

Top 5 Steps to Practice Evidence-Based Veterinary Medicine

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Veterinarians in all disciplines¹ should use optimal diagnostics, interventions, and medications to examine and treat veterinary patients. However, many veterinarians may not be using the newest information to aid clinical decision-making.

The principles of evidence-based veterinary medicine (EBVM) provide structured methods for processing the large amount and different types of clinical trials, studies, and other information available and applying that information to clinical case management.² In the context of a specific case, following the 5 steps of EBVM³ can help veterinarians avoid mistakes, be more circumspect in practice, and provide the best patient care.

1 Ask Formulate a relevant and answerable clinical question.

It is important for veterinarians to recognize knowledge gaps and limitations when facing a specific case. Using treatment protocols simply because they have “always been used” is often not appropriate in the rapidly developing veterinary field. Accepting that more valid

information is needed to make an appropriate clinical decision is the first step in using the concepts of EBVM.

After identifying a gap in knowledge, situations or concepts that are often complex should be broken down into a precise clinical question. For example, a veterinarian treating pyometra in a dog should not simply ask, *How should I treat a pyometra case?* Instead, the veterinarian should formulate a question that addresses all aspects of the case. The PICO approach is a practical way to formulate a question:

- ▶ P: Patient, population, and problem
- ▶ I: Intervention
- ▶ C: Comparison or control
- ▶ O: Outcome

In the pyometra example, the *patient* and *problem* element is a female dog with pyometra. *Interven-*

TOP 5 STEPS TO PRACTICE EVIDENCE-BASED VETERINARY MEDICINE

1. Ask
2. Acquire
3. Appraise
4. Apply
5. Assess

tion would involve hysterectomy, whereas choosing to do nothing would serve as a *control*. A hysterectomy as intervention can also be *compared* with the choice to treat with progesterone blockers or antibiotics. Finally, the *outcome* is considered: Will the patient survive or maintain fertility?

Considering each of the steps in the PICO approach leads to the precise clinical question, *In a 6-year-old female dog with open pyometra and only moderate clinical signs and slight WBC elevation, does hysterectomy have a better survival rate as compared with treatment with progesterone antagonists and antibiotics?* The clinician can then research surgical versus medical treatment for pyometra.

A PICO question can be adjusted to different situations, including treatment considerations (eg, *What medication is best? Is there risk for negative reaction?*) or diagnostic questions (eg, *Which diagnostic test provides the most reliable results?*).

2 Acquire

Access the best available information to answer your question.

With so much information available, it may not be practical to read all veterinary journals. Thus, veterinarians should develop skills to efficiently find relevant articles via literature databases (eg, PubMed, CAB Abstracts). After developing a PICO-based question, the terms determined in the PICO process can be used as search terms. In the pyometra case example, “pyometra in a dog,” “hysterectomy,” “surgical intervention,” “medical management,” “fertility,” and “antibiotics” could all be used to search for relevant data.

It can be difficult to determine whether an article or study will contain the expected information based on an abstract or title alone. Many journals charge considerable fees to access articles, making it difficult for veterinarians to decide whether an article is relevant and worth purchasing. To overcome these obstacles, some projects aim to provide knowledge synthesis, systematic reviews, and meta-analysis of journal content (see *Suggested*

CHECKLIST 1

CHECKLIST TO ASSESS THE QUALITY OF RESEARCH ON DIAGNOSTIC TESTS

Evaluation of diagnostic tests should include examination of the usefulness of new diagnostic tests. Results of a new diagnostic test are typically compared with current gold standard outcomes to establish the sensitivity, specificity, and likelihood ratios for the new diagnostic test.

