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Attitudes of small animal practitioners toward participation in veterinary clinical trials

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Abstract

OBJECTIVE—To determine attitudes of small animal practitioners toward veterinary clinical trials and variables influencing their likelihood of participating in such trials.

DESIGN—Cross-sectional survey.

SAMPLE—Small animal practitioners with membership in 1 of 2 online veterinary communities (n = 163 and 652).

PROCEDURES—An online survey was developed for each of 2 veterinary communities, and invitations to participate were sent via email. Each survey included questions designed to collect information on the respondents' willingness to enroll their patients in clinical trials and to recommend participation to clients for their pets.

RESULTS—More than 80% of respondents to each survey indicated that they spend no time in clinical research. A high proportion of respondents were likely or extremely likely to recommend clinical trial participation to clients for their pets when those trials involved treatments licensed in other countries, novel treatments, respected investigators, or sponsoring by academic institutions, among other reasons. Reasons for not recommending participation included distance, time restrictions, and lack of awareness of ongoing clinical trials; 28% of respondents indicated that they did not usually learn about such clinical trials. Most respondents (79% to 92%) rated their recommendation of a trial as important to their client's willingness to participate.

CONCLUSIONS AND CLINICAL RELEVANCE—Participation in veterinary clinical trials by small animal practitioners and their clients and patients appeared low. Efforts should be increased

to raise practitioner awareness of clinical trials for which patients might qualify. Specific elements of trial design were identified that could be modified to increase participation.

Clinical trials are important to the development and testing of treatments in human medicine. Through such clinical trials, safety and efficacy of various medical or surgical interventions are determined in the applicable target population. In human medicine, recruitment for clinical trials is often challenging, with low enrollment rates and often disproportionate representation of certain groups, such as people with particular demographic characteristics. This difficulty results in a prolonged duration and high financial cost for trials, while also limiting the generalizability of any findings.¹ Barriers to participation in human clinical trials commonly include a lack of awareness of trials for which subjects are being recruited, concerns about randomization to a placebo group, and logistical issues, such as transportation to clinical trial centers.²⁻⁴

In veterinary medicine, clinical trials are equally important, and safety and efficacy data for a particular intervention for a particular species cannot be presumed to apply to another species. The existence of a profound caregiver placebo effect⁵⁻⁸ further highlights the need for recruitment and enrollment strategies that result in clinical trials with representative populations and sufficient statistical power to detect any treatment effects that truly exist. For an animal to participate, the owner must participate to some extent as well, emphasizing the importance of the veterinarian-client-patient relationship. A similar dynamic exists in human clinical trials involving individuals unable to provide informed consent, particularly pediatric patients.

Much has been written about issues regarding recruitment and consent processes in human clinical trials that might extend to veterinary medicine.^{9,10} Personal relationships with physicians and trust in their recommendations can influence people's decisions to participate in a clinical trial.^{9,10} The reluctance of physicians to enroll patients has been called one of the most serious obstacles to trial success, given that patients will rarely participate unless actively encouraged by their physician.^{11,12} Pediatricians' perceptions of the burden that trial participation might have on their patients influence the likelihood of caregivers refusing participation, suggesting that subtleties in the language with which a potential trial is discussed with caregivers is influential in their decision to enroll.¹³

In a survey of cat owners,¹⁴ several variables were identified to influence the likelihood of owners participating in a clinical trial with their cat, including trust in the organization performing the trial, whether the cat had a disease that would benefit from the trial, and the recommendation of their veterinarian to participate. A large proportion (80%) of cat owners said that recommendation from their veterinarian would be important (24%) or extremely important (56%) to their participation.

Although several studies^{4,13,15-17} have been performed to identify variables that influence physician enrollment of patients in clinical trials and recommendation of trial participation to their patients, this type of research has not yet been thoroughly performed in veterinary medicine. The objectives of the study reported here were to survey small animal practitioners to ascertain their attitudes toward enrollment of their patients in veterinary

clinical trials, particularly the influence of experimental and other trial variables on their likelihood of recommending clinical trial participation to clients for their pets.

Materials and Methods

Survey development

Questions for the survey were generated de novo on the basis of expert input and review of the human medical literature regarding physician views on clinical research and clinical trial participation. Expert input was solicited in 2 phases: first by means of a focus group with General Practice Service faculty and faculty members engaged in clinical trials at North Carolina State University, and then via feedback from pilot testing and a group of survey evaluators at VIN.

An initial 83-item version of the survey was sent to 40 small animal veterinarians known to authors for pilot testing, with 35 veterinarians completing the survey. Mean completion time for the pilot survey was 26.1 minutes, with 10 respondents indicating that the duration was satisfactory. The remaining respondents indicated that the survey was long but feasible ($n = 22$), a bit too long (2), or much too long (1). On the basis of their responses, changes were made to delete 2 items from the survey and to clarify or improve items as suggested in free-text responses.

The final survey consisted of 81 items grouped into 8 sections. The first section contained 8 items for collection of demographic information, and the second section included questions about prior clinical trial participation. For questions in the next 5 sections, respondents were asked to rate the importance or influence of certain variables in their willingness to recommend participation in a veterinary clinical trial to clients for their pets or their opinion on the importance of those variables to those clients. Items in the final section were designed to gauge the respondent's general feelings about clinical trials and ideas about the best ways to advertise a clinical trial to attract participation and best incentives to encourage owner and animal participation.

On August 19, 2014, an email invitation to participate in the 81-item survey was sent to 1,657 veterinarians and veterinary health professionals whose contact information was included in a database maintained by the professional organization VP. Veterinary Professionals Ltd is a UK-based company that provides information and advice to pet owners and veterinary professionals through its website, books, and continuing professional development courses. Veterinary professionals who have accessed any of these resources are registered in the database.

