How to Start Practicing Evidence-Based Veterinary Medicine: A Practical Guide for Over-Worked Practitioners

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1. Introduction

Although many busy clinicians may appreciate the compelling rationale for the scientific approach employed by evidence-based veterinary medicine (EBVM), they may also question how it can possibly be incorporated into the routine of a busy equine clinic. In an academic institution with its wealth of students, library resources, and possibly, time, we might be able to turn every clinical decision into a comprehensive search for the evidence and then appraise every paper. This is clearly not a practical option when working out of the back of a truck or dealing with acute problems in the barn. Therefore, what practical steps can be taken to adopt an EBVM philosophy while simultaneously retaining one’s sanity and work/life balance?

This paper describes three scenarios where an EBVM approach can be adopted to ensure that the best evidence is incorporated into the clinical decision-making process. The examples represent situations when a veterinarian might traditionally have relied on sources of information such as a review article or a textbook to make the decision. The examples describe a more systematic or methodical approach that does involve some additional time and effort, but it is not excessively burdensome. The examples also attempt to illustrate the process starting from the clinical problem presented by the client and/or patient through to the final veterinary decision. The first example discusses the process that many veterinarians are already using, but this paper emphasizes appraising the evidence from a single paper. The second example illustrates how evidence from a number of papers on the same topic might be compared, and the third example introduces the formal presentation of evidence in the form of a critically appraised topic.

2. Example One: Complications of Equine Castration

A colleague returns from a third revisit to check up on a castration that was performed 2 wk ago and subsequently, has become infected (in a standing horse, open technique). Our clinic has good surgical facilities, and although we have traditionally performed most of our castrations this way, some castrations are performed at the clinic under general anesthesia. A tired and irritable veterinarian asks if there is recent evidence that would support the view that castrations are best performed closed on a recumbent patient. We know that the compli-
The complication rate of field surgery is greater than fully aseptic surgery, but what are the actual rates? This begs the clinical question: “what are the complication rates of standing open versus recumbent closed castration in the equine?”

What information is in the literature? The quickest and easiest way to find papers is to search the National Library of Medicine database; this is performed using Pubmed. Typing “equine castration complications” into the search textbox yields the titles of 74 papers. Many of the papers listed are clearly of no use for our question, but a paper by Mason et al. published in the Equine Veterinary Journal stands out as likely to be helpful.

The paper describes a retrospective survey of 217 horses castrated by a veterinary clinic in Newmarket, United Kingdom, over an 18-mo period. There were 121 open standing castrations and 96 recumbent closed castrations. Complications and costs of the two groups were compared.

There are three questions that we have to ask ourselves. First, are the techniques and types of horse relevant for our clinic? In this case, they are not identical but not so different that we are not interested in the results. Second, can we trust the results? Anything that would clearly bias or confound the results will make us suspicious. If all the standing castrations were performed by one surgeon and all the recumbent castrations performed by another, then we might just be looking at a comparison between one good surgeon and one bad surgeon. Third, were all the standing castrations performed at the same premises? If they were at the same place, then we might just be looking at the effect of particularly good or bad husbandry or yard staff. All we need to know is in the materials and methods section, and although we can find minor flaws and some unanswered questions, we fail to find a major problem that would stop us from looking at the results.

In the results section, we find out that the complication rate in the standing castration group was 27% of 121 and that the complication rate in the recumbent castration group was 6% of 96. The complication rates are 22% and 6%, respectively.

Needless to say, the paragraph in the paper is more complex than this information, because it also reports the results of the statistical analysis. With ~100 horses in each group and a reasonably substantial difference of 16% between the two groups, we might not be surprised to find that this result is statistically significant. However, when the number of subjects is small, even quite large differences may not be significant. The \( \chi^2 \) test used here is the appropriate way to establish that the difference observed is likely to be a true observation and not just a chance finding. Another piece of information presented in this paragraph is an uncertainty range for each proportion. We are told that the 95% confidence intervals are 15–30% for the standing castrations and 1–11% for the recumbent castrations. These ranges give an estimate for where the true result lies. If we were to replicate the study 100 times, we would expect that an average of 95 of 100 results would fall in this range. If the confidence intervals do not overlap, we expect that the difference will be statistically significant (at the 5% significance level).

