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A Review

A Bayesian approach for inductive reasoning to clinical veterinary medicine: The math of experience

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A Bayesian approach (BA) is well-used in veterinary medicine as it has been used for inductive reasoning regarding interventions, treatments and diagnoses. The objectives of the current article were (1) to examine the state of BA used for inductive reasoning in veterinary medical problems and (2) to illustrate how veterinarians update states of knowledge (prior clinical experience) to a new state of knowledge (posterior clinical experience). When veterinarians are managing patients, they start with their inference from history and a clinical sign to an underlying cause using inductive reasoning. In updating from a prior clinical experience to a posterior clinical experience, the strength of evidence plays an important role. Nevertheless, if an experienced veterinarian uses his/her previous experience of a current patient's clinical signs, he/she may not move from the prior clinical experience to a posterior clinical experience and is less likely to change his/her treatment decisions. In comparison, for a novice veterinarian who would have less prior clinical experiences with given clinical signs, his/her prior clinical experience would easily be changed to a posterior clinical experience after taking history and physical examination. In brief, the more prior clinical experience a veterinarian has, the more rapid a diagnosis is made. The stronger the evidence, the more precise inference will be.

Key words: Bayesian, inference, reasoning, inductive, veterinarian.

INTRODUCTION

In clinical practice, experience is an unmeasured aspect in making a diagnosis. To make a diagnosis, veterinarians imply the association from cause to effect. For example, if pigs were infected with influenza A virus

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(IAV), they may present with coughing as their primary clinical sign, or if dogs are exposed to canine parvovirus (CPV), they may present with bloody diarrhea. On the other hand, when managing most patients, veterinarians start their inference from a clinical sign to an underlying cause. The former reasoning (from cause to effect) pathway cannot be made since veterinarians rarely know the true cause of a disease. They have to reason in an opposite direction (from clinical sign to cause). In the statistical perspective, the former pathway of thinking is called “deductive reasoning” while the latter pathway (from clinical sign to cause) is called “inductive reasoning” (Cockcroft, 2008).

Since the 1970s, inductive reasoning has been employed in clinical veterinary medicine (Lorenz, 2009). It was originally called, “pattern recognition” and more recently “problem-oriented approach (POA)” and “evidence-based veterinary medicine (EBVM)”. In the 1980s, the term “evidence-based medicine” (EBM) was minted at McMaster Medical School in Canada (Rosenberg and Donald, 1995). EBM is defined as “the conscientious, explicit, and judicious use of the current best evidence in making decisions about the care of individual patients” (Sackett et al., 1996). EBM can be practiced in any situation where there is doubt about an aspect of clinical diagnosis, or prognosis (Rosenberg and Donald, 1995). In veterinary medicine, EBVM would be defined similarly as it uses the current best evidence to make clinical decisions concerning the care for animal patients. EBVM has been described as “just in time learning (as opposed to just in case learning), science into practice or from publication to patient” (Cockcroft, 2008).

The veterinarian uses all of the information collected from evidence, such as signalment, patient history, physical examination and laboratory results to answer the question, “What is the cause(s) of the problem that is associated with the clinical presentation (that is, disease effect)?” From a statistical point of view, the veterinarian is answering the question, “What is the probability of a potential cause?” For instance, the probability of classical swine fever (CSF) in coughing pigs in the United States (US) may be near zero, since CSF is no longer in the US and will therefore be excluded from the differential diagnosis. Similarly, the probability that dog with bloody diarrhea is infected with CPV is near zero due to the low prevalence of CPV in the US; therefore, CPV will be removed from the differential diagnosis. This type of probability is called “inverse probability”, which is different from the probability (direct probability) of having a sign if an animal is exposed to the agent (Holland, 1986).

Inverse probability is typically used as a basis for making inductively statistical inference and finding the “probability of causes” and future events derived from a past event (starting with the conclusion desired or desirable proposition and seeking for premises which make it true or probable) (Dale, 1999; Hald, 1998). It is “inverse” because it involves inferring backwards from the present day to the past or “from effects to causes” (Fienberg, 2006). The term "inverse probability" is also known as the “Bayesian approach (BA)" (Aldrich, 2008; Bayes and Price, 1763; Fienberg, 2006; Stigler, 1986).