Study Design

The disease/condition to be tested is clearly defined.	1 point
Clear thresholds for physiologic/nonphysiologic conditions are defined.	2 points
Clear inclusion/exclusion criteria for patients/samples are reported.	1 point
An appropriate number of patients/samples was included in the study.	1 point
The test procedures are described in detail.	1 point
The study was blinded.	2 points

Test Characteristics

The test was compared to an acknowledged gold standard.	1 point
Sensitivity and specificity of the test are given.	2 points
Repeatability of the test is good (same results when test is repeated).	1 point
Possible bias or other problems of the test (preanalytical/analytical) are discussed.	1 point

Practical Relevance

Quality of the test results is discussed in context to other diagnostic tools for the given disease/condition.	1 point
Applicability and reliability of the test in practice is discussed objectively.	1 point

Add the given rating points to obtain the overall rating score. _____ points

15-13 = very good, 12-10 = good, 9-7 = satisfactory, 6-4 = adequate, 3-2 = inadequate, 1 = fail

EBVM = evidence-based veterinary medicine

Reading, page 66).⁴ Meta-analyses summarize information and statistically analyze the results of different clinical trials relating to a specific topic to formulate concise and advanced conclusions. Systematic reviews aim to collect and interpret all available information on a specific topic without a statistical approach but with a defined and rigorous search method. Knowledge syntheses (also referred to as critically appraised topics) are standardized summaries of research evidence around a specific clinical question, usually generated from a specific case or problem. Inclusion of case reports in knowledge syntheses is uncommon, as they are prone to bias. No quantitative assignments exist for meta-analyses, systematic reviews, or knowledge syntheses.

CHECKLIST 2

CHECKLIST TO ASSESS THE QUALITY OF REVIEWS

Literature reviews in journals aim to objectively summarize recent knowledge on a specific topic. In general, these knowledge compilations can be helpful. However, sometimes it is unclear how cited publications were selected and what the authors based their conclusions on. This checklist aims to provide an objective assessment of bias in literature reviews.

Literature Search & Inclusion

Literature search was conducted systematically via databases and is well documented.	4 points
The used search terms are documented.	2 points
More literature was searched in reference lists of acquired articles.	1 point
Inclusion and exclusion criteria for papers are well documented.	2 points

Assessment

The quality of each paper was assessed systematically.	4 points
The findings and conclusions are discussed objectively.	2 points

Add the given rating points to obtain the overall rating score. _____ points

15-13 = very good, 12-10 = good, 9-7 = satisfactory, 6-4 = adequate, 3-2 = inadequate, 1 = fail

A knowledge synthesis may be helpful if the specific clinical question is very similar to the posed PICO question. In other cases, reviews might provide a broader overview about different options and give helpful background information. Large-scale reviews of evidence, common in human medicine, would be helpful in veterinary medicine but are not generally available.

3 Appraise

Assess the quality of the relevant evidence found.

After reading a study, trial, or article, the clinician must assess the information's quality. Evidence can be ranked from weak to strong based on methodology.⁵ The following questions may be helpful in assessing information⁵:

- Is the information relevant to my clinical question or my patient(s)?
- Is the study design appropriate to answer my clinical question?
- Is the level of evidence and the quality of the paper good enough to rely on the results?

Checklists are available to guide veterinarians through determining whether the level of evidence and quality of the paper are good enough to rely on the results (*Checklists 1*, previous page, **2**, and **3**). However, checklists are not comprehensive and do not cover all possible scientific research approaches.⁶ The literature evaluation form (*Checklist 3*) can be helpful in assessing the quality of treatment information in a study but is not the only method available for determining quality. When using it to assess the quality of information, clinicians should first determine the evidence level (eg, meta-analysis, clinical trial, case report, expert's opinion or experience). Quality criteria such as study design, information content, and objectivity should then be assessed.

By assigning a subjective score for each area in the checklist and totaling these ratings to obtain an overall score (*Checklists 1*, previous page, and **2**), an impression of the quality and practical

CHECKLIST 3**CHECKLIST TO ASSESS THE QUALITY OF RESEARCH ON INTERVENTIONS****Step 1: Evidence Level**

Meta-analysis (statistical combination of the results of several studies)	<input type="checkbox"/>	5 points
Clinical trial	<input type="checkbox"/>	3 points
Case report	<input type="checkbox"/>	2 points
Expert's opinion or experience	<input type="checkbox"/>	1 point

Step 2: Additional Quality Criteria (Regarding the Corresponding Evidence Level)