It is interesting to translate the absolute risks to the number needed to treat (NNT). This figure represents the number of castrations you would have to perform to have one less complication if you were to choose to undertake a recumbent closed castration rather than a standing open castration. The absolute risk reduction (ARR) is 22%–6% or 16%. The NNT is calculated as 1/ARR. In this case, 1/0.16 = 6.25 or 6, because we do not operate on a quarter of a horse. One way to compare the two techniques is to say that for every six horses castrated in the clinic, we will have one less patient with complications.

But, of course, the reason our clients prefer standing castrations is economic. This paper has calculated the average cost of the four possibilities (standing uncomplicated, standing with complications, recumbent uncomplicated, and recumbent with complications) using the cost of a standing castration as a standard cost unit. If we factor in the complication rates, we can calculate the average cost of the two techniques as illustrated in the decision tree shown in Figure 1. Thus, the average cost of a standing castration is 1.18 standard cost units compared with an average cost of 3.14 standard cost units for a recumbent castration. It seems unlikely that we are going to see a big increase in the number booked in for castrations under general anesthetic.

A final interesting piece of information contained in this paper is a consideration of the clinical treatment of complications after open castration. Horses treated with repeated opening and flushing of the scrotal cavity with 10 ml of 3% hydrogen peroxide in conjunction with IM injection of procaine benzyl penicillin for 5 days were compared with horses that received flushing only, penicillin only, or trimethoprim sulphonamide only. Only 1 of 8 horses receiving the more aggressive treatment required further treatment; 10 of 17 horses receiving more conservative treatment required additional treatment. The differences were statistically significant and translate to an ARR of 46% with a NNT of 2. This is good evidence to support this treatment option.

Collecting the equivalent data in our own practice would not be difficult. This would serve two purposes. First, it would enable us to compare our own performance with a published benchmark figure, and second, we could make a decision on best practice for our own clinic patients based on the population of horses and veterinarians that will be the best predictor of our performance.

3. Example Two: Risk of Death Associated With Equine General Anesthesia

After the third death of a horse under general anesthesia, the veterinarians working in a large equine
clinic have a discussion about risks associated with anesthesia. The client waiver documentation indicates that the risk is ~1% with a considerably increased risk with colic surgery. Where did the 1% figure come from? Is this clinic’s mortality figures higher or lower than this figure?

A member of staff is given the task of investigating. Taking the EBVM approach, the staff member turns the problem into an answerable question.

Patient: general equine population (no restrictions)
Intervention: general anesthesia
Comparison: not applicable
Outcome: death, during or shortly after surgery

From this, it would seem that a Medline search on Pubmed using the words equine, anesthetic, and death might be appropriate. This search yields ~16 papers, of which 4 seem directly relevant. The search is repeated with the word deaths substituted for death, and it reduces the yield to two result. Re-spelling the word anaesthetic with anesthetic also changes the papers returned. It is important to note at this stage that Pubmed is not a perfect searching tool and the Medline database is not comprehensive. Although the majority of veterinary journals are included, some are not, and some journals may not be included before a certain date.

The useful papers we find are Bidwell et al., Johnston et al., and Mee et al. An additional two papers, a second paper by Mee et al. and a second paper by Johnston et al. were not revealed by the Pubmed search but were identified by looking through the lists of references in the papers. The second paper by Johnston et al. incorporates the results from the first paper; therefore, the first paper is no longer considered. The papers providing the evidence are summarized in Table 1.

The methods section of the paper is examined to look for any potential source of bias or confounding factor that might cast doubt on the likely truth or value of the results. An obvious source of bias would be the spurious exclusion of any patients that might distort the result; all the papers seem to be satisfactory in this regard. All the studies describe results from a large number of patients, but only one of the studies is a survey of multiple clinics. The main source of bias in these papers would be any aspect of the caseload or anesthetic procedure that might reduce or increase the mortality risk compared with our own clinic. The multiclinic study included 149 participating clinics from 19 countries including the United States. This study was also
the only prospective survey, which should have helped to assure the quality of the data. Although it should be acknowledged that retrospective data on mortality are unlikely to be flawed, the standardization of recording of anesthetic data such as duration, agents used, surgical position, etc. is easier to achieve in a prospective study design. If we were to rank the general quality of each study, we consider the Johnston et al. paper as providing the best evidence based on the quality of the study design (prospective and multiple clinics) and the number of subjects (~42,000). The remaining studies have similar designs; however, because the Bidwell et al. study includes >10 times the subjects of the Mee et al. studies, it should be accorded more weight when considering methodology alone. Readers should be aware that any comments on quality are only relevant in the context of answering the clinical question under consideration. Readers should be aware that many studies provide a valuable contribution to our understanding even when they are not able to be used for clinical decision making.