In clinical veterinary medicine, veterinarians always deal with a rapidly changing body of evidence obtained from physical examination, patient history and laboratory results. When new evidence is uncovered, a veterinarian’s clinical decisions may be changed as well as the lists of differential diagnoses will be reduced. A utility of BA for veterinary diagnostic test has been well-addressed elsewhere (Bonde et al., 2010; Branscum et al., 2005; Gardner, 2002; Greiner and Gardner, 2000; Paul et al., 2013; Toft et al., 2005). Therefore, the objectives of the current article were to examine the state of BA used for inductive reasoning in veterinary medical problems and to illustrate how veterinarians update states of knowledge (prior clinical experience) to a new state of knowledge (posterior clinical experience).

A BAYESIAN APPROACH

A Bayesian approach is a statistical method of the conditional distribution of parameters and unobserved evidence, given the observed evidence (Gelman, 2008). It is considered as the natural statistical framework for both EBM and EBVM in order to make decisions that incorporate an integrated summary of the available evidence and associated uncertainty (Ashby and Smith, 2000). It is a more natural formalization of the normal scientific process of evaluating evidence (Dunson, 2001), integrating and synthesizing EBM in a systematic way (Ashby and Smith, 2000). It provides a common framework for problem solving and improving communication and understanding between owners and their animals from different backgrounds (prior experience) (Rosenberg and Donald, 1995). It is used to integrate individual clinical expertise (prior clinical experience) with the best available external clinical evidence from systematic research (Sackett et al., 1996). It is a synthesizing of the available external clinical evidence using Bayesian meta-analysis (Ashby and Smith, 2000). In addition, it can gauge the strength of prior clinical experience by evaluating whether evidence can dominate the prior experience or not (Greenland, 2006). It has been shown that a major change of prior clinical experience would require solid clinical evidence and then clinicians will logically update their prior clinical experience to updated clinical experience (Higgins et al., 2014).

A Bayesian approach was independently developed by Tomas Bayes and Pierre-Simon Laplace over 300 years ago (Aldrich, 2008; Bayes and Price, 1763; Fienberg, 2006; Stigler, 1986). However, the fundamentals of BA have been followed by the Laplace-Jeffreys objective

school, with additional modern refinements (Berger, 2006). The influence of BA can be seen in mathematics, statistics, computer science, bioinformatics, economics, physics, ecosystem, parasitology, and epidemiology as well as in human and veterinary medicine (Ashby and Smith, 2000; Basáñez et al., 2004; Dowd and Meyer, 2003; Fienberg, 2006; Gardner, 2002). A classic example of applying BA in order to make inductive reasoning from an effect to a cause is during 1855 to 1865 in London, England, where John Snow had used BA as his inductive reasoning to scientifically convince audiences that a source of cholera transmission was from a private water supplier company (Koch and Denike, 2006).

Components of a Bayesian approach

A Bayesian approach comprises three mathematical terms: (i) evidence[1], "p(x)" (a.k.a. the marginal likelihood, or the probability of evidence), (ii) the prior experience[2], "p(θ)" and (iii) strength of evidence[3], "p(x|θ)" (a.k.a. likelihood of evidence given a hypothesis). The posterior experience, "p(θ|x)[4]" (a.k.a. updated posterior experience from prior experience after having seen the evidence) is equal to the product of prior experience times strength of evidence divided by the evidence. Mathematically, it is written as:

$$p(\theta|x) = \frac{p(x|\theta) * p(\theta)}{p(x)}$$

Simply, the posterior experience is proportional to the strength of the new evidence times prior experience (Higgins et al., 2012b, 2014). To further illustrate this, we will use an example of coughing pigs, where the posterior experience was reversely inferred from the strength of the new evidence and the prior experience.

Example: Coughing pigs

A veterinarian observes coughing pigs (evidence) and wishes to make a diagnosis (inference) by asking the question, "Is coughing in pigs caused by IAV infection?" He/she needs to inductively infer the cause from a posterior clinical experience (posterior probability) as shown in Figure 1.

However, the coughing could be caused by multiple pathogens including classical swine fever, metastrongylus, *mycoplasma hyopneumoniae*, porcine respiratory coronavirus, classical swine fever virus, porcine circovirus type 2 virus, porcine reproductive, respiratory syndrome (PRRSv) virus, or IAV, etc. (Zimmerman et al., 2012) (Figure 2).

From the Bayesian notation, the theorem is applied to the inference of coughing in pigs caused by IAV infection written as:

$$p(flu|coughing) = \frac{p(coughing|flu) * p(flu)}{p(coughing|flu) * p(flu) + p(coughing|\sim flu) * p(\sim flu)}$$

The denominator is called the "probability of evidence" of coughing event (marginal likelihood). The Bayesian terms, notations and definitions were detailed in Table 1.