Meta-Analysis	Agree	
The literature search was exhaustive and reproducible.	<input type="checkbox"/>	2 points
The included trials were comparable from a clinical point of view.	<input type="checkbox"/>	4 points
Trials of a high quality (eg, randomized, controlled, blinded) were included.	<input type="checkbox"/>	2 points
Results are discussed objectively and critically, including questions regarding comparability and publication bias.	<input type="checkbox"/>	2 points

Clinical Trial	Agree	
The trial comprised a sufficient number of animals or samples.	<input type="checkbox"/>	2 points
Essential information regarding the animals are given (eg, number, breed, age, sex, inclusion criteria, housing).	<input type="checkbox"/>	1 point
The trial comprised an adequate control group.	<input type="checkbox"/>	3 points
The trial is randomized.	<input type="checkbox"/>	1 point
The trial is blinded.	<input type="checkbox"/>	1 point
Examinations and interventions are described in detail. Results are presented completely.	<input type="checkbox"/>	1 point
Adequate statistic procedures were used. Data is complete, or missing data is documented sufficiently.	<input type="checkbox"/>	1 point
Results are discussed critically.	<input type="checkbox"/>	1 point
The bibliography is adequate (extent and up to date).	<input type="checkbox"/>	1 point

Case Report	Agree	
Essential information regarding the animals are given (eg, number, breed, age, sex, inclusion criteria, housing).	<input type="checkbox"/>	2 points
Examinations and interventions are described in detail.	<input type="checkbox"/>	2 points
Results are discussed critically.	<input type="checkbox"/>	2 points
The bibliography is adequate (extent and up to date).	<input type="checkbox"/>	1 point

Expert's Opinion or Experience	Agree	
Results are discussed critically.	<input type="checkbox"/>	1 point
The bibliography is adequate (extent and up to date).	<input type="checkbox"/>	1 point

Step 3: Summate Rating Points to Obtain the Overall Rating Score. _____ points

15-13 = very good, 12-10 = good, 9-7 = satisfactory, 6-4 = adequate, 3-2 = inadequate, 1 = fail

From Arlt SP, Heuwieser W. Training students to appraise the quality of scientific literature. *J Vet Med Educ.* 2011;38(2):137. doi: 10.3138/jvme.38.2.135. Reprinted with permission from University of Toronto Press (<https://utpjournals.press>). © 2018 AAVMC. All rights reserved.

applicability of the information in a given study or paper can be formed.

The methods section should be reviewed to determine the study type and whether possible bias was addressed appropriately. Common sources of bias in veterinary literature include a small number of animals, lack of or incomparable control groups, missing specifications of diagnostic procedures, or missing definitions of diseases. Earlier studies have shown that common flaws in many papers include poor reporting of essential information (eg, age and medical history of the animals in the study), small sample size, missing enrollment criteria, and missing information on allocation and blinding.^{1,7} These are all factors that determine the quality of information and should be considered when deciding whether a study or paper is reliable.³

It is not possible or necessary for the reader to recalculate all the statistics given in a paper. However, by assessing other factors, the clinician can make some determination of quality.

4 Apply Implement the evidence into clinical practice.

After new information is proven to be of good quality, the information should be assessed to determine if it is appropriate for a patient's condition. The availability of the suggested therapies, availability of equipment, the veterinary team's skills, whether the circumstances of the study are similar to the patient's circumstances, the owner's wishes, and legal and ethical aspects should all be considered. In the pyometra case example, step 4 involves discussing intended treatment extensively with the owners, including potential complications and recurrence.

Any new clinical applications or approaches should be communicated to the veterinary team and the pet owner. Even small changes concerning specific cases, practice protocols, or other routines in the practice may have a large impact on clinical outcomes, the practice, and the clinician's professionalism.

5 Assess Evaluate the impact of the changes.

Because improving clinical practice is a never-ending task,⁸ clinicians should assess whether changes implemented as a result of EBVM really led to better outcomes. Although it is easy to reflect on cases in which something went wrong or that had an unexpected outcome, it is also important to reflect on what went well in cases with positive outcomes. Assessment can be as simple as a personal reflection on individual cases at the end of a busy day. A more thorough assessment could include a reflection on the PICO-based clinical question, answers found through research, and a comparison to the actual outcome of the case. Finally, a formal practice-wide audit based on these 5 steps could be conducted.