The invitation included a link to an online survey,^a which allowed for anonymous responses (Supplemental Appendix S1, available at: <http://avmajournals.avma.org/doi/suppl/10.2460/javma.250.1.86>). The survey link remained active for 2 months, and follow-up invitations were emailed to database members twice after the initial invitation (once 2 weeks afterward and again 5 weeks afterward).

^aFormsite, Vroman Systems Inc, Downers Grove, Ill.

During the VP survey, the instrument was adapted for distribution to members of an online veterinary community (VIN), with suggestions from the VIN survey representative (MR) to increase the response rate and geographic distribution of respondents. To increase participation, the survey was shortened, while retaining the original language as much as possible (Supplemental Appendix S2, available at: <http://avmajournals.avma.org/doi/suppl/10.2460/javma.250.1.86>). This survey was created to be more dynamic than its predecessor so that a participant's response to a particular item could direct the presentation of relevant subsequent items. All respondents were asked whether they had looked into a clinical trial for which recruitment was underway. If the response was no, then respondents were asked for the reason. If the response was yes, then respondents were asked whether they had ever recommended clinical trial participation to clients for their pets. If the response to that question was no, then respondents were asked for the reason. If the response was yes, then respondents were asked whether they had ever successfully enrolled clients and their pets and about their general perceptions of clinical trials and the impact of certain variables on their willingness to promote participation. All respondents, regardless of whether they had looked into a clinical trial, were asked about the importance of certain variables on their willingness to promote participation and their perception of the importance of certain variables to their clients.

On April 9, 2015, an invitation to participate in the VIN survey was emailed to 30,088 VIN members (excluding students, academicians, and veterinarians in industry) by use of a list of contact information for current members provided by VIN staff, and a reminder invitation was sent 2 weeks later. Invitations included a link to an online survey, which allowed for anonymous responses.

Statistical analysis

Responses generated through the electronic survey were stored in datasets, which were subsequently downloaded for analysis. To reduce the possibility of redundancy in respondents, data from VP survey respondents who had identified themselves as VIN members were deleted. In addition, all nonveterinarian responses were deleted. Graduation dates in the VP survey were manually coded to correspond with the categories used in the VIN survey. The VIN categories consisted of 10-year periods, with the exception of the period from 2010 through 2014, in which only graduates from the past 5 years were represented.

For both surveys, Likert-type responses were converted to an ordinal scale. For items concerning importance of a variable (ie, importance items), the scale ranged from 1 (not at all important or irrelevant) to 5 (extremely important or essential). For items concerning likelihood of a variable (ie, likelihood items), the scale ranged from 1 (most or extremely unlikely) to 5 (most or extremely likely). For items concerning agreement with a variable (ie, agreement items), the scale ranged from 1 (strongly disagree) to 5 (strongly agree), with 3 indicating neutral. Responses provided as free text were categorized manually by keyword or theme, and those with an identical or common theme were grouped together.

Distributions of responses by graduation-year category were compared by an analysis of means of proportions, whereby proportions of respondents within a certain category that

were significantly ($P < 0.05$) higher or lower than the overall mean of all proportions for that variable were considered significantly larger or smaller, respectively, than the overall mean of all proportions for that variable. For the VP survey and for importance items on the VIN survey, frequency of each response category was compared between respondents who had, or had not, recommended clinical trial participation to clients in the past by use of the χ^2 or Fisher exact test, as appropriate. To identify whether general themes or groups of variables were associated with being more or less likely to look into or recommend clinical trial participation, factor analysis was used, followed by logistic regression. All analyses were performed by use of a statistical software program,^b and values of $P < 0.05$ were considered significant.

Results

Response rate

A total of 249 people responded to the VP survey, representing a 15% response rate; 815 people responded to the VIN survey, representing a 3% response rate. To reduce the possibility of redundancy among respondents, VP survey respondents who identified themselves as VIN members ($n = 43$) were deleted, leaving 206 respondents in that portion of the study. Following removal of incomplete, nonveterinarian, or VIN member responses ($n = 86$), 163 (65%) VP survey respondents had useable data and were included in the study. For the VIN survey, 163 surveys were incomplete, yielding 652 (80%) respondents with complete data. Given the dynamic application of the VIN survey, the number of responses for individual questions varied.

Demographic information

Distributions of graduation year and type of practice among respondents were summarized for each survey (Figures 1 and 2). Veterinary practices of VIN survey respondents were located mainly in the United States ($n = 526$ [81%]), with 81 (12%) respondents from Canada and 45 (7%) respondents from other countries. The most commonly represented other country was Australia ($n = 16$ [2%]), and no other country was represented by $> 5\%$ of respondents. In contrast, veterinary practices of VP survey respondents were mainly located in the United Kingdom ($n = 136$ [83%]), with 27 (17%) in other countries (none of which had $> 5\%$ of respondents). Most respondents to each survey identified themselves as veterinarians whose practices were characterized as small animal with or without exotic animal (77% and 83% for VIN and VP surveys, respectively) or mixed animal (5% and 4% for VIN and VP surveys, respectively).

Time spent in clinical research

Most respondents indicated that they spent no time in clinical research (82% of VIN survey respondents and 88% of VP survey respondents) or $< 10\%$ of their time in clinical research (16% of VIN survey respondents and 5% of VP survey respondents).

^bJMP Pro 11.0, SAS Institute, Cary, NC.