There is a wealth of information contained in the papers we have found concerning many aspects of perioperative mortality and potential risk factors, but they do not help us answer our particular question. One thing we do have to address is our case definition. Horses die at or around the time of surgery for many reasons: they may be euthanized, they may die during surgery, they may die after surgery from a complication, and they may die shortly after surgery for a reason not associated with either the surgery or the anesthetic. In this case, we decide to make no distinction. Before surgery, clients probably want to know the total or overall risk. To them, it is a subtle distinction between the surgeon’s decision that the condition is inoperable or the horse’s development of complications during recovery. Inevitably, each of the papers reports the results in a different way. Mee et al. separates the results from their study into two papers that analyze the results from elective surgery and the results from emergency surgery. It is clear from reading the two papers together that they cover the total surgical load that received general anesthetics during the study period. Therefore, it would seem appropriate to combine the results from the two papers to obtain an overall mortality figure. All the studies provide some breakdown of the results according to the nature of the surgery or presenting condition. Our personal experience tells us that emergency surgery, particularly colic surgery, represents a greater mortality risk, and this is confirmed by the results from our literature search. It is clear from reading the two papers together that they cover the total surgical load that received general anesthetics during the study period. Therefore, it would seem appropriate to combine the results from the two papers to obtain an overall mortality figure. All the studies provide some breakdown of the results according to the nature of the surgery or presenting condition. Our personal experience tells us that emergency surgery, particularly colic surgery, represents a greater mortality risk, and this is confirmed by the results from our literature search.

Although it is of some use to let clients know overall mortality risk, we do not want to be overly pessimistic with clients facing elective surgery or overly optimistic with clients whose horses are admitted for more risky surgery. Although Mee et al. categorizes surgery as emergency or elective, these are, to some extent, subjective, and this distinction is not made in the other studies. However, it is possible to obtain separate figures for colic and non-colic surgery from all three studies. This is a practical

<table>
<thead>
<tr>
<th>Paper</th>
<th>Study Type</th>
<th>Population</th>
<th>Result</th>
<th>Proportion With Confidence Interval (%)</th>
<th>NNH</th>
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<tbody>
<tr>
<td>Mee et al.⁵</td>
<td>Retrospective</td>
<td>Elective surgical cases at a UK teaching hospital</td>
<td>46/1279 total anesthetics</td>
<td>3.6 (2.7–4.8)</td>
<td>20–37</td>
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<tr>
<td>Mee et al.⁶</td>
<td>Retrospective</td>
<td>Emergency surgical cases at a UK teaching hospital</td>
<td>312/995 total anesthetics</td>
<td>31 (29–34)</td>
<td>2–3</td>
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<td>Mee et al.⁵,⁶</td>
<td>(combined results)</td>
<td>Retrospective survey</td>
<td>All surgical cases at a UK teaching hospital</td>
<td>31/203 non-colic surgery 31/203 non-colic surgery 312/995 total anesthetics</td>
<td>2–3</td>
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<tr>
<td>Bidwell et al.³</td>
<td>Retrospective</td>
<td>All anesthetics at a U.S. private referral practice</td>
<td>42/17,961 total anesthetics</td>
<td>0.23 (0.17–0.32)</td>
<td>312–588</td>
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<tr>
<td>Johnston et al.⁷</td>
<td>Prospective</td>
<td>Multiple international clinics (62)</td>
<td>7/1046 colic surgery 35/16,915 non colic surgery 785/41,824 total anesthetics</td>
<td>0.67 (0.32–1.4) 0.20 (0.15–0.29) 1.9 (1.8–2.0)</td>
<td>71–312</td>
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<td>328/35,107 non-colic surgery 457/6717 colic surgery</td>
<td>0.9 (0.84–1.0) 6.8 (6.2–7.4)</td>
<td>100–119</td>
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Table 1. Summary of the Methodology and Main Results From Papers Reporting the Results From Studies Attempting to Measure the Risk of Perioperative Mortality Associated With Surgery Requiring General Anesthesia.
and useful distinction when providing advice to clients. The summarized results from the studies are shown in Table 1. Some arithmetical manipulation was required to produce the standardized results in the table and to produce the confidence intervals. The confidence intervals can be readily calculated using one of the many statistical calculators available on the Internet such as that found on the VassarStats website. A 95% confidence interval represents the range within which there is a 95% probability that the true result lies within the given range. For clinical purposes, 95% confidence intervals are a useful standardized method of conveying the uncertainty range. They generally indicate whether or not a result is statistically significant at the two-sided, 0.05 level of significance (when they do not cross the no-difference point). Also, they convey the uncertainty or imprecision of an estimate, and they incorporate information about the sample size involved. In the results from these papers where large sample sizes were involved, the confidence intervals are quite narrow, but when sample sizes are small, the breadth of the confidence intervals may render the results unusable. The final calculation provides the number needed to treat divided by the harmed; this represents the number of patients that will produce one extra good or bad result.
**Conclusion:**