Figure 3 numerically illustrates BA (inverse probability) pathway for diagnosing coughing pigs**.** Based on previous experience (prior clinical experience), the veterinarian may expect that 29% of coughing cases are caused by IAV infection, even though multiple swine pathogens can cause some degree of coughing (Choi et al., 2002; Olsen et al., 2000). While the prior knowledge may or may not be accurate, the prior clinical experience is useful to estimate such a percentage when there is lack of clinical information and a need to make a decision for clinical intervention (Higgins et al., 2012a). A Bayesian approach allows the veterinarian to update the probability of IAV infection by obtaining new information given his previous knowledge and the strength of evidence, $p(coughing|flu)$. If the probability of IAV infected pigs having coughing as a clinical sign, $p(coughing|flu)$, is for example 0.3, the posterior clinical experience, $p(flu|coughing)$, is 0.17. The calculation is illustrated in Figure 3. As BA measures a degree of prior clinical experience (hypothesis), from such posterior experience, it is implied from his/her clinical experience that there is a probability of 0.17 that those coughing pigs have IAV infection. Therefore, he/she has less confidence (low probability) concerning his/her prior clinical experience after he/she has had new evidence. In other words, if weak evidence is found, the prior experience stands; when moderate evidence is found, the prior clinical experience and the new evidence can be combined, modifying the moderate posterior clinical experience. If strong evidence is uncovered to discredit the prior clinical experience, this modifies the prior clinical experience, which changes intervention strategies (strong posterior clinical experience). A major change of prior clinical experience would require solid clinical evidence to update prior clinical experience to posterior clinical experience (Higgins et al., 2014). However, it is unlikely to be sufficient to warrant an intervention when using only prior clinical experience for implementing an intervention.

There is first-rate and fallacious evidence for guiding decisions of intervention. For any evidence, we also need to estimate the probability that first-rate evidence is obtained from clinical examination or diagnostic results. Thus, the definition of the observed first-rate evidence is

[1] "x" is data that has been observed.
[2] "θ" is a prior clinical experience about a disease.
[3] "x|θ" is data that have been observed based on a prior clinical experience.
[4] "θ|x" is a potential disease after having seen the data.

Table 1. Representation of the Bayesian terms, notations and definitions related to an example of influenza A virus (IAV) infection.

Bayesian term	Notation	Definition
Prior clinical experience	$p(flu)$	Probability that pigs have IAV infection (prevalence)
The strength of evidence	$p(coughing\|flu)$	Probability that IAV infected pigs are coughing as a clinical sign
-	$p(coughing\|\sim flu)$	Probability that pigs negative to IAV infection have coughing as a clinical sign
-	$p(\sim flu)$	Probability that pigs have no IAV infection
Posterior clinical experience	$p(flu\|coughing)$	Probability that coughing is caused by IAV infection

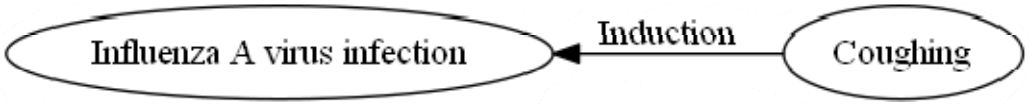


Figure 1. The representation of inductive inference from posterior clinical experience posterior clinical experience (posterior probability).

