 1 1 1 1 1	Reproduction/ lactation	10	2	20	2	1	2	0	2	0
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Wound closure/coaptation	6	0	0	1	51	0	NA	0	ε
Antacid 4 0 1 0 1 2 0 0 0 Other 6 0 0 3 2 0 1 0 Other 6 0 0 3 2 0 1 0 Ophthalmic/oral care/euthansia) 0 0 1 0 </td <td>Endocrine</td> <td>6</td> <td>0</td> <td>0</td> <td>1</td> <td>0</td> <td>1</td> <td>0</td> <td>4</td> <td>0</td>	Endocrine	6	0	0	1	0	1	0	4	0
Other 6 0 0 3 2 0 1 0 (phthalmic/oral care/euthansia) (phthalmic/oral 0 1 0 0 1 0 </td <td>Antacid</td> <td>4</td> <td>0</td> <td>0</td> <td>1</td> <td>0</td> <td>1</td> <td>2</td> <td>0</td> <td>0</td>	Antacid	4	0	0	1	0	1	2	0	0
Unclassifiable 5 0 0 2 3 0 0 0 0 0 10 Total 451 71 141 86 87 70 42 32	Other (ophthalmic/oral care/euthanasia)	9	0	0	0	ç	2	0	1	0
Total 451 71 141 86 87 70 42 32	Unclassifiable	5	0	0	2	3	0	0	0	0
	Total	451	71		141	86	87	70	42	32



FIGURE 2 Information accompanying advertisements by product category

Finally, half of all included advertisements contained no supporting information or only provided company contact details. Further investigations to determine why limited information is provided are warranted.

One possible interpretation for the low frequency of PRR-containing advertisements found in this sample is the relative scarcity of veterinary clinical trials focused on efficacy. However, peer-reviewed controlled trials or diagnostic accuracy studies were able to be identified elsewhere for the majority of products assessed in this study. No advertisements from several therapeutic product classes (emetic, endocrine and antacid) contained PRR despite the fact that suitable available references were identified at the time for all therapeutics in these categories. Similarly, no advertisements for diagnostic tests had PRR and more frequently lacked any accompanying information, despite available published diagnostic accuracy studies. Finally, antiparasiticides were the most frequently advertised product and very rarely contained PRRs; however, peer-reviewed articles reporting safety and efficacy trials for all products in this class were identified.

Interestingly, although many of the advertised products captured in the sample were regulated in the UK by the VMD or the EMA, few advertisements referenced authorisation or compendium documents representing or summarising SPC or public assessment reports (EPAR or UKPAR). Information accompanying veterinary pharmaceutical advertisements in the UK is not prescriptively regulated by the UK Vet-

erinary Medicines Directory.¹⁶ This contrasts with the situation in the USA. All prescription medication advertisements in the USA require 'adequate provision' of prescribing information,¹⁷ which must include FDA-approved indication, quantitative effectiveness and adverse effects data, as well as contraindications. In actual practice, print advertisements directed at veterinarians in the USA contain a reproduction or summary of the FDA-approved package insert, which contains this information. Even without PRR, package insert information is usually sufficiently detailed and comprehensive to allow for an initial assessment of quantified risk/benefit information by practitioners (see Supporting Information 3 for exemplar FDAapproved drug package insert information). Detailed trial data on effectiveness and adverse events that allow calculation of number needed to treat and number needed to harm (as well as confidence intervals) can typically be obtained from the package insert. If there is insufficient quantitative information on the package insert, the full summary of the documents submitted for FDA approval can usually be freely obtained online using the NADA number. In contrast to the information available from FDA-approved package inserts, efficacy and safety trial data are not generally available from the SPC in the UK. Adverse reaction data are presented but consist of categorical, as opposed to numeric, outcome data (see Supporting Information 3 for exemplar SPC, package leaflet or public assessment report information).¹⁸ Because clinical trials performed for regulatory approval may **TABLE 3** Availability of published controlled clinical trial, diagnostic accuracy study or US Food and Drug Administration (FDA) approval application details for advertised product categories at the time advertisements were published in two veterinary periodicals between July 2017 and July 2018

