Below are the documents related to a series of assignment in the pharmacology course in the second year of a 4-year DVM program. We start with practice writing PICO-style clinical questions in a class session, and then two PICOs are submitted for a grade. This is followed with a session in which students practice critical appraisal using pre-assigned articles and a form (see below). Students then search on their own time for 3 articles that are relevant to one of their graded clinical questions, and they are graded on their choice of articles and appraisals using the form. (Searching skills are introduced and reinforced in the previous semester of the curriculum.) In another class period, students learn how to use and then practice using the Fact Box for extracting treatment effect estimates from articles. The last assignment is to apply the evidence extracted from their own articles to answer their clinical question and make a clinical recommendation.

Rubric for grading PICO-style clinical questions

3 points (Excellent)	**2 points (Acceptable)**	**1-0 points (Needs work)**
PICO parts are specific and complete, and the question is highly relevant to clinical practice (that is, it takes into consideration mechanisms of action and known usages of drugs)	PICO parts are specific and complete	Missing important parts of PICO

Points may be subtracted for any of the following common mistakes:

Missing one of the elements (PICO)
Lack of specificity in any of the elements (words like “more effective” or “better” are not specific)
Asking about a drug that doesn’t make sense physiologically or clinically

Step 3: Critical appraisal of the evidence

Instructions for Completing the Form for Evaluating the Evidence for Therapeutics

1. Decide what **type of evidence** you have using your knowledge of study design using the table on the next page. An excellent resource for study design is the book you used in public health and in pharmacology: Petrie and Watson, Statistics for Veterinary and Animal Science, 3rd edition, 2013.

2. Use the **checklist** to help you assess the quality of the evidence for each paper. In light of the type of evidence and your responses on the checklist, provide an overall quality assessment of each paper.

Some common pitfalls

- Starting with the wrong study design type – the only options are in the table on the next page. Retrospective, which may be an important distinction when assessing accuracy of reporting, does not make a difference in terms of bias or strength of evidence. Case-control studies are not typically helpful for evaluating therapeutics, so be cautious about whether that type of study is appropriately identified.

- Using the incorrect check boxes for the type of evidence. This may give you a false impression of the number of "YES" or "NO" boxes checked, leading to an incorrect assessment of quality.

- Misidentifying a narrative review as a systematic review.

- Identifying a study of clinically-derived samples as a case series. For example, reports of antimicrobial susceptibility testing often describe the clinical cases from which the cultures were taken, but unless other information about the outcomes of the cases were provided, this would be an in vitro study.

- Confusing a case series and a cohort study. A cohort study has more than one group of animals that are compared in some way, but they were not randomized to treatment group.

    - A before-and-after type of study is not a cohort study for the purposes of assessing therapeutic interventions.

- Misidentifying a randomized controlled trial because there is not a placebo group. RCTs do not have to be placebo-controlled.

- Giving too high a quality rating for a study that is inherently lower quality due to study design.

- Considering any reported p value to be related to the estimate of precision of the treatment effect. This particular estimate refers to NNT or some other treatment effect calculation, and is uncommonly provided in veterinary literature.

Common types of evidence (study designs)

Studies are sorted based on the potential for risk of bias (lower is better) and strength of evidence

Evidence Type	Description	Primary Research or Research Summary	Potential for risk of bias	Ability to assess the risk of bias	Estimate of treatment effect/ effect size*	Precision of the effect
Systematic review with meta-analysis of RCT	Attempts to identify all relevant literature related to a specific condition or treatment with specific inclusion and exclusion criteria using a team of authors; qualitatively reviews and summarizes all results in a clear and repeatable manner; meta-analysis pools and quantifies data from the literature	Summary	Low	High	Yes	High
Systematic review without meta-analysis	Attempts to identify all relevant literature with specific inclusion and exclusion criteria using a team of authors; qualitatively reviews and summarizes results in a clear and repeatable manner.	Primary	Low	High	No	-
Large randomized controlled trial (RCT)	At least two groups of individuals are included, one with the treatment of interest and one with placebo or comparison treatment; randomization to group is required; >150 per group	Primary	Low	High	Yes	High
Small randomized controlled trial (RCT)	Same as large RCT, with <150 per group	Primary	Low	High	Yes	Low
Cohort study	Follows a group of individuals over time; comparison is group with different exposure or different treatment	Primary	High	Low	Yes	Variable
Case series	Reports on the treatment of individuals with the same condition; no control groups	Primary	High	Low	No	-
Case reports	Very small case series (<5 patients)	Primary	High	Low	No	-
Narrative review	Description of conditions or treatments; sources of data are not reviewed or graded; no data pooling performed; literature inclusion and exclusion criteria not specified	Summary	High	Low	No	-
Opinion	May be oral or written; may be based on one's own clinical experience	N/A	High	Low	No	-
Pharmacokinetic studies	Measures drug concentrations in plasma or other tissues	Primary	Cannot assess	Cannot assess	No	-
In vitro studies	Performed on cells or tissues outside of animals	Primary	Cannot assess	Cannot assess	No	-

*This might be a treatment effect, effect size, risk ratio, or other estimate, and it might be included in the report or it might need to be calculated by the reader.