EBVM = evidence-based veterinary medicine

See page 66 for references.

Semintra® (telmisartan oral solution) 10 mg/mL

For oral use in cats only

Angiotensin II Receptor Blocker

Brief Summary: Before using SEMINTRA, please consult the product insert, a summary of which follows:

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

Description: SEMINTRA (telmisartan oral solution) is a clear, colorless to yellowish viscous solution containing 10 mg/mL telmisartan.

Indication and Usage: SEMINTRA is indicated for the control of systemic hypertension in cats. The initial dose of SEMINTRA is 1.5 mg/kg (0.68 mg/lb) orally twice daily for 14 days, followed by 2 mg/kg (0.91 mg/lb) orally once daily. The dose may be reduced by 0.5 mg/kg (0.23 mg/lb) increments to a minimum of 0.5 mg/kg (0.23 mg/lb) orally once daily to manage SEMINTRA-induced hypotension. SEMINTRA can be administered directly into the mouth, or next to or on top of a small amount of food. Do not mix into food.

SEMINTRA should be administered using the dosing syringe provided in the package. The dosing syringe fits onto the bottle and has 0.1 mL incremental marks. The dose should be rounded to the nearest 0.1 mL. After administration close the bottle tightly with the cap. Rinse the dosing syringe with water and let air dry.

If the cat vomits within 30 minutes of dosing, the cat may be re-dosed.

Information for Cat Owners: Adverse reactions can occur with use of SEMINTRA. The most common adverse reactions reported during the field studies included vomiting, diarrhea, lethargy, weight loss, anemia and dehydration.

Contraindications: Do not use in cats with a hypersensitivity to telmisartan.

Human Warnings: Not for human use. Keep out of reach of children.

SEMINTRA is an angiotensin II antagonist/angiotensin receptor blocker (ARB). Pregnant women should avoid contact with SEMINTRA because substances that act on the renin-angiotensin-aldosterone system (RAAS) such as angiotensin receptor blockers (ARBs) can cause fetal and neonatal morbidity and death during pregnancy in humans.

Precautions: SEMINTRA can cause mild anemia or non-regenerative anemia. Cats should be monitored for anemia when initiating treatment with SEMINTRA. SEMINTRA may cause inappetence and weight loss in some cats. Cats should be monitored for weight loss when initiating treatment with SEMINTRA. Use with caution in cats with a history of vomiting, inappetence or weight loss. SEMINTRA has not been evaluated in cats with systolic blood pressure >200 mmHg.

The safe use of SEMINTRA in cats with hepatic disease has not been evaluated. SEMINTRA is metabolized by the liver.

The safe use of SEMINTRA has not been evaluated in cats less than 9 months of age, or in cats that are pregnant, lactating, or intended for breeding. **See Human Warnings.**

The safe use of other anti-hypertensive medications has not been evaluated.

Adverse Reactions: The safety of SEMINTRA was evaluated in a 28-day field study in 192 cats. Adverse reactions that occurred include vomiting 46 (24.0%), diarrhea 18 (9.4%), lethargy 13 (6.8%), weight loss 13 (6.8%), decreased appetite/inappetence 13 (6.8%), non-regenerative anemia 11 (5.7%), dehydration 10 (5.2%), retinal lesions (target organ damage) 4 (2.1%).

The long-term safety of SEMINTRA was evaluated in an open label, 5 month field effectiveness and safety study in 107 cats that received at least one dose of SEMINTRA. Adverse reactions that occurred in this study are weight loss 37 (34.6%), vomiting 32 (29.9%), dehydration 18 (16.8%), non-regenerative anemia 17 (15.8%), anorexia 14 (13.1%), diarrhea 12 (11.2%), lethargy 12 (11.2%), decreased appetite/inappetence 11 (10.3%), heart murmur 10 (9.3%), death, euthanasia, found dead 9 (8.4%), cough 8 (7.5%), and retinal lesions (target organ damage) 6 (5.6%).

Nine cats died or were euthanized during the study. Three cats had progressive chronic kidney disease that may have been affected by telmisartan treatment, concurrent disease, or inadequate control of hypertension. The other six cats died of causes unrelated to treatment (eg, neoplasia).