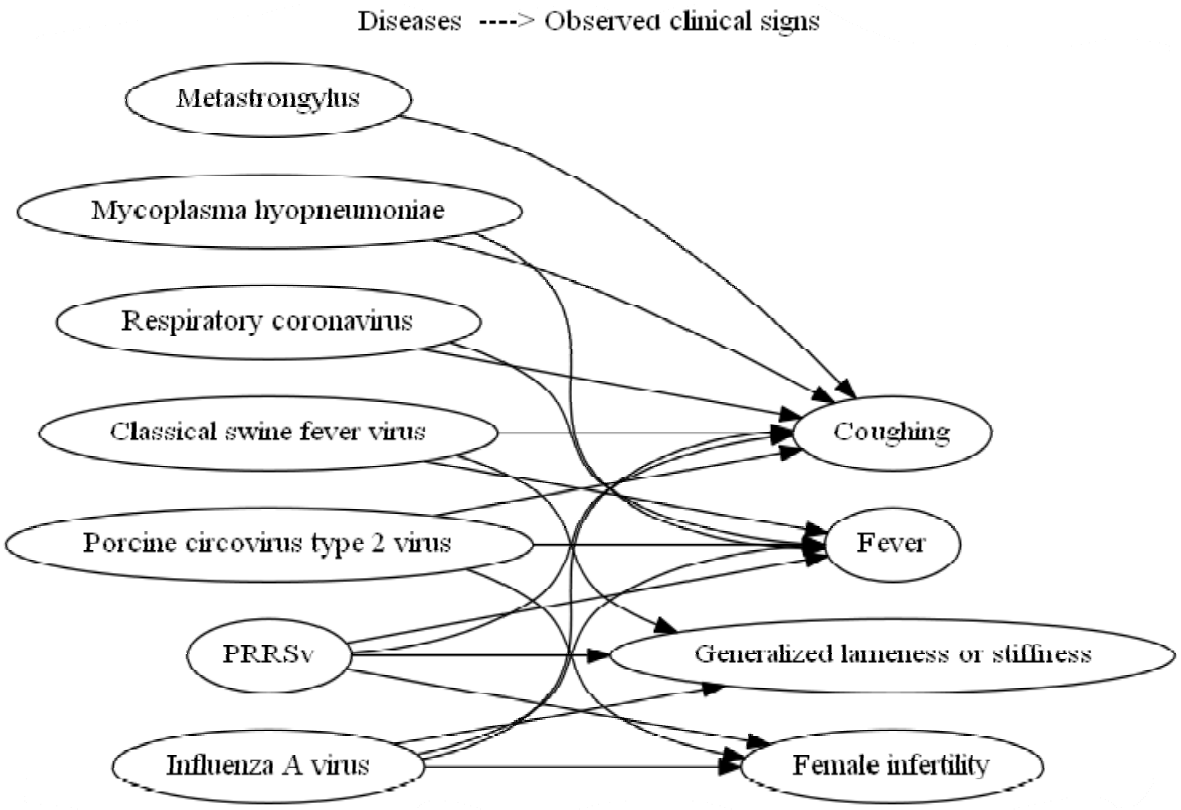
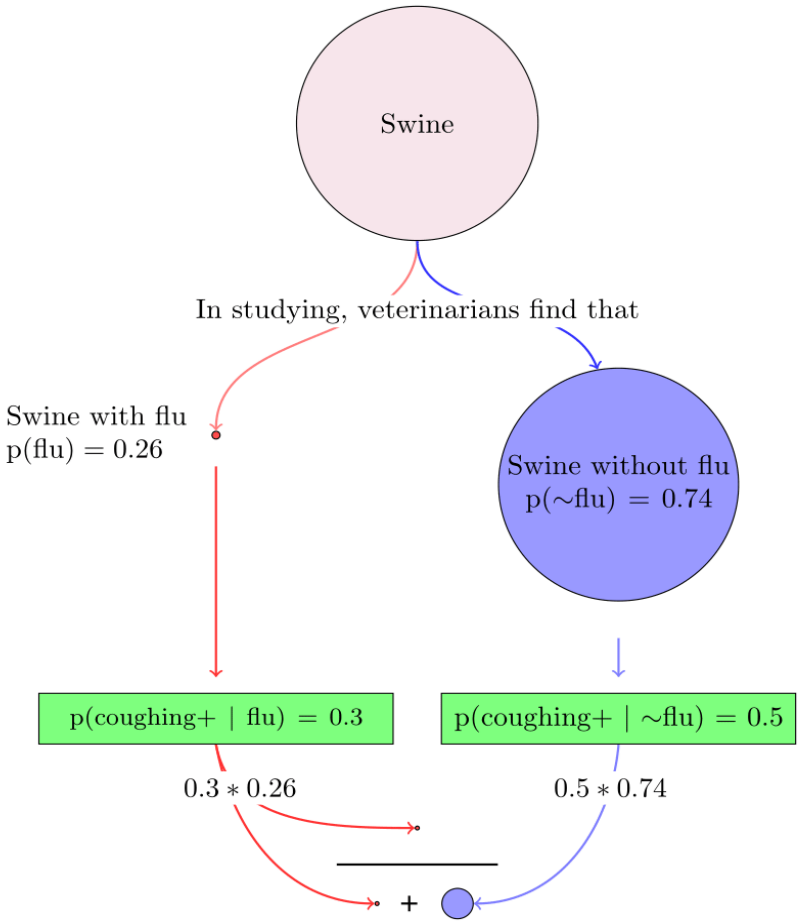