Factors associated with clinical trial participation

VIN survey—In the VIN survey, respondents who had never looked into enrolling a patient in a clinical trial ($n = 198$ [30%]) were asked to indicate a reason; 179 (90%) provided responses. The most common specific reasons selected were “Clinical trial centers are too far away from my practice” (37%) and “There are no clinical trials or diseases for patients that I deal with” (30%). For those who selected the general category other (37%) and entered a free-text response, the most common theme was lack of awareness about clinical trials for which subjects were being recruited, including which clinical trials were available, the process for enrolling a patient in a clinical trial, and where to look for available clinical trials.

Respondents who had looked into possibly participating in a clinical trial in the past ($n = 454$ [70%]) were asked about the frequency with which they had done this, whether they had ever recommended participation to clients for their pets, and whether they had ever successfully enrolled a patient in a clinical trial. Of those who had looked into a clinical trial in the past, 41% did so less than once a year, 24% did so at least yearly, and 14% did so at least semiannually; only 9% did so more frequently. When these respondents were asked whether they had ever recommended clinical trial participation to clients for their pets, 87% (395/454) responded that they had; 67% (265/395) of respondents who had recommended participation reported that they had successfully enrolled at least 1 small animal patient in a clinical trial.

The most common reasons provided by respondents who had looked into a clinical trial but had not recommended participation to clients (59 respondents; 56 of whom provided reasons) were distance to clinical trial centers (68%), lack of availability of clinical trials in which their patients might participate (48%), and lack of interest from clients (20%). The most common reasons provided by respondents who had recommended participation in the past but were unsuccessful in enrolling a patient (130 respondents; 126 of whom provided a reason) were distance to clinical trial centers (55%), lack of interest from clients (44%), and lack of clinical trials in which their patients might participate (25%). Few (< 1%) respondents indicated that clinical trial participation was against current practice policy or that they had no time for (3%) or interest in (8%) participating in clinical trials. Less than 1% of respondents indicated that they did not want to lose the client to the study investigators, whereas 6% indicated that their clients were not interested in participating in clinical trials.

Across respondents regardless of graduation date category, the overall proportion who had looked into participation in a clinical trial was 70%. A significantly (χ^2 test; $P < 0.001$) more than expected proportion of respondents who had graduated between 1980 and 1989 (79%) and between 1990 and 1999 (78%) had looked into enrolling a patient in a clinical trial, whereas a lower than expected proportion of respondents in the most recent graduation date category (2010 through 2014; 55%) had done the same.

Of respondents who had looked into enrolling a patient in a clinical trial, the overall proportion who had recommended clinical trial participation to clients for their pets was 87%. Significantly (χ^2 test; $P = 0.001$) fewer than expected (73%) respondents in the most

recent graduation date category had recommended clinical trial participation. No significant (χ^2 test; $P = 0.07$) difference was identified among graduation date categories with respect to whether respondents had successfully enrolled their small animal patients into a clinical trial.

VP survey—In the VP survey, 44% (72/163) of respondents indicated they had recommended clinical trial participation to a client for their pet in the past, and 56% (91/163) indicated they had not done so. Respondents in this survey were not asked about reasons for not recommending clinical trial participation. No significant ($P = 0.07$) difference in the distribution of respondents by graduation year category was identified between those who had or had not recommended clinical trial participation to a client for their pet in the past.

Agreement items

Responses to agreement items were asked of 395 of the 653 (61%) VIN survey respondents (392 [99%] provided responses) and all 163 VP survey respondents (157 [96%] provided responses; Table 1). For either survey, no significant difference in proportions of respondents within specific graduation year categories was identified for any item. In general, small animal practitioners who had recommended clinical trial participation to clients for their pets strongly agreed that clinical trials were important in veterinary medicine or agreed that they felt comfortable discussing clinical trials and informed consent with their clients.

When asked about their level of agreement with a series of statements, most VIN survey respondents disagreed or strongly disagreed that anecdotal information is sufficient to support most therapies (76%) and that their clients were aware of veterinary clinical trials in which they might participate (76%). In the VP survey, no significant difference in distributions of responses to most agreement items was identified between respondents who had or had not recommended clinical trial participation to their clients for their pets in the past. However, in response to the statement, “I feel comfortable discussing clinical trials and informed consent with my clients,” significantly (χ^2 test; $P = 0.002$) lower agreement was identified for respondents who had not (vs had) previously recommended participation (Table 2).

The VIN survey respondents who had recommended clinical trial participation to clients for their pets in the past ($n = 395$; 59 responded that they had not done so) and all VP survey respondents were asked to rate the likelihood that they would recommend clinical trial participation on the basis of certain experimental, methodological, and additional elements (Table 3). For the VP survey, no significant differences in the distribution of responses were identified between those who had and had not recommended clinical trial participation to a client in the past, except for 1 additional item, “Trial is run by a respected investigator,” to which respondents who had recommended clinical trial participation provided responses that indicated this would make them more likely to recommend a trial.

With respect to experimental variables, responses to the VP survey were generally in the same direction as for the VIN survey. The exception was “Trial involves a rare disease,” for which a high proportion of VP survey responses were in the less likely range of the Likert

scale, whereas in the VIN survey, a high proportion were in the more likely range. With respect to methodological variables, high proportions (> 50%) of responses were in the more likely range. A high proportion of survey respondents were less likely to recommend clinical trial participation to their clients when the trial involved invasive sample collection (VIN and VP survey respondents) or disruption of daily activity (VIN survey respondents only).