Product category	Number of searchable named products	Number of products for which at least one advertisement contained peer-reviewed published reference	Number of products for which peer-reviewed controlled trials or diagnostic accuracy studies available at the time the advertisement could be located	Number of products for which FDA FOIA new animal drug application summary available online
Antiparasitic	18	3	18/18	8 ^a
Nutraceutical/probiotic	14	0	0/14	NA
Cardiovascular	2	2	2/2	2
Dermatologic/steroid	13	2	8/13	3 ^b
Vaccine	9	2	7/9	NA ^c
NSAID	6	3	6/6	2 ^d
Antimicrobial	4	1	ND	ND ^e
Sedative/anaesthetic	6	1	6/6	3
Emetic	1	0	1/1	NA ^f
Diagnostic test	4	0	3/4	NA ^g
Antiemetic	2	1	2/2	1^{h}
Therapeutic diet	7	1	ND	NA ⁱ
Reproduction/lactation	8	1	8/8	4 ^j
Wound closure/coaptation	3	0	ND	NA ^k
Endocrine	3	0	2/3	1^1
Antacid	2	0	2/2	1^{m}
Other (ophthalmic/oral care/euthanasia)	4	0	2/4	NA ⁿ
Unclassifiable	0	0	ND	ND
Total	106	17	67/92	25

Abbreviation: FOIA, Freedom of Information Act drug approval submission documents.

^aEight products consisted exclusively of topical pesticides that are not regulated by the FDA. Of the 10 remaining products, all had FDA FOIA information available for similar active pharmaceutical ingredient (API) but only eight were products distributed by the same manufacturer in both the USA and the UK.

^bOne dermatologic product was a biologic that is not regulated by the FDA; five others were topical products not regulated by the FDA. Of the seven remaining products, three are not labelled veterinary products in the USA and one is available only through a manufacturer that it not distributed in the USA; for the latter, FDA FOIA approval documents are available for a similar product made by a different manufacturer.

^cVeterinary biologics are not regulated by the FDA and documents submitted for approval are considered proprietary by the regulating agency (United States Department of Agriculture (USDA)).

^dFDA approval documents were available for three products sold in both countries by the same manufacturer; an additional advertised product contains an identical API and indication as one of these FDA-approved products. Of the two remaining products, one is not marketed in the USA and the other (phenylbutazone) is available as a large number of generic forms approved under abbreviated new animal drug application rules.

^eDue to proprietary product-line naming and lack of specific product details, unable to match products to the FDA Animal Drug database.

^fNo similar approved product in the USA.

^gVeterinary diagnostic testing is not regulated in the USA.

^hBoth products contained the same API; FDA FOIA documents were available for the proprietary brand name version.

ⁱVeterinary diets are not considered prescription drugs by the FDA.

ⁱFDA documents were available for the four products labelled and distributed in both countries by the same manufacturers. A fifth product has available approval documents submitted to the FDA by a manufacturer different from that in the UK. Two products are not marketed in the USA and a third is considered a feed additive.

^kNot regulated for veterinary patients in the USA.

¹Only one of the two pharmaceuticals in this category is a branded and approved animal drug in the USA. The other is widely available as a generic human drug used off-label. The third product was an unregulated diabetes monitoring app.

^mBoth products contained the same API; FDA FOIA documents were available for the proprietary brand name version.

ⁿThree products in this category are not regulated by the FDA; the fourth is a euthanasia solution available as a generic under abbreviated new animal drug applications in the USA.

also be published in the peer-reviewed literature, veterinarians in the UK may still be able to access more detailed information about specific product claims for appraisal; however, we found that few advertisements signposted available articles and the search strategies we used to find peer-reviewed evidence for safety and efficacy required more time than may be available to busy clinicians. Easily accessible information is likely to be key for enhancing evidence integration into practice. If PRR on safety and efficacy prove difficult to access, clinicians can look to other options; for example, subscribing to information services offered by organisations such as Veterinary Prescriber (www. veterinaryprescriber.org/).