There is reasonable evidence that dantrolene sodium is an effective prophylactic treatment for the prevention of RER in Thoroughbred horses. Neither of the two papers describing clinical trials is of sufficient power to provide conventional statistical confidence in the absolute risk reduction (see notes below). However, the best evidence available, based on the results from these two studies, suggests that dantrolene is 100% effective in preventing an episode of exertional rhabdomyolysis in susceptible animals. Different dosing regimes were used in the two trials; the lower dose of 800mg/horse given 1 hr before exercise would appear to be sufficient.

**References:**


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1 The trial described by Edwards et al (2003) used a well-defined, clinically relevant population (Thoroughbreds in training) which had returned to exercise after a two-day lay off on two separate occasions (following public holidays). The horses used by McKenzie et al (2004) were related horses with a history of RER that were maintained in a university facility. These horses might be regarded as a less clinically relevant population as they may not represent the type of spontaneous case seen by equine practitioners.

2 The case definition used has been created for the purposes of this CAT. In both clinical trials the authors concentrated on the actual differences in plasma CK levels following exercise regardless of any other clinical manifestation of disease. An arbitrary level of >900iu/l was selected as a case definition to provide a means of counting the number of animals which might be described as constituting a case of exertional rhabdomyolysis (ER). Clinical cases of ER may exhibit considerably greater levels of CK and it should not be implied that lower CK levels may not be associated with clinical signs of ER.

3 The key results are presented as Absolute Risk Reductions (ARR) and Relative Risk Reductions (RRR). The ARR indicates the proportion of all horses in the treatment group that have an improved clinical outcome as a result of the intervention (dantrolene in this case) in order to have one animal with a favourable outcome (i.e. to prevent one horse developing exertional rhabdomyolysis). The NNT is calculated as the inverse of the ARR (1/ARR). When a treatment is 100% effective the NNT = 1 (every time you treat a patient we have an extra favourable outcome).

4 The NNT (number needed to treat) is a figure representing the number of animals that would need to receive the intervention (dantrolene in this case) in order to have one animal with a favourable outcome (i.e. to prevent one horse developing exertional rhabdomyolysis). The NNT is calculated as the inverse of the ARR (1/ARR). When a treatment is 100% effective the NNT = 1 (every time you treat a patient we have an extra favourable outcome).

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As part of the appraisal process for a CAT the author would normally establish the confidence intervals of the ARR (and any values derived from it). Even when the results would indicate complete success it is not possible to provide a meaningful estimate of the confidence intervals of the results when the numbers involved are less than 5. Although it may be argued that Fisher’s Exact test yields a one-tailed probability value of 0.05 for the Edwards trial which would render the result statistically significant the evidence is on the border line. If we could assume that any study that had produced a negative result had been published (sadly not always the case) we might feel that the repetition of the result in both studies adds to the weight of evidence. In both the clinical trials appraised statistical significance was achieved when the overall analysis of the changes in plasma CK levels were examined. It is only when the data is converted to ‘clinical cases’ that it becomes impossible to establish statistical certainty (or to be more exact – a lack of uncertainty) due to the low numbers of ‘cases’.