With respect to additional variables, the distribution of responses to all variables was in the same direction from neutral agreement for both surveys, except for “Trial is funded by a corporation or industry.” In that situation, the distributions of responses to the VP survey were at or below neutral and those to the VIN survey were above neutral. Only 1 additional variable from the VIN survey, “Trial is not funded,” had a majority (84%) of responses in the neutral or below (less likely) categories. Across both surveys, the top 3 variables that increased the likelihood of respondents recommending clinical trial participation to their clients included a respected investigator running the trial, a promise to inform the veterinarian of the trial results, and sponsoring of the trial by an academic institution.

In the VP survey, a significant (Fisher exact test; $P = 0.042$) difference was identified in the distribution of responses to a respected investigator running the trial between those who had or had not recommended participation to clients for their pets in the past, with the distribution of responses shifted more toward the neutral range of the scale for those who had not recommended clinical trial participation in the past (Table 2).

Importance items

A total of 765 respondents (618 from the VIN survey and 147 from the VP survey) provided usable responses to prompts regarding the importance of certain variables, either to themselves in their decision to recommend clinical trial participation to a client or to their clients in considering participation. Because of the limited number of VP survey respondents, factor analysis was performed on responses to these importance items in the VIN survey only.

With respect to the decision to recommend clinical trial participation to clients for their pets, variables receiving a higher proportion of responses in the high importance range of the scale included belief in the value of the study, concern about putting the study needs and protocol before the pet’s needs, and inconvenience to the owner. With respect to their clients considering participation, such variables included the pet having a disease that could benefit from the trial, safety of the treatment, cost of participation, distance to the trial center, and chance of pet being placed in the placebo group (VIN survey), among others (Table 4). A high proportion (37%) of VIN survey respondents rated 1 variable, the need for the pet to be unfed for recheck examinations, as less important to owners, suggesting that the respondents did not believe that withholding food from a pet would be difficult for owners to accomplish.

For both surveys, significant differences were identified in the distributions of responses regarding certain variables between respondents who had and had not recommended clinical trial participation to clients for their pets in the past (Table 2), with remarkable concordance between the 2 surveys. Variables with concordant data included concern about putting the study needs and protocol before the pet’s needs, concern about the respondent’s relationship

with the client, loss of trust from a client, loss of control of case management, and time required to explain the trial to the client.

Factor analysis of importance items from the VIN survey

Factor analysis across the 22 importance items was performed for responses to the VIN survey for which complete data were provided ($n = 609$ [93%]). Six factors explained 61% of the total variance in responses (Table 5).

A logistic regression model was fit with the probability that a respondent had looked into enrolling a patient in a clinical trial as the response variable; 434 respondents had done so, whereas 175 had not. Factors 2 ($P = 0.002$), 3 ($P < 0.001$), and 4 ($P = 0.005$) were all significantly associated with looking into patient enrollment. Each factor represented a mixture of positive and negative influences on the overall factor score—influences that appeared to group together. These factors were deemed to represent the following themes: factor 2, veterinarian-client-pet relationship (positive loading) and features related to logistics (negative loading); factor 3, features important to the client (positive loading) and features related to time (negative loading); and factor 4, features related to time. Increases in factor 2 (OR, 1.34; Wald 95% CI, 1.12 to 1.61) and factor 3 (OR, 1.45; Wald 95% CI, 1.20 to 1.74) were associated with an increased likelihood of looking into patient enrollment, whereas an increase in factor 4 was associated with a decreased likelihood of looking into patient enrollment (OR, 0.78; Wald 95% CI, 0.65 to 0.93).

Clinical trial awareness

VIN survey—In the VIN survey, all respondents were asked how they obtained information about clinical trials for which subjects were being recruited and the most effective ways to promote clinical trial participation to veterinarians in their area; 606 provided responses. At least 40% of respondents indicated that they obtained information about veterinary clinical trials from email notifications, word of mouth, and promotions on VIN. Twenty-eight percent (170/606) responded that they did not usually learn or know of clinical trials in their area. For the most effective ways to advertise subject recruitment for clinical trials, 70% of respondents selected email to the practice, 60% selected a clinical trials website, and 54% selected printed information sent to the practice. Only 43% selected a visit from the study investigator.

VP survey—In the VP survey, respondents were also asked how they obtained information about clinical trials in their area and for their opinion on the 2 most effective ways to promote clinical trial participation to veterinarians in their area. As in the VIN survey, 36% of respondents indicated that they did not typically learn of clinical trials in their area; 37% selected email and 25% selected mailed flyers as the most effective advertising strategies for educating them about clinical trials. Forty-six percent of respondents indicated that they obtained information about available clinical trials through journals; this option was not provided in the VIN survey. Opinions regarding the most effective ways to promote clinical trials were somewhat different from those in the VIN survey, with 45% of respondents selecting email to the practice and 54% selecting a visit from the study investigator. Only

20% selected a clinical trials website for the region, whereas 30% indicated that continuing education seminars would be effective.

Respondents in the VP survey were also asked about their overall feelings regarding clinical trials in veterinary medicine as well as the incentives they believed would be best for encouraging pet and owner participation, with 140 providing responses. Overall, 75% (105/140) of respondents had positive feelings about clinical trials in veterinary medicine, with 23% having neutral (32/140) and only 2% having negative (3/140) feelings. Most respondents (122/140 [87%]) selected free services (eg, laboratory tests, radiographs, or examinations) as the best owner incentive for participation with their pet in a clinical trial.

Discussion

The present study revealed that small animal practitioners are interested in veterinary clinical trials, and several variables associated with those trials were important and influential in their decision to recommend clinical trial participation to clients for their pets. The study represents the first of its kind in veterinary medicine, although similar studies have been conducted in human medicine.

