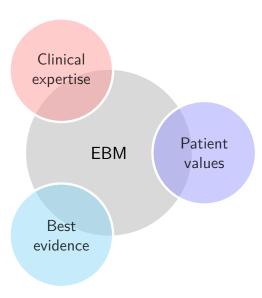
# Evidence Based Veterinary Medicine

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"Evidence based medicine is the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients. The practice of EBM means integrating individual clinical expertise with the **best available** external clinical evidence from systematic research." (Sackett et al., 2000)

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The practise of
Evidence-Based Veterinary
Medicine (EBVM) is the use of
best available scientific
evidence, in conjunction with
clinical expertise and
consideration of owner and
patient factors, to make the
best clinical decisions for
patients.



"... the primary difference between evidence-based medicine and evidence-based veterinary medicine is that, in the latter, the emphasis must be necessarily placed on poorer sources of evidence." (Kastelic, 2006)

Over recent decades, there have been massive increases in the availability of **information**, both in the medical and veterinary literature, but also in mainstream media.



"Clients have access to many of the same resources that veterinary professionals do, but some will lack the clinical knowledge and judgement to assess whether the advice they find online is sensible.

They may have attempted diagnosis, and even worse, treatment, before seeking veterinary advice, and the veterinary surgeon now has an important role in educating owners and debunking myths."

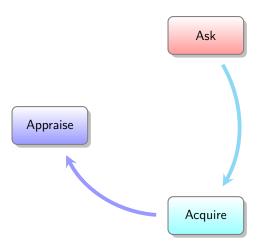
Veterinarians need to be aware of the evidence available, read it, decide on its quality and relevance, and then, if appropriate, incorporate it into clinical decision-making.



defining a clinical question that is of interest and (hopefully!) answerable



finding the best available evidence to answer the question

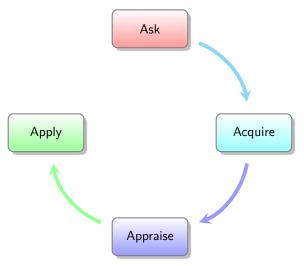


assessing the quality of the relevant evidence found

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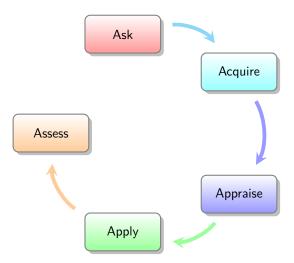


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implementing the evidence into clinical practice where appropriate

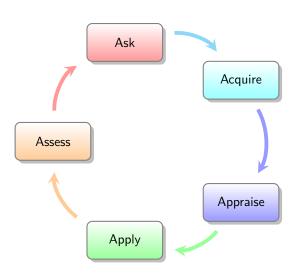
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evaluating the impact of the implementation and changes in clinical practice

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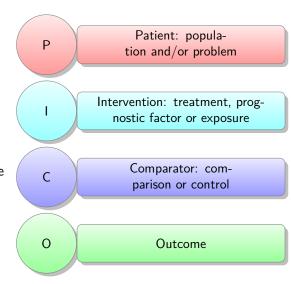
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Formatting your question correctly is important in ensuring that your search for evidence is structured, systematic and complete.

The most common way to format a question is to use the PICO system (https://pico.vet/).



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Treatment These types of questions refer to treatment choices a veterinarian would need to make in order to achieve a desirable outcome. These choices can include drugs or medicines to be used, surgical methods, changes in diet or management, and many more. These types of questions are best answered by randomised controlled trials when they are available.

Which diet is best to feed cats with chronic renal disease?

**PICO:** In [cats with chronic renal disease] does [feeding a renal prescription diet] compared with [not feeding a renal prescription diet] impact on [survival time]?

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Prognosis and Incidence These types of questions relate to the likelihood of disease or the progression of disease over time. These questions are best answered by **cohort** studies.

Does sex affect survival in flat-coat retrievers with cancer?

**PICO:** In [flat-coated retrievers with cutaneous lymphoma], does [being a male] compared with [being a female] affect [average life expectancy]?