Nutraceuticals and probiotics were the second most common type of product advertised. This product

class is not regulated by VMD or FDA, and perhaps as a reflection of this, there were no peer-reviewed reports cited in any of the advertisements. A clinician interested in further evaluating claims for one of these products would need to perform their own literature searches to find relevant evidence. These searches were not attempted due to the lack of specific keywords and because some advertisements marketed product lines for multiple indications rather than a single product. Given the burgeoning market for these supplements,¹⁹ it is suspected that clinicians are often asked for professional advice on these foods and supplements without access to adequate resources to find and evaluate any available evidence. Similarly, veterinary diagnostic tests are unregulated (in contrast to human diagnostics) Given that diagnostic test accuracy is critical to clinical decision making, the lack of PRR in these advertisements is concerning, particularly when published literature was available for three of the four diagnostic tests identified in the present study.^{20,21}

We consider the results of this exploratory study as motivating a number of areas for further investigation. There is a need to understand the effects of advertising on veterinarians' prescribing habits as well as the influence of different regulatory frameworks on the characteristics of advertising in veterinary professional publications. Moreover, veterinarians obtain information on therapeutic and diagnostic products from a variety of sources, some of which may involve other interactions with industry (including promotions using professional social networks and continuing professional education).²² The reason for the limited information provided with advertisements in these publications is likely to be multifactorial and vary geographically. It could include factors such as pharmaceutical advertising rules (regulatory and voluntary), advertising policies of journals and stakeholder appetite for scientific references. There is a need to understand the effects of advertising and other promotional activities on veterinarians' prescribing habits as well as the influence of different regulatory frameworks on the characteristics of advertising in veterinary professional publications. Do veterinary professionals rely primarily on manufacturers for information on diagnostic and therapeutic interventions or do they seek additional SOI? Is additional information seeking by clinicians more frequent or efficient if additional data are provided in the form of published therapeutic trials or diagnostic accuracy data, whether from regulatory documents or peer-reviewed publications? What role do different regulatory structures play in the quality and frequency of citations contained in veterinarian-directed advertising?

LIMITATIONS

The data set accrued from this study represented a limited number of advertisements for a limited num-

ber of products in a single regulatory jurisdiction over a limited time frame, collected 6 years ago. This limits statistical power for being able to analyse associations and may not be generalisable to other regions or time periods. More recent advertisements may contain more information. Additionally, the impact of regulatory changes in response to the UK formally leaving the European Union in January 2020 could have an impact on current advertising practices. Advertisements were also not assessed for alignment of product claims with either citations within the advertisements or with available peer-reviewed scientific articles or regulatory documents identified by our independent searches. Other variables not assessed but potentially of interest to investigate could be whether the advertisements were printed in colour or the location of the references (e.g., within the body or at the end of the advertisement). Finally, only print advertising was examined. Online sources of advertising or product promotion, which is a growing portion of manufacturer promotional efforts, were not included in this assessment. However, the authors hope that the information reported here helps to start conversations in the veterinary professions about the importance of companies providing, or at the very least signposting to, good-quality research-based evidence relating to any products that are advertised.

CONCLUSION

Our findings emphasise a distinct lack of peerreviewed supporting information for veterinary product advertisements in both a trade periodical and a biomedical journal. This is an important issue for EVM because it may limit efficient access to high-quality information for veterinary professionals making decisions in conjunction with clients about therapies or diagnoses for clinical cases.

AUTHOR CONTRIBUTIONS

Marnie Brennan, Rachel Dean and Lisa Morrow conceived this study. Rachel Dean contributed to the data collection. Natasha Basham, Simran Floyd, Marnie Brennan and Lisa Morrow contributed to the data collection and initial analysis. Constance White was responsible for the data cleaning, final analysis and writing. All the authors reviewed the manuscript prior to submission.

A C K N O W L E D G E M E N T S

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CONFLICT OF INTEREST STATEMENT The authors declare they have no conflicts of interest.

DATA AVAILABILITY STATEMENT

Additional data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

This study received ethical approval from the Committee for Animal Research and Ethics at the School of Veterinary Medicine and Science at the University of Nottingham (approval number 2975 191015 UG) for the advertisement assessments.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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