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outcome when subject to a particular intervention, and it is calculated as the inverse of the absolute risk (e.g., a 5% risk gives a NNT of 20).

The clinical conclusion from the evidence presented in the papers will depend on how well the patient population in our clinic correlates with the populations surveyed in the particular studies. The total anesthetic risk will depend on the relative numbers of emergencies or colics compared with our non-emergency caseload. The Mee et al. study is heavily biased in this way and is unlikely to reflect the risks seen in a general equine practice. The Johnston et al. study provides evidence from the broadest population base, and unless our clinic profile closely matches that described in another study, it should be used as the best source from which to estimate the risk of perioperative mortality.

Returning to the scenario presented at the beginning of this section, we can say that the best evidence in the literature indicates that we can expect one perioperative fatality for every 100–119 general anesthetics for non-colic surgeries. For colic surgery, we can expect a fatality for every 13–16 cases. Using a figure of 1% (or 1:100) when communicating with clients, the risks associated with non-colic surgery seems to be justified.

It is interesting that the Bidwell et al. study yields NNT figures of 344–666 for non-colic surgery and 71–312 for colic surgery. This indicates that a lower level of fatalities is achievable, although the Johnston et al. survey suggests that this clinic is performing far better than the majority of equine clinics. The best advice on the risk of mortality for our clients is that derived from our own recent records. We should keep a track of our own performance; this enables us to monitor possible deterioration of our performance and also allows comparison of our results with those of colleagues in other clinics as part of a clinical audit process. It is essential that we calculate the confidence intervals for our own figures, particularly if the number of general anesthetics is relatively low. This should help us avoid false interpretation of a particularly good or bad result when the confidence intervals are quite wide.

4. Example Three: Prevention of Exertional Rhabdomyolysis

Having just finished treating a client’s horse for tying up (exertional rhabdomyolysis [ER]), a client asks for advice about preventing this condition; the horse in question is used for eventing and has a history of this condition. When discussing this with colleagues or remembering an article we have read, we learn that a drug called dantrolene has been suggested as a suitable treatment when other dietary or exercise management techniques fail to control the condition. Before embarking on this treatment option, we want to establish the probability that this treatment is going to work so that we can advise the client appropriately.

Our decision to look for and appraise the evidence in this case is motivated by the fact that we have not used this drug before in our clinic. Additionally, it will be an “off label” use of the drug, and it provides an opportunity to discuss our clinic’s approach to ER at one of our monthly educational gatherings over pizza and beer.

The first stage is to turn our clinical problem into an answerable question. Patient, intervention, comparison, and outcome (PICO) is often used to provide a useful checklist.

- Patient: 6-yr old, Warmblood mare in athletic work with a history of ER
- Intervention: a preventive pharmacological treatment
- Comparison: any drug that will prevent ER
- Outcome: the prevention of ER

At first, this might seem to be a slightly tortuous way of formulating what is an obvious question. However, it is useful to focus on particular characteristics of the patient that need to be considered when looking at the evidence from clinical research performed on very different animals. It is also valuable to consider other interventions or comparisons.

The remaining part of the process requires a search of the scientific literature and the appraisal of any relevant clinical research papers. A good way of summarizing this is to write a critically appraised topic (CAT). An example of a CAT on the use of dantrolene in ER is shown in Figure 2.

This CAT follows a format that is used on the BestBET’s website, which contains a large number of CATs produced mainly by and for emergency doctors working in human medicine.

This CAT seeks to appraise the current literature on the use of dantrolene to prevent ER in horses. The CAT starts with a three-part question that carefully defines the population, intervention, and outcome. These elements are important, because they define the literature from which the conclusions are to be reached. In other words, they provide the definition of the literature search. It also helps to describe the clinical scenario in which the CAT might be used; this is provided in the next section.

