Editorial

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Editorial: Towards Evidence-Based Veterinary Medicine

Evidence-based medicine has been defined as the conscientious, explicit and judicious use of current best evidence in making decisions about individual patient care[1]. Evidence-based practice seeks to combine the clinical judgement and expertise that clinicians acquire through training and experience with the best available scientific evidence (especially the results of patient-centered clinical research) in order to provide patients with more effective, efficient, and compassionate care. A serious movement toward evidence-based veterinary practice will require that a large body of high quality patient-centered research be made available to veterinarians willing and able to access and critically appraise the quality and applicability of clinical trials. With the increasingly frequent publication of patient-centered clinical research such as the study by Chun, et al that appears in this issue, the JVIM has confirmed its commitment to making the results of patient-centered research available to interested practitioners.

The need for more patient-centered veterinary research is obvious. A brief perusal of the National Library of Medicine's holdings that might potentially provide relevant information to a veterinarian interested in the current best evidence regarding the treatment of lymphosarcoma in dogs (Advanced PubMed search string: ((lymphoma OR lymphosarcoma) AND (dog OR dogs OR canine OR canines) AND (randomized controlled trial [publication type] OR drug therapy [subject heading] OR therapeutic use [subject heading] OR random* [word])) returned less than 60 studies published since 1995. Only a handful of those studies are clinical trials that were designed to address important therapeutic issues. For comparison, an identical search string that allowed the inclusion of human subjects returned 5,400 studies published during the same time period, many of which provide the results of randomized, placebo-controlled therapeutic trials. There are a number of important reasons for this discrepancy, and our plight as veterinarians is not as hopeless as it might appear from those superficial results.

Funding and performing patient-centered veterinary research has been and will probably continue to be challenging. For starters, the veterinary pharmaceutical market (with the exception of products that are widely used in healthy animals such as flea control) represents only a tiny fraction of the pharmaceutical industry. It would be unrealistic to expect a for-profit industry to mount a research and development effort totally out of proportion to its potential returns. Even if companion animal health were a higher societal priority (and large amounts of money were available from government or private agencies to address clinical concerns in companion animals), a shortage of well-trained clinical researchers would probably limit the rate at which high quality clinical veterinary evidence could be generated. The entire membership of the ACVIM Specialty of Oncology, for example, would barely provide enough oncologists to populate the oncology division of a single university-based medical school and regional cancer center. Universities also contribute to the difficulty of doing high quality veterinary patient-centered research by following tenure and promotion policies that penalize faculty for time-consuming participation in large collaborative studies, regardless of their potential impact on the profession. Veterinarians are nothing if not resourceful, however, and it is remarkable how much patient-centered research can be and is being done on what would be vanishingly small budgets by human clinical trial standards.

While high-quality research is being done on small budgets, in clinical research (as in life), you often get what you pay for. We are thus obligated as a profession to understand, recognize, and acknowledge both the advantages and limitations inherent in the evidence generated by a variety of clinical trial designs. Yusef and his colleagues have popularized an adaptation of the hierarchy of clinical evidence originally generated by Sackett and colleagues at the Oxford Center for Evidence Based Medicine that assigns a letter grade that reflects the probability that the conclusions and subsequent recommendations made by a research study will be reliable.[2] The most reliable evidence (Class A) is obtained from the results of systematic reviews (e.g. meta-analyses) of multiple, randomized, blinded, placebo-controlled trials designed specifically to address the clinical question of interest. Such virtually unassailable evidence is currently unavailable in veterinary medicine because there have been too few such trials performed on any single topic. Individual randomized, placebo-controlled clinical trials that yield narrow confidence intervals for producing a relevant clinical effect also provide Class A evidence, and represent the next best thing to systematic reviews of multiple high-quality studies.

While it is widely recognized that blinded, placebo-controlled, randomized clinical trials provide the best available evidence, such trials are almost always expensive in terms of money, manpower, and case requirements. In addition, they are administratively taxing, and can potentially pose ethical dilemmas depending on the clinical problem and treatment(s) studied. Because of the constraints commonly present in veterinary practice, and the difficulties associated with randomized clinical trials, other trial designs are often utilized to address clinical questions. As a profession, we can not afford to exclude or ignore evidence from easier to perform, nonrandomized (historically controlled) or even uncontrolled (case series) trials. However, we can also not afford to uncritically embrace the results of such studies.

Therapeutic evidence obtained from high quality clinical trials using historical controls (Class B evidence) is significantly less reliable that that obtained from high quality randomized clinical trials. Although there are many potential reasons for this difference, the basic problem is that an inappropriately large percentage of historically controlled trials find in favor of the experimental therapy. Sacks et al. found many years ago that historical control groups gen-

erally don't fare as well clinically as those included in randomized control groups.[3] The same authors evaluated the outcomes of clinical trials of 6 different therapies that were performed using both historical and randomized controls. They discovered that while 84% of the trials using historical controls found the therapy to be effective, only 11% of the randomized controlled trials evaluating the same therapy yielded positive results.[4] In general, positive results from a trial utilizing historical controls should be interpreted to mean that the therapy evaluated might hold promise, and a randomized controlled trial is needed. Negative results from historically controlled trials are more likely to be true.

Evidence obtained from an uncontrolled case series (Class C evidence) is generally less reliable than that obtained from trials utilizing historical controls. There are famous (or infamous, in the case of diethylstilbestrol administered to women in the 1940s and 50s) examples of therapies that were adopted following enthusiastic reports of several large case series, only to find that the positive results evaporated (or worse, evidence of harm appeared) when the treatments were subjected to randomized, placebo controlled trials.[5]

The least reliable category of evidence (Class D) is the most plentiful in veterinary medicine—evidence derived from expert opinion, and/or extrapolated from bench research or physiologic studies. These sources currently fill the huge void created by the relative dearth of high quality patient-centered clinical research. This is not to say that experts are unimportant to the profession, or that we should abandon untested treatments that make pathophysiologic sense if no better therapy is available. Expert opinion, bench research, and pathophysiologic inference are all rich sources of direction for future clinical trials, and provide meaningful guidance in the absence of more reliable evidence. There is no doubt, however, that one benchmark of our professional progress in this century will be our ability to wean ourselves away from these easy but unreliable answers by enhancing the quality and quantity of the evidence used daily in our practices.

References

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