Making Therapeutic Decisions: Evidence for Effectiveness and Adverse Effects
Form for Evaluating the Evidence for Therapeutics

Evidence (article or source title):

1: Use the table of types and sources of evidence (see instructions document) to determine the type of evidence, and check the boxes below that apply to the risk of bias and your ability to assess the risk of bias.

Evidence Type: _____

Risk of bias ☐ Low ☐ High ☐ Cannot assess
Ability to assess risk of bias ☐ High ☐ Low ☐ Cannot assess

2: Use the checklist below, based on the type of evidence. Once you completed the checklist, and in light of your responses to Step 1, circle which quality assessment you would give this evidence.

High Moderate Low Very Low

	YES	NO
<u>For all evidence types</u>		
Results were discussed critically	☐	☐
The bibliography is adequate (complete and up to date)	☐	☐
<u>Systematic review (with or without meta-analysis)</u>		
The literature search was exhaustive and reproducible	☐	☐
Trials of high quality (randomized, controlled, blinded, trials) were included	☐	☐
Comparability and publication bias were discussed	☐	☐
<u>Randomized controlled trial (RCT)</u>		
Randomization procedure was described	☐	☐
The trial comprised an adequate number of animals (e.g., a sample size calculation was performed)	☐	☐
The control group was completely described and was appropriate for the study	☐	☐
The trial was blinded (single, double, triple)	☐	☐
<u>RCT, cohort study, or case series</u>		
Data are complete, or missing data were documented	☐	☐
Essential information regarding the animals were given: number, breed, age, sex, housing, inclusion criteria, etc.	☐	☐
Exposures and outcomes were described in detail	☐	☐
Appropriate statistical assessments were used	☐	☐
See flow chart on front and back covers of "Statistics for Veterinary and Animal Science" to aid your assessment of the statistics – you know enough to make this judgment!		
<u>PK study</u>		
Regimen was comparable to clinical use	☐	☐
Data exist about concentrations required for pharmacological effect	☐	☐
<u>In vitro study</u>		
Cells or system used were similar to in vivo setting	☐	☐
Drugs or concentrations used were comparable to those achievable in vivo	☐	☐

RUBRIC FOR CRITICAL APPRAISAL:

10 points (Excellent)	**5-9 points (Acceptable)**	**0-4 points (Needs work)**
Article type accurately categorized, all quality assessment questions answered appropriately, and final quality assessment thoughtfully and appropriately assigned	Article type accurately categorized, most assessment questions answered appropriately, and final quality assessment appropriately assigned	Article type not accurately categorized, most or all assessment questions answered inappropriately, or final quality assessment not assigned appropriately

Points may be subtracted for any of the following common mistakes:

Do not use a narrative review for this assignment – you need to find some other primary evidence.
If one of your articles is in a volume of Veterinary Clinics of North America, it is most likely a narrative review, so see previous comment.
Not identifying the correct study type
Make sure you can differentiate case series from in vitro, narrative review from systematic review
Inappropriate quality rating for the type of study
Study design is correlated with quality rating: study designs with a higher likelihood (or unknowable likelihood) of bias should be rated lower
Confusing a p value with treatment effect
Not understanding that a lack of statistically significant differences between treatment groups is the same thing as no treatment effect (or no relative treatment effect)

EBVM Step 4: Applying evidence – how to use a Fact Box

Fact Boxes can be used to help decide what the treatment effect is. For high quality study designs such as systematic reviews, randomized controlled trials, and cohort studies, you should attempt to estimate a treatment effect by completing the Fact Box. For other study designs such as case series or in vitro studies, you will not be able to estimate a treatment effect.

Generally speaking, this means what is the difference between the treated and the untreated animals, or what does the drug do? You can calculate the number needed to treat (NNT) as an estimate of the treatment effect, but you can also extract an estimate based on the data in the paper. For example, if 80% of the dogs stop itching with Drug A, and only 20% in the control group, then the treatment effect is 60%.

Using the Fact Boxes below, practice estimating treatment effects for the articles given to you. Add columns for groups if needed, if there are more than 2 treatment groups that are relevant to your clinical question.

	Group 1	Group 2
List one parameter that was evaluated (this is an "outcome" in the studied animals)	List the treatment given to this group	List the treatment given to this group
What is the mean or average for the outcome you're interested in in each group? Alternatively, how many animals, or what percentage of animals, experienced the outcome in each group?		
What is the numerical difference between the two groups in the outcome (this is the **treatment effect** or "relative" treatment effect if there is not a placebo-controlled group)?		