Responses to several survey items were restricted to respondents who had recommended clinical trial participation in the past because this subset of small animal practitioners was considered more likely to recommend clinical trial participation than those who had not made such a recommendation. This subset was also considered the group for whom it would be most valuable to explore the elements of clinical trials that influence the likelihood of recommendation.

Overall, agreement was high that veterinary clinical trials are important and that small animal practitioners feel comfortable discussing informed consent. This finding was expected, although lower agreement could have existed for respondents who had not previously looked into or recommended clinical trial participation in the past. That possibility could not be evaluated with the data obtained in the VIN survey, but responses to the VP survey for items pertaining to comfort discussing clinical trials and informed consent were generally more negative for small animal practitioners who had not (vs had) recommended clinical trial participation in the past. In human medicine, a physician's lack of confidence in explaining clinical trials to patients is a reported barrier to trial recruitment.¹⁸

Small animal practitioners who had recommended clinical trial participation to clients did not generally believe that their clients would be "fearful about participating in a clinical trial," although 78% disagreed or strongly disagreed that their clients were aware of veterinary clinical trials in the recruitment phase. This is in agreement with findings from a survey¹¹ involving pediatricians, in which respondents believed that community awareness of randomized clinical trials in the recruitment phase was low. Even among those veterinary practitioners who strongly believed that clinical trials are important and who had actively recommended participation to patients, some degree of failure to recommend participation was identified, given that only 49% agreed or strongly agreed that veterinarians should

recommend clinical trial participation to clients for their pets as often as possible, whereas 34% agreed that veterinarians should recommend participation only to select clients (Table 1).

Failure to recommend a trial to potential participants is a considerable problem in the subject recruitment stage of clinical trials in human medicine, even for groups of clinical trial investigators.¹⁹ Reasons for failure to recommend participation in human clinical trials include concerns about characteristics of the project or protocol, perceptions of the patient or family, and anticipated refusal of patients to participate. Protocol-related concerns in human clinical trials include the involvement of invasive procedures (including blood sample collection), inclusion of a placebo group, and randomization.^{2,11,20}

In the present study, small animal practitioners generally gave no indication that any of the specified clinical trial elements would make them less likely to recommend clinical trial participation. The exceptions were a trial that was not funded (VIN survey) or involved invasive sample collection or a rare disease (VP survey). However, shifts in response distributions toward a lower likelihood of recommending participation (or a more negative influence) were evident for trials involving a new treatment for a condition with a currently successful therapy, and those that involved invasive sample collection or interfered moderately with daily activities. Respondents believed that the chance of the pet being placed in a placebo group was important to clients in considering a clinical trial (74 selected important or extremely important), but whether this variable influenced the decision to recommend participation was not examined.

Nearly 30% of VIN survey respondents stated that they did not generally learn of clinical trials being conducted in their area. In addition, among the most common reasons given for not looking into or recommending clinical trial participation were lack of awareness of the trials and the process for enrolling a patient. Similarly, distance to clinical trial centers was selected as a reason for not looking into clinical trial participation by 37% of VIN respondents and by nearly 70% of those who had looked into enrolling patients in a trial but had not recommended it to clients. However, respondents were not asked to define their perception of a clinical trial center, which could have included referral hospitals, universities, or private clinics. Future research should incorporate additional questions to determine how and where veterinarians believe clinical trials are conducted, given that this may represent an educational opportunity. For human clinical trials, proximity to a clinical trial center has been associated with increased likelihood of physician referral of patients with Alzheimer disease for trials.²⁰

In the present study, positive influences on recommending trial participation included running of the trial by a respected investigator, sponsoring of the trial by an academic institution, and promises to inform participating small animal practitioners about the trial results. This suggested that increasing communication between trial investigators and veterinary practitioners could facilitate subject recruitment to veterinary clinical trials.²¹

Population attitudes and beliefs often manifest as latent traits that can be only indirectly and sometimes imperfectly measured by use of standard questionnaires. Factor analysis is a

method for estimating these latent traits from question-level survey data by determining the question responses that group together. Results of factor analysis in the present study indicated that response items with high loading for a certain factor were thematically related and that small animal practitioners' beliefs about the importance of these factors may have influenced whether they recommend clinical trial participation to their clients. Only the factors that had a significant relationship with the likelihood of a veterinarian looking into clinical trial participation were considered, as they were the only factors providing meaningful insight into the characteristics of the population studied. Overall, higher scores on factors 2 and 3 (representing relatively higher scores for issues related to doctor-client relationship and lower scores for logistical issues and relatively higher scores for features believed to be important to the client and lower scores for issues related to time, respectively) were associated with an increased likelihood of respondents looking into enrolling a patient in a clinical trial. On the other hand, a higher score on factor 4 (appearing to represent variables related to time) was associated with a decreased likelihood of a respondent looking into enrolling a patient in a clinical trial.

Concerns related to time investment required for trial participation are important to acknowledge in general veterinary practice, where free time is often restricted and the time needed to look into trials, discuss trials with owners, and pursue participation may be a strain for veterinarians when avenues for identifying upcoming trials for which subjects are being actively recruited and the requirements for those trials are not clearly outlined. This problem has been identified in studies^{4,22–24} concerning clinical trials in human medicine as well. For example, a study¹³ involving pediatricians revealed that spending more time in the initial interview or discussion with potential clinical trial participants led to lower refusal rates, which is a strategy that is not always feasible in busy general practices.