Figure 2. The processes of deduction (from diseases to observed clinical signs) and induction (from observed clinical signs to diseases) used in veterinary inference with an example of partially-selected swine diseases.

useful in the context of diagnosing disease and making an intervention decision. A simple approach may be to increase the sample size to strengthen the evidence given the prior experience. Consider the following



$$p(\text{flu} \mid \text{coughing+}) = \frac{p(\text{coughing+} \mid \text{flu}) * p(\text{flu})}{p(\text{coughing+} \mid \text{flu}) * p(\text{flu}) + p(\text{coughing+} \mid \sim\text{flu}) * p(\sim\text{flu})}$$

$$0.17 = \frac{0.3 * 0.26}{(0.3 * 0.26) + (0.5 * 0.74)}$$

Figure 3. The calculation using Bayes' theorem for inductive inference processes from coughing to influenza A virus infection.

examples; an inexperienced veterinarian is monitoring a healthy sow herd (negative sow herd) for H1N1-IAV using an ELISA test kit with the test specificity = 99.7% (95% CI: 99.5–100%). Randomly, 5 sows were tested at once and one is positive, "p(x)". Given the prior clinical experience "p(θ)" and inductive thinking, the one positive is questioned. He/she is unsure if one positive sample represents 20% (1/5), "p(θ|x)" being the strength of evidence of prevalence of H1N1-IAV given what is previously known (that is, the prevalence of IAV was 29% with 13% SD (Choi et al., 2002; Olsen et al., 2000), by prior clinical experience of H1N1-IAV prevalence in US swine herd) (Figure 4). If 10 more samples were analyzed with 2 positive samples, or 20 samples with 3 positive samples, strength of evidence "p(x|θ)" will increase and then can create the posterior clinical experience p(θ|x)." Based on the first-rate evidence, the prior clinical experience will change from 29% to the posterior clinical experience of 20% prevalence (the most likely H1N-IAV prevalence), and thereby the veterinarian has learned something new. With a sample size of 20, the confidence in the posterior clinical experience and the precision about the estimate relatively increases as compared to the prior clinical experience, represented by narrower credible interval (confidence interval used in BA) is as shown in Figure 5. By choosing narrower credible intervals, inference and decision-making are better served, compared to chance (Poole, 2001). More