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Aetiology and Risk These types of questions investigate the origin of disease or the factors influencing development of a certain condition or disease. These questions are best answered by **cohort** studies, **case-control** studies or **cross-sectional** studies.

What are the risks of general anaesthesia in ferrets?

**PICO:** In [ferrets], is [general anaesthesia by triple injectable agent] compared with [general anaesthesia by induction and inhalational agent] associated with [an increased risk of death]?

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Diagnosis These types of questions involve identification of a disorder based on the animal's presenting signs. These questions are best answered by diagnostic test validation studies (also known as diagnostic evaluation studies).

Which diagnostic test is most reliable for diagnosing fascioliasis in dairy cattle?

**PICO:** In [lactating dairy cattle] does [milk ELISA] compared with [serum ELISA] have [a better sensitivity and specificity for diagnosing fascioliasis]?

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Prevalence These questions consider the frequency of disease at a certain point in time, and are best answered by cross-sectional studies and surveys.

What is the prevalence of cardiac disorders in Welsh Section A mountain ponies?

**PICO:** In [horses], does [being a Welsh Section A mountain pony] compared with [being any other breed] increase the [prevalence of cardiac disorders]?

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#### Where to find the evidence?

Ideally, clinical decisions will incorporate the most current and relevant scientific research, but where is the best place to search for the evidence base for veterinary medicine?

Unfortunately, there is no "one-stop-shop", and so a variety of search tools, databases and methods must be used.

- Look for synthesised evidence
- Search the bibliographic databases
- Review the references of relevant papers
- Read key publications
- Contact researchers and experts
- Use unpublished data

Reporting a search: PRISMA

http://prisma-statement.org/PRISMAStatement/

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- Does the paper have the right study design to answer my clinical question?
- Is the quality of the paper good enough to help me answer my particular question?
- Is the paper relevant to my clinical question, my population or my patient?
- Not everything you read is true!
- Scientific literature is extremely important, but not always entirely valid.
- Which level of evidence does the paper provide?

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#### **Evidence hierarchy**

More RCTs

Randomized Clinical

**T**rials

Non-randomized clinical trials

Observational studies (case-control, cohort, cross-sectional)

Case studies, case series, anecdotes, personal opinion

#### Hierarchy level: Anecdote

- Acute diarrhea is a common, often self-limiting, cause of presentation for veterinary care, yet there is a paucity of data on frequently-prescribed treatments.
- Two anecdotally-recommended treatments: a probiotic and metronidazole
- Sixty dogs without concurrent comorbidities were randomized into three treatment groups (placebo, probiotic, metronidazole).
- Dogs presenting with acute diarrhea were treated.
- Acceptable fecal consistency after  $3.5\pm2.2$  days when receiving probiotic,  $4.6\pm2.4$  days with oral metronidazole, and  $4.8\pm2.9$  days with placebo.
- p = 0.17

#### Hierarchy level: Non-random allocation trials

- Bias is a major problem with non-randomised trials.
- True randomisation involves the use of a formal randomising method and should not be confused with the arbitrary assignment of animals to treatments.
- Selecting alternate cases for treatments, or using a different treatment on certain days of the week are examples of arbitrary selection and may introduce confounding factors, however unlikely it may seem.
- True randomisation is extremely easy to achieve and is only avoided as a result of ignorance or laziness.

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#### SIGN classification for grading evidence

- 1++ High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
  - 1+ Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
    - 1- Meta-analyses, systematic reviews, or RCTs with a high risk of bias
- 2++ High-quality systematic reviews of case-control or cohort studies High-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
  - 2+ Well-conducted case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
    - 2- Case-control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
    - 3 Non-analytic studies; for example, case reports, case series
    - 4 Expert opinion

SIGN: Scottish Intercollegiate Guidelines Network

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#### **Applying evidence to practice**

- How relevant is the evidence?
- Discuss important evidence
- Prepare a strategy for change:
  - Who?
  - When?
  - What?
  - How?