In the present study, respondents' ratings of importance items highlighted several variables they believed to be extremely important to clients in considering clinical trial participation with their pets. The variable that received the highest importance rating in the VIN survey was having a pet with a condition that could benefit from the trial, reported by 71% of respondents. This finding was similar to that in a study¹⁴ of cat owners' views on clinical trial participation, in which 73% of respondents gave this item the highest importance rating (5-point scale). Veterinarian endorsement of the trial was also rated as important, although only 33% of VIN survey respondents and 26% of VP survey respondents gave this the highest importance rating. This finding was likely an underestimation, given that physician recommendation has been cited as a critical feature of clinical trial participation in human medicine,¹¹ and in the study¹⁴ of cat owners, 56% assigned the highest importance rating (5-point scale) to the item "My veterinarian recommended the trial." Additional research would be useful to compare attitudes of pet owners (including dog owners) with attitudes of small animal practitioners to identify commonalities (and gaps) between importance ratings.

A few studies^{11,21,25,26} in human medicine have involved use of small groups of physicians and more in-depth discussions to explore attitudes toward clinical research. Although such studies generally have far fewer participants, the ability to ask follow-up questions can provide details not accessible through a survey tool, even with free-text options. This approach could be explored in veterinary medicine.

The present study had several limitations. Considering the number of veterinarians in small animal practice, overall participation and response rate in the survey were low; however, the number of participants was similar to that in another veterinary survey.²⁶ These characteristics may have limited the ability to generalize the findings to a broader veterinarian population. Also, studies involving internet-based surveys are subject to volunteer bias, whereby the attitudes of those who participate might not represent the attitudes of those who declined participation or the target population.

Several items on the VIN survey were asked only of respondents who had recommended clinical trial participation to clients, so it remains unknown how small animal practitioners who had not recommended participation would have rated the same items. Differences in response patterns were identified between VIN survey and VP survey respondents, which might have been attributable to differences in the survey instruments or differences in the populations from which respondents were selected. Given these differences, it was not possible to make direct comparisons between results from these surveys. Although all respondents were veterinarians, and the majority from each survey self-identified their practices as small animal practice, exotic animal practice, or both, differences aside from country of residence may have existed. In the future, efforts to obtain international participation on the same survey instrument delivered in the same manner could be helpful in the evaluation of potential geographical differences in attitudes. Respondents in the present study were also limited to small animal practitioners, and findings for other types of practitioners toward clinical trials in their own specialties could be expected to differ from those reported here.

Despite the aforementioned limitations, results of the present study emphasized the importance of understanding the elements of clinical trials that are important to small animal practitioners and those that they believe are important to clients as well. Opportunities exist to improve the awareness small animal practitioners regarding clinical trials for which subjects are being recruited, and a means of achieving this may be through a searchable clinical trials website or registry, such as that initiated by the AVMA.²⁷ Conduction of clinical trials at multiple rather than single sites could also help to minimize the distance that clients would need to travel with their pets to participate, thereby increasing the likelihood of small animal practitioners successfully enrolling patients or recommending participation to clients. In addition, development of educational materials designed to streamline the practitioner's discussion of a clinical trial with clients could help to provide information, raise awareness, and relieve some of the time constraints that hinder clinical trial recruitment.

Results also suggested that even when small animal practitioners were aware of a clinical trial, they may not have attempted to enroll patients if they did not believe in the value of the study or distrusted other protocol or patient care elements. Additional research is needed to investigate the impact of interventions, such as increasing involvement of small animal practitioners in study design and communication of results, on recruitment efforts.

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ABBREVIATIONS

CI	Confidence interval
VIN	Veterinary Information Network
VP	Veterinary Professionals Ltd

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Figure 1. Distribution of year of graduation for small animal practitioners who responded to an online VP (n = 163) or VIN (652) survey regarding attitudes toward enrolling their patients in veterinary clinical trials.

Figure 2. Distribution of practice types for small animal practitioners who responded to an online VP (n = 163) or VIN (652) survey regarding attitudes toward enrolling their patients in veterinary clinical trials.

Table 1

Distributions of responses by small animal practitioners to various statements regarding clinical trial participation of clients and their pets in 1 of 2 online surveys circulated via email to VIN and VP members.

Statement	VIN survey (n = 392)					VP survey (n = 157)				
	Strongly agree	Agree	Neutral	Disagree	Strongly disagree	Strongly agree	Agree	Neutral	Disagree	Strongly disagree
Veterinary clinical trials are important in advancing veterinary medicine	0.83	0.16	0.01	0.00	0.00	0.58	0.38	0.04	0.00	0.00
I feel comfortable discussing clinical trials and informed consent with my clients	0.47	0.43	0.08	0.02	0.00	0.09	0.44	0.31	0.15	0.01
Veterinarians should recommend clinical trials to owners as often as possible	0.19	0.30	0.43	0.69	0.00	—	—	—	—	—
Veterinarians should recommend clinical trials only to select clients	0.00	0.34	0.31	0.22	0.12	0.00	0.48	0.30	0.11	0.11
Most of my clients are fearful about participating in a veterinary clinical trial	0.02	0.15	0.48	0.33	0.02	0.03	0.03	0.39	0.27	0.02
Most of my clients are aware of veterinary clinical trials	0.02	0.08	0.14	0.56	0.20	0.01	0.03	0.07	0.48	0.41
Anecdotal information is sufficient for most therapies	0.12	0.04	0.18	0.50	0.26	—	—	—	—	—

— = Not asked in the VP survey.

Responses to these agreement items were solicited only from the 395 VIN survey respondents who had recommended clinical trial participation in the past (392 provided responses), whereas responses were solicited from all 163 VP survey respondents, regardless of whether they had recommended participation (157 provided responses).

Table 2

Distributions by survey and response scale of responses by small animal practitioners to the surveys in Table 1 regarding variables hypothesized to influence whether they had or had not recommended clinical trial participation to clients for their pets in the past and for which a significant ($P < 0.05$) association was identified.