	Group 1	Group 2
List one parameter that was evaluated (this is an "outcome" in the studied animals; treatment effects are benefits, adverse effects are harms)	List the treatment given to this group	List the treatment given to this group
What is the mean or average for the outcome you're interested in in each group? Alternatively, how many animals, or what percentage of animals, experienced the outcome in each group?		

What is the numerical difference between the two groups (this is the **treatment effect** or "relative" treatment effect if there is not a placebo-controlled group)?	

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EBVM STEP 4: Integrate appraisal to make decision about using a drug

The point of this step is to make a decision about a patient or group of patients. We would like the data to provide clear evidence that the desirable consequences of an intervention clearly outweigh the undesirable consequences, with the result that a "strong recommendation" can be made. The alternative is a "weak recommendation," which requires more equivocation on the part of the clinician.

Your answer can be simple, but you must explain WHY you are convinced of the answer. You should also provide a prediction or expectation of how much you expect the drug to do, or the "treatment effect," in the Fact Box.

APPLY ASSIGNMENT:

Upload a Microsoft Word file or pdf that includes the following:

1. The PICO question you are addressing
2. Citation for the evidence you appraised (citation should include the first author, title of article, title of journal, year of publication, and issue/page numbers; format is not important)
3. FINAL quality assessment of the article you appraised (options are high, moderate, low, very low) - do not include the entire literature evaluation form
4. A completed Fact Box with one line for each article you used to make your recommendation
5. The answer to your clinical question based on your appraisal of the evidence, and the recommendation you would make to a client based on that answer. Include at least one sentence that explains or provides your rationale for the answer and the recommendation.
6. The strength of the recommendation (options are either strong recommendation or weak recommendation)

Making Therapeutic Decisions:
Applying Evidence for Effectiveness or Adverse Effects Apply (3 articles)

Clinical Question:

Evidence (article or source title):

Article 1:

Article 2:

Article 3:

Based on your appraisals and in the context of your clinical question, what is your quality assessment for each article? (High, Moderate, Low, or Very Low)

Article 1:

Article 2:

Article 3:

Estimate at least one treatment effect (or adverse effect) by completing the Fact Box below (or explain why you couldn't complete it). You may need to add columns for additional treatment groups, depending on study design.

		Group 1	Group 2
	List one parameter that was evaluated in each article (this is an "outcome" in the studied animals)	List the treatment given to this group	List the treatment given to this group
Article 1			
	What is the mean or average for the outcome you're interested in in each group? Alternatively, how many animals, or what percentage of animals, experienced the outcome in each group?		
	What is the numerical difference between the two groups in the outcome (this is the **treatment effect** or "relative" treatment effect if there is not a placebo controlled group)?		
Article 2			

	What is the mean or average for the outcome you're interested in in each group? Alternatively, how many animals, or what percentage of animals, experienced the outcome in each group?		
	What is the numerical difference between the two groups in the outcome (this is the **treatment effect** or "relative" treatment effect if there is not a placebo controlled group)?		
Article 3			
	What is the mean or average for the outcome you're interested in in each group? Alternatively, how many animals, or what percentage of animals, experienced the outcome in each group?		
	What is the numerical difference between the two groups in the outcome (this is the **treatment effect** or "relative" treatment effect if there is not a placebo controlled group)?		

Based on your review of this evidence:

a. answer your clinical question

b. make your clinical recommendation

c. assess the strength of your recommendation based on your assessment of the quality of the evidence (the only options are Weak or Strong)

RUBRIC FOR APPLYING EVIDENCE:

10 points (Excellent)	**5-9 points (Acceptable)**	**0-4 points (Needs work)**
Completely describes how the article(s) and your critical appraisal helped answer your clinical question; includes at least one estimate of treatment effect; includes the clinical question and the citation	Is incomplete in describing how or why the article(s) and your critical appraisal helped answer your clinical question; or leaves out the clinical question, the citation, or the treatment effect	Provides no explanation of how or why you answered the clinical question; leaves out the clinical question and the citation

Points may be subtracted for any of the following common mistakes:

Confusing a p value for significance of comparisons with treatment effect

Describing a treatment effect for inappropriate study types (treatment effect cannot be determined in case series, in vitro studies, or many systematic reviews)

Inappropriate strength of recommendation compared to the quality of the papers cited

Not making a specific recommendation ("either would be fine" is not a recommendation)

Leaving out or not providing a complete Fact Box (or incorrectly stating that one cannot be completed)

Leaving out an explanation of how the quality of the articles supported your assessment – study design type is not enough, and instead a brief explanation of characteristics of the study and their application to your recommendation