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 If you're still not convinced that the evidence fully pertains to you, one way to start putting evidence into practice might be to run a sort of 'pilot' to assess the possible effects of your new approach in the context of your practice.

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The only way we can establish if the care of patients is improved by the application of evidence to practice is to measure the effect of the apply stage.

It is vital to assess what we do in practice in order to ensure our practice is moving with the times and adapting and responding to the advances in the profession.

A simple way of assessing your own performance as an EBVM practitioner is to **ask yourself some questions**, and to provide truthful answers!

Some suggested questions are:

- Do I identify and prioritise problems to be solved (specifically in relation to what information I need to make my best decisions)?
- Do I perform a competent and complete examination of each animal, in order to establish the likelihood of alternative diagnoses?

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- Do I have an accurate knowledge of disease manifestations, the sensitivities and specificities of the clinical signs I am looking for, and the frequency of occurrence of different combinations of clinical signs within a disease?
- Do I search for missing information when I know I am lacking it?
- Do I appraise information I am given in terms of scientific validity?
- Do I understand terms such as specificity and sensitivity, which enable me to interpret important information in my daily practice?
- Do I have the resources to access the Internet and use these to the best of my ability?
- Am I aware of the veterinary information databases?
- Do I actively consider if the application of new information I am given is scientifically justified and sensible for the situation to which I might apply it?
- Do I explain the pros and cons of the different options to owners, taking into account and making clear their different utilities?

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#### Narrative reviews:

- Tend to cover a subset of studies based on availability or author selection.
- This can introduce an element of selection bias.

# Systematic reviews:

- Employ standardised and rigorous methodologies to review scientific literature, with a view to minimising bias.
- They conduct a comprehensive literature search to identify, appraise, and synthesise all the relevant studies on a particular topic.
- They will formally and openly report the sources they use as well as the search strategies used to find those sources, so that searches can be peer-reviewed and replicated.
- Evidence synthesis:

meta-synthesis: if a systematic review inspects qualitative data meta-analysis: if homogenous quantitative evidence is assessed

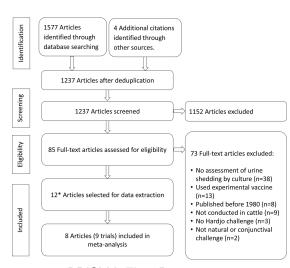
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"A collection of techniques whereby the results of two or more independent studies are statistically combined to yield an overall answer to a question of interest."

- Fixed effects (FE) model:
  - assumes that each observed individual study result is estimating a common unknown overall pooled effect
  - the research question concerns whether treatment has produced an effect, on the average, in the set of studies being analysed
  - there is **no interest in generalising** the results to other studies.
- Random effects (RE) model:
  - assumes that each individual observed result is estimating its own unknown underlying effect
  - is estimating a common population mean
  - allows for the existence of between-study heterogeneity as well as within-study variability
  - when the research question involves extrapolation to the future

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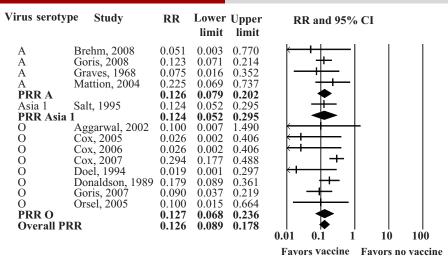
- Leptospirosis is a zoonosis often associated with occupational exposure from livestock that can be prevented by animal vaccination.
- Several trials have assessed vaccine efficacy in livestock but there have been no attempts to evaluate these trials jointly.
- This systematic review and meta-analysis aimed to estimate vaccine efficacy to prevent urinary shedding of Leptospira serovar Hardjo (Hardjo) in cattle.