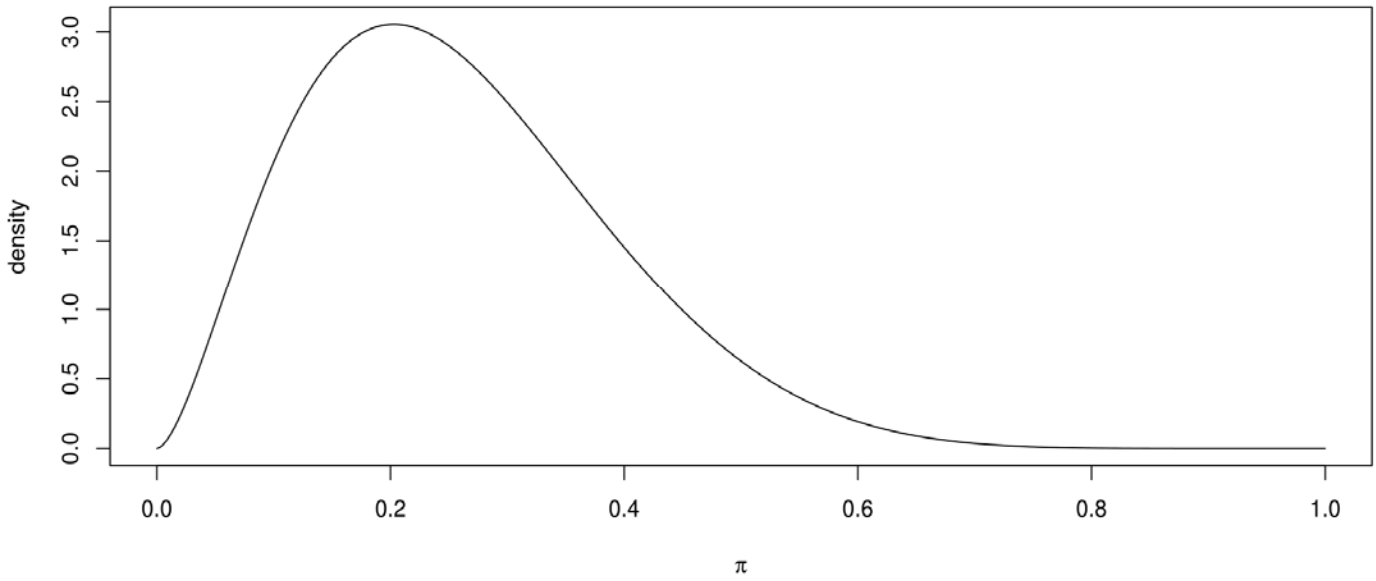


Figure 4. The distribution for prior clinical experience of an inexperienced veterinarian regarding prevalence of H1N1- influenza A virus in the United States swine herd (a horizontal axis is the prevalence with 29% most likely and standard deviation of 13%).

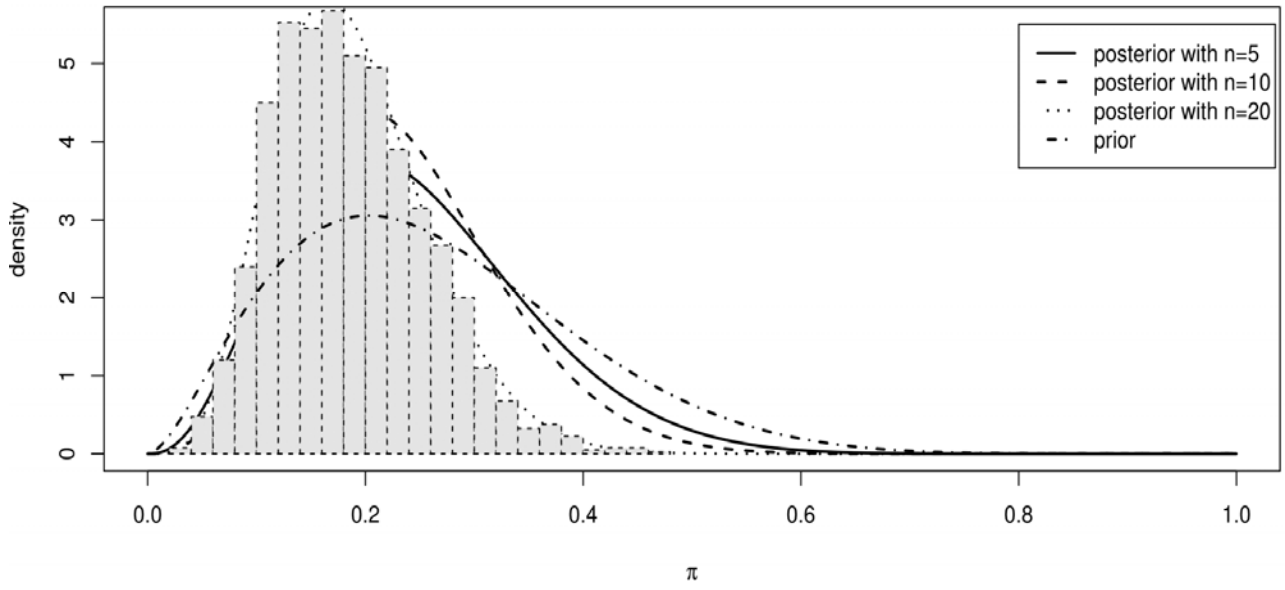


Figure 5. The represent of increasing strength of evidence as probabilistic graph using Beta-binomial model with 1, 2 and 3 positive samples out of 5, 10, 20 total samples, respectively.

precision (narrower credible interval) in the posterior clinical experience is the sum of precisions in the two sources of information (the strength of evidence and the prior clinical experience). The combined strength of these two sources of information lead to increasing precisions in understanding of evidence (Carlin and Louis, 2008). With more prior clinical experience, the veterinarian's decision regarding clinical intervention or treatment will be more precise. Similarly, as the veterinarian finds stronger evidence, his/her decision regarding clinical intervention or treatment will also be more precise.