To report suspected adverse drug events, for technical assistance, or to obtain a copy of the Safety Data Sheet (SDS), contact Boehringer Ingelheim Vetmedica, Inc. at 1-866-638-2226. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or at <http://www.fda.gov/AnimalVeterinary/SafetyHealth>.

Effectiveness: Effectiveness was demonstrated in a 28-day multi-center, controlled, randomized and masked field study in client-owned cats with hypertension, and in an open-label 5-month field study.

28-Day Field Study

In a 28-day study, 288 cats with hypertension (systolic blood pressure [SBP] 160-200 mmHg) were enrolled in the study and randomized to treatment with SEMINTRA (telmisartan oral solution) (n=192) or vehicle control (n=96). The study population included cats with hypertension associated with chronic kidney disease or controlled hyperthyroidism, or idiopathic hypertension. The per protocol population for effectiveness was 141 SEMINTRA treated cats and 79 control cats. SEMINTRA was administered orally at 1.5 mg/kg twice daily for 14 days, then 2 mg/kg once daily until study end; the vehicle control was administered at a mL/kg volume equivalent to SEMINTRA. The two primary variables for effectiveness were comparison of the SEMINTRA and control group mean SBP (mSBP) from baseline to Day 14, and a decrease in mSBP >20 mmHg in the SEMINTRA group from baseline to Day 28. Cats with SBP >180 mmHg at Days 14 or 28 were rescued and removed from the study. There was a statistically significant difference between the mSBP for the SEMINTRA group compared to the control group at Day 14 (p=0.0005). At Day 14 the SEMINTRA group mSBP decreased by 23.2 mmHg, and the control group mSBP decreased by 7.3 mmHg. At Day 28, the SEMINTRA group mSBP decreased 23.9 mmHg compared to baseline.

5-Month Field Study

One hundred-seven cats from the SEMINTRA group that had successfully completed the 28-day study were enrolled in a 5-month open-label study. At the beginning of the 5-month study most cats were administered SEMINTRA at 2 mg/kg once daily. Cats that experienced hypotension (defined as SBP <120 mmHg) at 2 mg/kg once daily could have the SEMINTRA dose reduced to 1 mg/kg once daily. Cats that experienced hypotension at 1 mg/kg once daily could have the SEMINTRA dose reduced again to 0.5 mg/kg once daily. Cats were evaluated for SBP, target organ damage (TOD), primarily assessed by retinal photographs), clinical pathology and adverse reactions. SBP was measured on Days 28, 56, 98, 140 and 182 and retinal photographs and clinical pathology were collected on Days 28, 98 and 182. Seventy-three (68.2%) cats completed the study (Day 182), 8 cats were removed for hypertension (SBP >180 mmHg), 2 cats were removed for hypotension, 10 cats were removed by the owner or for owner non-compliance, 8 cats were removed for new or worsening TOD, and 6 cats were removed for adverse reactions unrelated to TOD. Twenty-six cats had dose reductions to 1 mg/kg once daily to manage hypotension. Of these 26 cats, 10 had an additional dose reduction to 0.5 mg/kg once daily.

NADA 141-501, Approved by FDA

Manufactured for:

Boehringer Ingelheim Vetmedica, Inc.

St. Joseph, MO 64506, U.S.A.

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Reference: Package Insert 449201-00 Revised 03/2018

09/2018

Amitriptyline

CORRECT RESPONSE



Stress is thought to contribute to the development of FIC.⁹⁻¹¹ Amitriptyline, a tricyclic antidepressant that has both anxiolytic and analgesic action, may be beneficial in managing patients with severe or recurrent disease. Side effects include sedation, salivation, urine retention, thrombocytopenia, and neutropenia. Although there is insufficient evidence to support use of amitriptyline as a short-term medication, long-term use of this drug may be considered if or when other evidence-based methods of control—which include moist diet, veterinary therapeutic urinary diet, and multimodal environmental modification or environmental enrichment¹¹—have not delivered a desired response. ■■■

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FIC = feline idiopathic cystitis

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