Variable, by survey and scale	Had recommended					Had not recommended				
	1	2	3	4	5	1	2	3	4	5
VIN survey										
Importance scale										
Belief in the value of the study	0.01	0.02	0.02	0.47	0.48	0.04	0.04	0.13	0.51	0.29
Concern about putting the study needs and protocol before the pet's needs	0.03	0.06	0.11	0.43	0.37	0.07	0.14	0.18	0.44	0.16
Concern about my relationship with my client	0.04	0.10	0.17	0.47	0.22	0.18	0.14	0.24	0.35	0.09
Loss of trust from client	0.05	0.12	0.15	0.39	0.29	0.33	0.11	0.29	0.20	0.07
Time required to explain the trial to the client	0.12	0.29	0.26	0.28	0.05	0.27	0.40	0.18	0.13	0.02
Loss of control of case management	0.15	0.27	0.32	0.19	0.07	0.40	0.33	0.22	0.02	0.04
Need for pet to wear a monitoring device	0.02	0.16	0.31	0.41	0.10	0.07	0.18	0.43	0.18	0.13
Need for pet to be unfed for recheck examinations	0.07	0.39	0.30	0.18	0.06	0.18	0.24	0.31	0.22	0.04
VP survey										
Importance scale										
Concern about putting the research study needs and protocol before the pet's needs	0.03	0.00	0.15	0.42	0.39	0.01	0.01	0.10	0.23	0.64
Concern about my relationship with my client	0.08	0.14	0.30	0.38	0.11	0.01	0.09	0.31	0.27	0.32
Paperwork that would be required by the trial	0.03	0.05	0.38	0.36	0.18	0.01	0.06	0.15	0.43	0.35
Time required to explain the trial to the client	0.03	0.20	0.35	0.27	0.15	0.00	0.10	0.25	0.42	0.23
Loss of trust from client	0.08	0.18	0.35	0.32	0.07	0.01	0.14	0.27	0.30	0.28
Loss of control of case management	0.06	0.20	0.47	0.21	0.06	0.04	0.16	0.28	0.38	0.14
Veterinarian endorsement of the trial	0.00	0.05	0.11	0.53	0.32	0.01	0.00	0.24	0.54	0.21
Need to keep a daily log	0.00	0.11	0.26	0.53	0.11	0.00	0.16	0.25	0.34	0.25
Agreement scale										
I feel comfortable discussing clinical trials and informed consent with my clients	0.00	0.16	0.54	0.21	0.09	0.05	0.36	0.39	0.19	0.01
Likelihood scale										
Trial is run by a respected investigator	0.00	0.01	0.09	0.68	0.22	0.00	0.00	0.23	0.52	0.25

In the VIN survey, 383 practitioners responding to these items had recommended clinical trial participation and 55 had not recommended participation; in the VP survey, these numbers were 66 and 81, respectively. For both surveys, Likert-type responses were converted to an ordinal scale. For items concerning importance of a variable, the scale ranged from 1 (not at all important or irrelevant) to 5

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(extremely important or essential). For items concerning likelihood of a variable, the scale ranged from 1 (most or extremely unlikely) to 5 (most or extremely likely). For items concerning agreement with a variable, the scale ranged from 1 (strongly disagree) to 5 (strongly agree), with 3 indicating neutral.

See Table 1 for remainder of key.

Table 3

Distributions of responses by small animal practitioners to the surveys in Table 1 regarding how likely they were to recommend clinical trial participation to clients for their pets with respect to certain experimental, methodological, and other variables.

Variable	VIN survey (n = 395)					VP survey (n = 163)				
	1	2	3	4	5	1	2	3	4	5
Experimental										
Trial involves a therapy licensed elsewhere	0.00	0.02	0.09	0.47	0.42	0.01	0.02	0.30	0.49	0.18
Trial involves a rare disease	0.00	0.07	0.14	0.46	0.33	0.06	0.42	0.34	0.14	0.04
Trial examines a novel therapy	0.00	0.05	0.19	0.55	0.20	—	—	—	—	—
Trial examines an anecdotal therapy	0.02	0.10	0.24	0.48	0.14	—	—	—	—	—
Trial involves a surgical intervention	0.01	0.09	0.37	0.44	0.09	—	—	—	—	—
Trial examines a new treatment for a disease with a currently successful therapy	0.02	0.23	0.30	0.34	0.11	0.02	0.33	0.39	0.19	0.06
Methodological										
Trial is noninvasive	0.00	0.00	0.02	0.36	0.61	0.00	0.01	0.11	0.50	0.38
Trial is minimally invasive	0.00	0.01	0.05	0.59	0.35	0.00	0.04	0.26	0.55	0.14
Data collection interferes minimally with daily activities	0.00	0.03	0.10	0.55	0.32	—	—	—	—	—
Trial involves invasive sample collection procedures	0.02	0.21	0.36	0.36	0.05	0.19	0.53	0.19	0.08	0.00
Data collection interferes moderately with daily activities	0.02	0.25	0.38	0.32	0.03	—	—	—	—	—
Other										
Trial is run by a respected investigator	0.00	0.00	0.03	0.47	0.49	0.00	0.01	0.16	0.59	0.24
You would be informed of the trial results	0.00	0.00	0.06	0.48	0.46	0.00	0.01	0.10	0.60	0.28
Trial is sponsored by an academic institution	0.00	0.00	0.13	0.46	0.40	0.00	0.03	0.16	0.60	0.21
Client was compensated for their time	0.01	0.00	0.24	0.50	0.25	0.01	0.02	0.19	0.62	0.16
You retain management of the case	0.00	0.02	0.31	0.39	0.28	—	—	—	—	—
Trial results are guaranteed to be published	0.00	0.01	0.33	0.39	0.26	0.00	0.01	0.09	0.47	0.43
You were compensated for your time	0.00	0.01	0.46	0.34	0.18	0.00	0.03	0.38	0.43	0.15
Trial is funded by a corporation	0.00	0.08	0.37	0.42	0.13	0.03	0.19	0.64	0.13	0.01
Trial is not funded	0.09	0.35	0.40	0.13	0.03	—	—	—	—	—

For both surveys, Likert-type responses were solicited and converted to an ordinal scale from 1 (most or extremely unlikely) to 5 (most or extremely likely).