Based on numerical example (Figure 3), it is important to note that the inferences from deductive and inductive reasoning are not equal (Poole, 2001). The inference from deductive reasoning, "$p(x|\theta)$", had the probability of 0.30 that IAV infected pigs would be coughing as an

observed clinical sign. On the other hand, that from inductive reasoning, "p(θ|x)", had the probability of 0.17 that coughing in pigs was caused by IAV infection. It is important to elucidate that performing statistical inference as deductive reasoning (frequentist) and as inductive reasoning (Bayesian) can end up with different conclusions. This is because the methods are answering different questions of making inference, and also both depict the opposite direction of causal models (Fienberg, 2006). However, if very strong evidence "p(x|θ)" has been found or theoretically when samples sizes is large (as $n \rightarrow \infty$) no matter what direction of a causal model is being made, both inductive and deductive inference will be identical (Geyer, 2012).

Example: Dog with pancytopenia

A young vaccinated dog is admitted to the small animal teaching hospital with a problem of pancytopenia, a decrease in the number of platelets, and red and white blood cells. The veterinarian investigates pancytopenia from signalment to identify a probable cause of pancytopenia. However, if the veterinarian uses deductive reasoning of making an inference, he has to use a number of tests to check each body system, which might cause pancytopenia. In contrast, if the veterinarian applies BA of making an inference, he/she will start from his/her prior clinical experience and then update that posterior clinical experience by accumulating new evidence (information) from history taking, physical examination and diagnostic results.

Starting from the prior clinical experience, a veterinarian would ask whether the dog has been showing diarrhea or vomiting. If the patient's history revealed no exposure to radiation, toxins or medications that could reduce the numbers of platelets, and red and white blood cells, from history taking and prior clinical experience, he/she would then update his/her posterior clinical experience (posterior distribution) using BA. The cause of pancytopenia may be infectious including parvovirus, canine distemper or ehrlichia infection. He/she would like to have stronger evidence (than from taking patient's history) to update his/her prior clinical knowledge of infectious diseases causing pancytopenia and also would like to coalesce evidence from the past concerning whether the patient has been showing diarrhea or vomiting. He/she continues to investigate more evidence using signalment, history and physical examination in order to increase the precision of the inference.

The broad category of infectious diseases is narrowed down to which one of the three infectious diseases would be a primary cause of pancytopenia with some certain probability. It is found that the patient has not had diarrhea or vomiting, the most likely cause of pancytopenia would be chronic ehrlichiosis with some degree of certainty. To have stronger evidence, the patient's serum is tested using a specific diagnostic test- ImmunoComb® Canine Ehrlichia Antibody Test Kit (Biogal Galed Lab., Israel). If the diagnostic test was positive, following Bayesian reasoning, a feasible cause of pancytopenia of the young dog patient may be chronic ehrlichiosis with some certain probability relying on veterinarian's prior clinical experience of knowing *Ehrlichia canis* prevalence (Davies and Shell, 2002; Singla et al., 2011).

As a veterinary diagnostician, one prefers to make an inference of the serological positive result if such a result is truly positive and truly caused by a chronic *E. canis* infection. The true positive result is simply measured by the sensitivity of the ELISA kit. However, making inference that the serological positive result is truly caused by *E. canis* infection requires BA (3 points). In statistical terms, what is the probability that the serological positive test result would really be caused by *E. canis* infection? This is the mathematical way of incorporating the serological evidence accompanied with prior clinical experience concerning the previous prevalence of *E. canis*. One then updates the estimate of how likely is the serological positive test caused by *E. canis* infection (posterior clinical experience). This result is known as the predictive value of the test. Subsequently, the veterinarian updates the posterior clinical experience by making inference of how likely is pancytopenia caused by *E. canis* infection.

HETEROGENEITY OF PRIOR CLINICAL EXPERIENCE

Veterinarians' prior clinical experiences are heterogeneous. They range from being pessimistic to being enthusiastic (Higgins et al., 2014). Therefore, their clinical (posterior) expectations would be different. The strength of evidence needed concerning clinical expectations for them to agree with each other would also be different. Thus, two veterinarians that are different in experiences may provide a different decision for giving treatment options. The evidence will provide a factual basis for the decision, which will dictate the patient's care (Rosenberg and Donald, 1995).

When we consider the BA notation, BA has three terms in itself: prior clinical experience "p(θ)", evidence "p(x)" and strength of evidence "p(x|θ)". If two veterinarians disagree about a treatment option, they are disagreeing based on one of these three terms. If a veterinarian uncovers the same evidence, for example, the positive serologic test of *E. canis*, an experienced veterinarian with strong belief in his/her prior clinical experience may think the result is a false positive because he has seen similar cases (based on his prior clinical experience). Given his prior clinical experience, stronger evidence is needed, "p(x|θ)", to update his posterior clinical experience. For a veterinarian with little experience, serological evidence may be sufficient given the lack of

his/her prior clinical experience to update his posterior clinical experience. One, then, treats the patient with Doxycycline. No matter the result of the treatment to the dog patient (improving, stable or worsening pancytopenia), the veterinarian will learn from this experience. A Bayesian approach, however, is a mathematical way to learn from past experience and measure the strength of evidence given a prior clinical experience "p(x|θ)" (Ashby and Smith, 2000).