# PRISMA Flow Diagram

Trial	Vaccinated Shed(+) Total		Con Shed(+)			Relative Risk [95% CI]
Cortese et al., 2014	0	41	10	11	<b>∢•</b>	0.014 [0.001, 0.216]
Zimmerman et al., 2013	4	18	18	18	<b>⊢</b>	0.243 [0.108, 0.547]
Rinehart et al., 2012b	0	21	11	11	<b>←</b>	0.024 [0.002, 0.368]
Zuerner et al., 2011	0	8	7	7	•	0.059 [0.004, 0.881]
Bolin et al., 1989a	1	15	5	5	<b></b>	0.102 [0.022, 0.478]
Broughton et al., 1984_Calves	0	9	6	10	•	O.085 [0.005, 1.318]
Broughton et al., 1984_Heifers	2	8	9	10	<b>├</b>	0.278 [0.082, 0.939]
Allen et al., 1982	2	39	13	42	<b>⊢</b>	0.166 [0.040, 0.688]
Mackintosh et al., 1980	2	8	9	10	l—————————————————————————————————————	0.278 [0.082, 0.939]
Mantel-Haenszel fixed effects model				•	0.113 [0.068, 0.190]	
Bayesian random effects mod	el				•	0.101 [0.051, 0.194]
					0.010 0.200 1.0	00

Sanhueza et al. (2018)



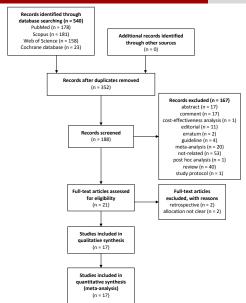
FMD: Forest plot of the relative risk (RR) of the clinical disease in vaccinated cattle for each of the 13 included studies, the pooled RR (PRR) per virus serotype and the overall PRR together with the 95% CI.

Halasa et al. (2011)



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- The greatest challenges for endoscopists performing biliary therapy in endoscopic retrograde cholangiopancreatography (ERCP) are to achieve selective biliary cannulation and prevent post-ERCP pancreatitis (PEP).
- Non-steroidal anti-inflammatory drugs have proven prophylactic effect in PEP.
- Diclofenac and indomethacin are the most studied drugs for preventing post-ERCP pancreatitis (PEP).
- Our aim was to evaluate all prospective trials published in full text that studied the efficacy of diclofenac or indomethacin and were controlled with placebo or non-treatment for the prevention of PEP in adult patients undergoing ERCP.

Author (Year)	Trea Events	ited Total	Con Events	trol Total					Weight	Risk Ratio [95% CI]
Diclofenac										
Abu-Safieh et al. (2014)	6	89	12	93	<b>—</b>		⊣		5.18%	0.52 [0.20, 1.33]
Cheon et al. (2007)	17	105	17	102		_ <del>_</del>	<del>-</del>		8.13%	0.97 [0.53, 1.80]
Khoshbaten et al. (2008)	2	50	13	50	<del> </del>	→ :			2.78%	0.15 [0.04, 0.65]
Lua et al. (2015)	7	69	4	75		<u> </u>	-	<b>→</b>	3.75%	1.90 [0.58, 6.22]
Murray et al. (2003)	7	110	17	110	$\vdash$				5.92%	0.41 [0.18, 0.95]
Otsuka et al. (2012)	2	51	10	53	<b>⊢-</b> -	——:			2.68%	0.21 [0.05, 0.90]
Park et al. (2015)	22	173	20	170		<del> </del>			8.68%	1.08 [0.61, 1.91]
Senol et al. (2009)	3	40	7	40	⊢		$\dashv$		3.33%	0.43 [0.12, 1.54]
Zhao et al. (2014)	4	60	12	60	<b>⊢</b> •	——(			4.31%	0.33 [0.11, 0.98]
RE model for subgroup	70	747	112	753						0.57 [0.36, 0.92]
Heterogeneity: 1 <sup>2</sup> = 54.29%, C Test for overall effect: p = 0.0	Q(df = 8) : 208	= 17.24,	0 = 0.0277							
	4	82	17	84		. :			4.470/	0.04 [0.00 0.00]
Andrade-Dávila et al. (2015) Döbrönte et al. (2012)	4 11	130	11	98		¬ :				0.24 [0.08, 0.69] 0.75 [0.34, 1.67]
Döbrönte et al. (2014)	20	347	22	318	-					0.83 [0.46, 1.50]
Elmunzer et al. (2012)	20 27	295	52 52	307		_ :	_			0.54 [0.35, 0.84]
Levenick et al. (2016)	16	223	11	226	,		_			1.47 [0.70, 3.11]
Montaño Loza et al. (2007)	4	75	12	75		_ i		'		0.33 [0.11, 0.99]
Patai et al. (2015)	18	270	37	269						0.48 [0.28, 0.83]
Sotoudehmanesh et al. (2007		221	15	221						0.47 [0.19, 1.12]
RE model for subgroup	107	1643	177	1598		''			3.0178	0.60 [0.43, 0.82]
Heterogeneity: $I^2 = 40.73\%$ , C Test for overall effect: $p = 0.0$	Q(df = 7) :			1596		•				0.60 [0.43, 0.62]
RE model for all studies	177	2390	289	2351		•			100.00%	0.60 [0.46, 0.78]
Heterogeneity: I <sup>2</sup> = 45.52%, C	Q(df = 16)	= 29.93	p = 0.0184			· .			0(-15 4)	0.0005 0.00
Test for overall effect: $p = 0.00$	JUI						est for subgrot	ip airrerenc	es. Q(at = 1)	= 0.0005, p = 0.98
					1		1	ı		
					0	1	2	3		
						Rick F	Ratio 95% CI			