See Table 1 for remainder of key.

Table 4

Distributions of responses of small animal practitioners to the surveys in Table 1 regarding the importance they considered certain variables to be to clients when considering clinical trial participation for their pet.

Variable	VIN survey (n = 618)					VP survey (n = 147)				
	1	2	3	4	5	1	2	3	4	5
Pet has a disease that could benefit from the trial	0.00	0.01	0.00	0.27	0.71	0.00	0.01	0.03	0.29	0.67
Safety of the treatment	0.00	0.01	0.00	0.29	0.70	0.00	0.03	0.02	0.20	0.75
Cost of participation	0.00	0.02	0.03	0.40	0.55	0.01	0.01	0.03	0.26	0.68
Distance to the trial center	0.00	0.01	0.06	0.48	0.45	0.00	0.04	0.14	0.44	0.38
Free evaluation and treatment	0.00	0.01	0.08	0.48	0.42	—	—	—	—	—
Number of recheck examinations required	0.00	0.02	0.07	0.53	0.38	0.01	0.01	0.14	0.48	0.36
Veterinarian's endorsement of the trial	0.00	0.01	0.05	0.59	0.33	0.01	0.02	0.18	0.53	0.26
Chance of pet being placed in the placebo group	0.01	0.03	0.22	0.50	0.24	—	—	—	—	—
Duration of each recheck examination	0.01	0.09	0.17	0.50	0.23	0.03	0.14	0.18	0.40	0.24
The treatment is experimental or novel	0.01	0.07	0.26	0.51	0.15	0.01	0.12	0.36	0.27	0.23
Need to keep a daily log	0.01	0.16	0.24	0.46	0.13	0.00	0.14	0.25	0.42	0.18
Need for the pet to wear a monitoring device	0.02	0.16	0.34	0.38	0.09	0.00	0.18	0.33	0.36	0.12
Need for the pet to be unfed for recheck examinations	0.01	0.36	0.32	0.19	0.04	0.04	0.27	0.29	0.29	0.10

For both surveys, Likert-type responses were solicited and converted to an ordinal scale from 1 (not at all important or irrelevant) to 5 (extremely important or essential).

See Table 1 for remainder of key.

Table 5

Factor loading patterns for responses of small animal practitioners (n = 434) to a VIN survey regarding the importance that certain variables played in whether they would look into clinical trial participation for their patients.

Variable	Factor 1	Factor 2	Factor 3	Factor 4	Factor 5	Factor 6
Belief in the value of the study	0.314	0.299	0.376	0.231	0.165	0.318
Concern about putting the study needs and protocol before pet's needs	0.433	0.353	0.275	-0.116	-0.269	0.159
Inconvenience to the owner	0.444	0.070	-0.023	0.044	-0.495	0.183
Concern about my relationship with my client	0.482	0.584*	0.192	-0.310	-0.167	-0.077
Time required to assess, treat, and enroll the pet	0.480	0.326	-0.435*	0.535*	0.106	-0.015
Loss of trust from client	0.465	0.603*	0.237	-0.306	-0.124	-0.129
Paperwork that would be required by the trial	0.508	0.274	-0.477*	0.491*	0.110	0.069
Time required to explain the trial to client	0.432	0.443*	-0.467*	0.224	0.046	-0.154
Loss of control of case management	0.414	0.528*	0.008	-0.263	0.012	-0.228
Pet has a disease that could benefit from the trial	0.263	-0.033	0.552*	0.333	0.153	0.172
Safety of the treatment	0.444	-0.116	0.391	0.036	0.230	-0.011
Cost of participation	0.505	-0.314	0.136	0.187	-0.072	-0.447
Distance to trial center	0.512	-0.475*	0.140	0.187	-0.400	0.011
Free evaluation and treatment	0.420	-0.278	0.163	0.172	0.100	-0.467
Number of recheck examinations required	0.623	-0.416*	-0.062	0.074	-0.394	0.077
Veterinarian's endorsement of the trial	0.307	-0.005	0.432*	0.180	0.276	0.363
Chance of pet being placed in placebo group	0.427	-0.184	0.272	-0.104	0.288	-0.340
Duration of each recheck examination	0.574	-0.355	-0.131	-0.152	-0.282	0.133
Treatment is experimental	0.461	-0.061	0.186	-0.069	0.256	-0.009
Need to keep a daily log	0.580	-0.295	-0.285	-0.311	0.310	0.115
Need for pet to wear a monitor	0.617	-0.222	-0.308	-0.319	0.202	0.217
Need for pet to be unfed for recheck examinations	0.468	-0.186	-0.370	-0.365	0.268	0.146

* Variables within significant factors that had high loadings (> 0.400 or < -0.400). Factors 2, 3, and 4 were significantly associated with small animal practitioners looking into clinical trial participation for their patients. For these significant factors, response patterns with high loadings would influence the likelihood of a small animal practitioner looking into a trial.