Having established the clinical question, the first task in the authoring process is to perform the literature search. In this case, a search of the National Library of Medicine database, Medline, was performed using Pubmed. There have not been many papers published on the use of dantrolene in horses, and therefore, a relatively simple query consisting of the terms dantrolene and equine was used in this case. The results were 11 papers of possible interest. The inclusion of the search terms helps readers and potential updaters of the CAT to repeat the search at a later date and identify any papers that should also be considered that were not ap-
praised when the CAT was first written. From the titles and abstracts that result from the literature search, it is possible to eliminate any that are not of direct relevance to the question. In this case, any paper that does not describe the use of dantrolene in the treatment of ER is not directly relevant to our question. If we were asking a question about adverse reactions to dantrolene, we might include information from the use of the drug in other conditions. The decision to exclude and include papers from consideration can usually be achieved from reading the abstracts provided by Medline. In this case, the two remaining papers were readily available in journals to which many equine veterinarians already have a subscription (Equine Veterinary Journal and American Journal of Veterinary Research). The full text of these two papers could also be obtained from the journal’s websites (Ingenta and AVMA) for $15–35 per article.

Having obtained full copies of the papers, the next task is to formally appraise the methodology and results. In the two papers providing the evidence here, a cross-over study was performed; therefore, the patients acted as their own controls. The appraisal process is essentially a case of being skeptical—could the way that the study was performed lead to bias? In clinical trials, randomization and blinding are methods that should be used to reduce the likelihood of bias. The peer-review process used by the journal to decide if the papers submitted should be published usually ensures that there are no serious faults or errors. Although objectivity is very important, there is inevitably some need for the author of the CAT to make some judgments and interpretations. The aim of the CAT is to summarize the content of primary research papers into a succinct report of the methods used and results obtained in such a form that they can be applied in a clinical situation. For this CAT, the author needed to provide a case definition that was applicable for both the papers that were appraised. The authors of the original papers had no particular need to do this in the context of their studies, and the fact that they did not provide a case definition is no criticism of their work; however, to develop a clinical conclusion from the combined results, a case definition is required. To some extent, the precise definition used was arbitrary, and veterinarians (or reviewers) may have different views on what they consider important or relevant. The summary of the papers is kept brief and focused on the clinical question being addressed, and if possible, it is best to use a tabular form to allow immediate comparison of the methodology or results from different papers. If the author of the CAT believes it to be valuable to identify particular issues arising from one or more papers, it is best to add these as footnotes.

The question addressed by the CAT is answered in the conclusion that provides the reader with the take home message. Look at all the evidence provided. Does the intervention work? What clinical outcome could a veterinarian expect to obtain based on the evidence from the literature appraised? The author of this CAT concludes that the evidence is good; this is a subjective judgment. The author of the CAT acts as a jurist. What if the only paper on the use of dantrolene had been a single case report? Would this represent good evidence? Although it would certainly be some evidence, we would probably not describe it as good. The readers of the CAT can make their own conclusions on the absolute quality of the evidence.

Although writing a CAT is undoubtedly a more time-consuming task than just quickly scanning the papers and reaching a subjective conclusion that dantrolene seems to work quite well, it is not an overly difficult or time-consuming task. The discipline of organizing one’s thoughts and formatting them in this way is an excellent way of developing appraisal skills. Reading and appraising the source papers inevitably raises side issues or identifies minor problems in the research. It is important to stay focused and only try to address the question at the head of the CAT. Brevity and succinctness are important; a CAT provides a structured set of notes that may be quickly and easily referred to and also updated when necessary. They are not intended to provide a rigid set of clinical guidelines but summarize the evidence provided by the research literature. The best research evidence can then be combined with the clinical judgment of the veterinarian and the patient’s individual circumstances; this information helps the veterinarian arrive at a decision.

In this case, it was decided that there was sufficient evidence that dantrolene would be effective in this case. The evidence was discussed with the client, and a protocol was established to identify high-risk circumstances when prophylactic use of dantrolene would be appropriate.

5. Conclusion

EBVM should be pragmatic rather than dogmatic. We need to develop skills in identifying answerable questions arising from our clinical questions, we need to be able to find the appropriate clinical research papers, and we need to be able to appraise these papers. If we can acquire and apply these skills in our clinical work, we can focus our reading on the literature we need now rather than trying to read everything—the aim is to move toward just-in-time reading and away from just-in-case reading.

References