- Cochrane Library □
- Joanna Briggs Institute □
- Campbell Collaboration □
- Centre for Evidence-Based Medicine □
- NHS Centre for Reviews and Dissemination □
- Bandolier □
- PubMed Clinical Queries: Find Systematic Reviews ☑

- RCVS Knowledge ☑
- The Centre for Evidence-based Veterinary Medicine at the University of Nottingham ☐
- Veterinary Evidence ☑

#### References

- Cockcroft, P. D. and M. A. Holmes (2003). Handbook of evidence-based veterinary medicine. Blackwell Publishing Ltd.
- Cuzick, J. (2005). Forest plots and the interpretation of subgroups. The Lancet 365(9467), 1308.
- Greenhalgh, T. (2010). How to read a paper: The basics of evidence-based medicine. John Wiley & Sons.
- Halasa, T., A. Boklund, S. Cox, and C. Enge (2011). Meta-analysis on the efficacy of foot-and-mouth disease emergency vaccination. Preventive veterinary medicine 98(1), 1–9.
- Heneghan, C. and D. Badenoch (2006). Evidence-based medicine toolkit. Wiley Online Library.
- Hothorn, T. and B. S. Everitt (2014). A handbook of statistical analyses using R. Chapman and Hall/CRC.
- Kastelic, J. (2006). Critical evaluation of scientific articles and other sources of information: an introduction to evidence-based veterinary medicine. Theriogenology 66(3), 534–542.
- Patai, Á., N. Solymosi, L. Mohácsi, and Á. V. Patai (2017). Indomethacin and diclofenac in the prevention of post-ERCP pancreatitis: a systematic review and meta-analysis of controlled trials. Gastrointestinal Endoscopy 85(6), 1144–1156.
- Sackett, D. L., W. S. Strauss, Sharon E Richardson, , W. Rosenberg, and R. B. Haynes (2000). Evidence-based Medicine: How to Practice and Teach EBM. Churchill Livingstone.
- Sanhueza, J., P. Wilson, J. Benschop, J. Collins-Emerson, and C. Heuer (2018). Meta-analysis of the efficacy of leptospira serovar hardjo vaccines to prevent urinary shedding in cattle. *Preventive veterinary medicine* 153, 71–76.
- Shmalberg, J., C. Montalbano, G. Morelli, and G. J. Buckley (2019). A randomized double blinded placebo-controlled clinical trial of a probiotic or metronidazole for acute canine diarrhea. Frontiers in Veterinary Science 6, 163.
- Thrusfield, M., R. Christley, H. Brown, P. J. Diggle, N. French, K. Howe, L. Kelly, A. O'Connor, J. Sargeant, and H. Wood (2018). Veterinary Epidemiology (4th ed.). Oxford, UK: Wiley.