If experienced and inexperienced veterinarians understand BA, they can focus on the area of disagreement (the prior clinical experience or weak evidence) and resolve the disagreement quicker. If a veterinarian is not using BA for diagnosing the patient, the patient may be subject to additional medical tests and unnecessary procedures. For instance, the patient may be evaluated for drugs and toxins depressing bone-marrow activity, or tested for parvovirus or canine distemper viral infection (Davies and Shell, 2002).

Evidence

What kind of evidence is useful and where does the strength of evidence originate? Strength of evidence may come from the number of patients (sample size) since as the samples size increases (as numerically showed previously), the Bayesian point and interval estimates will be driven more by the observed data and less by the prior clinical experience (Dunson, 2001). However, a Bayesian approach does not require a large number of samples but sequential analysis (the number of bits of information from the same patient) (Berger, 2006). For example, the strength of evidence increases as veterinarians make inferences based on new evidence obtained from history taking, physical examination and then the diagnostic serological test result. A Bayesian approach is remarkable not only in that it tells us what is and is not good evidence, but it helps us to quantify how strong the evidence is. A Bayesian approach tells us how much veterinarians should update their clinical experience or how much they should change their expectation when new evidence becomes available.

A Bayesian approach distinguishes between weak evidence and strong evidence. If the posterior clinical experience is very different from the prior clinical experience, something has been learned, and if posterior clinical experience is the same as the prior clinical experience, strength of evidence (useful information contented) is low. In many circumstances, a veterinarian finds very strong evidence.

Evidence that is sufficiently strong will permit a novice to make a discussion concerning clinical interventions or treatments with the confidence and precision as similar as an experienced veterinarian. Statistically speaking, this type of circumstance is called "a likelihood dominates a prior" (Carlin and Louis, 2008). Often, ones tend to believe results that support their preconceptions and disbelieve contradicting results (Gelman, 2008). Veterinary clinical decisions need to be supported by evidence because the evidence lets veterinarians decide whether an intervention or treatment can be reliable (Rosenberg and Donald, 1995). Therefore, appraising evidence is crucial.

CONCLUSION

In this article, particular attention has been paid to examine the state of BA used for inductive reasoning in veterinary medical problems and to illustrate how veterinarians update states of knowledge, not focusing on a utility of BA in veterinary diagnostic test. A Bayesian approach is considered to be the natural framework of thinking in veterinary medicine. Pattern recognition and problem-based approach are based on this kind of thinking, although some veterinarians may not realize that they are using BA when making an inductive reasoning (inverse probability).

Animals are not able to speak and provide limited information to a veterinarian. The veterinarian has to gather information from signalment, history, physical examination and laboratory results. In making decisions to treat a particular disease, there are relevant quantities or outcomes the veterinarian has observed or recorded and other relevant quantities or outcomes the veterinarian has not yet observed or recorded, and all are therefore uncertain.

We have demonstrated that veterinarian's physical examinations and history taking are the way of gathering information incorporating the prior clinical experience out-flowing to posterior clinical experience to make a clinical decision. Also, we have emphasized that veterinarian, whether they know it or not, are always using BA to update their posterior clinical experience by starting from their prior clinical experience. Some veterinarians may have a different prior clinical knowledge based on their previous experience. However, as evidence strengthens, their posterior clinical experiences are updated to meet clinical agreement.

No matter whether we call this learning process of solving problems from the present to the past, in reality, the data is meaningless by itself without having gone through thought processes (statistical modeling, or reasoning) incorporating previously observed information (prior experience) to synthesize a conclusion (posterior clinical experience).

However, the conclusion could be changed if we have more information and evidence. Veterinarian's diagnoses are based on evidence, and the best diagnosis should also be based on evidence and previous experience. The more prior experience a veterinarian has, the faster the diagnosis is made. The stronger the evidence, the more precise the veterinarian's inference will be. Veterinary education needs a more formal recognition and utilization of BA in the veterinary curriculum.

Conflict of interest

The authors declare they have no conflict of interest.

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