

# I'm not positive that's a positive. Become indispensable to your clients by knowing how to choose, interpret and incorporate diagnostic testing in bovine practice

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## Abstract

Diagnosis is central to the function of the medical professions, and yet, making a diagnosis is as much art as science. There are many sources of error that result in the wrong diagnosis, including lack of knowledge, our cognitive biases, and the inevitable use of imperfect tests. Strategic use of diagnostic tests can aid the diagnostic process and make the veterinary practitioner invaluable to their clients. Unfortunately, failure to understand cognitive error, causal logic, and the concepts of diagnostic interpretation have led many clinicians down preventable paths of incorrect diagnoses and inappropriate treatment decisions. Poor diagnostic strategies, especially when applied to population-based decision making, can lead to devastating and costly errors. Blindly following a diagnostic formula is not a substitute for clinical judgment, but neither is clinical judgment sufficient in the absence of critical thought. Quantitative assessment of the predictive value of a diagnostic plan complements clinical judgment to enhance the decision-making process. Diagnostic testing, in the hands of a clinician with an appreciation for physical examination and history taking, aware of their own cognitive biases, and understanding of the importance of the predictive value of the test, becomes a powerful tool for helping clients improve the health of their cattle.

**Key words:** diagnosis, bovine, sensitivity, specificity, predictive value, cognitive bias

## Résumé

Le diagnostic occupe une place centrale dans le fonctionnement de la profession médicale mais il s'avère que faire un diagnostic relève autant de l'art que de la science. Il y a plusieurs sources d'erreur qui mènent à un mauvais diagnostic, incluant le manque de connaissance, nos biais cognitifs et l'utilisation inévitable de tests imparfaits. L'utilisation stratégique des tests diagnostiques peut aider dans le processus diagnostique et rendre le praticien vétérinaire inestimable aux yeux de ses clients. Malheureusement, l'incompréhension de l'erreur cognitive, du lien de causalité et des concepts

de l'interprétation du diagnostic fait en sorte que plusieurs cliniciens établissent de façon prévisible un diagnostic incorrect et prennent des décisions de traitement inappropriées. De mauvaises stratégies de diagnostic, particulièrement lorsqu'elles sont appliquées à la prise de décision au niveau de la population, peuvent entraîner des erreurs coûteuses et désastreuses. Suivre aveuglement une formule de diagnostic ne remplace pas le jugement clinique bien que ce dernier ne soit pas suffisant en l'absence de pensée critique. L'évaluation quantitative de la valeur prédictive d'un plan de diagnostic s'ajoute au jugement clinique pour parfaire le processus de prise de décision. Le test de diagnostic, dans les mains d'un clinicien qui comprend bien l'importance de l'examen physique et des antécédents médicaux, qui reconnaît ses propres biais cognitifs et qui comprend l'importance de la valeur prédictive d'un test, devient un puissant outil pour aider les clients à améliorer la santé de leurs bovins.

## Introduction

*"Practice of veterinary medicine" means: To diagnose, prognose, treat, correct, change, alleviate, or prevent animal disease, illness, pain, deformity, defect, injury, or other physical, dental, or mental conditions by any method or mode...*

AVMA Model Practice Act<sup>3</sup>

The act of medical diagnosis is principal to all of the medical professions. For veterinarians, making a diagnosis of a medical condition precedes all other acts to prognose, treat, correct, change, alleviate or prevent animal diseases. The various types of diagnoses are differential, tentative, presumptive, definitive and etiological, pathoanatomic, and open or undetermined.<sup>13</sup> To this, I would make the case for assuring that the diagnosis is a functional one –a diagnosis that points to a solution.

Making a definitive etiological diagnosis almost certainly requires laboratory assistance because the history and clinical signs are rarely pathognomonic. Also, although a definitive etiological diagnosis may often seem to be desirable, it is not always possible, nor necessarily helpful, to achieve that level of knowledge about a particular morbid process.<sup>13</sup>

The pursuit of a definitive etiologic diagnosis may not lead to a functional diagnosis. Diagnostic investigations can become sidetracked, and both human and capital resources consumed, in the sole pursuit of a causative agent, rather than finding explanations for the disease that are more useful for solving the problem. By the nature of their training in infectious diseases, veterinarians often spend considerable time and money trying to identify a pathogen to blame for health problems. Sometimes, knowing the pathogen(s) involved in a disease outbreak can be useful. For example, it is probably useful to know that recent calf deaths were associated with infection with *Clostridium chauvoei* or *Listeria monocytogenes*. However, that information alone does not explain why calf deaths might suddenly have occurred from either of these widely distributed environmental-source pathogens. Knowing the name of the causative agent may provide an explanation for the observed morbid process and might provide therapeutic insight. However, that knowledge rarely explains the course of events that led to the outbreak or provides a solution for preventing future problems. For example, any number of disease agents might explain poor growth performance in the feedlot, and some number of such agents may be revealed in the course of a diagnostic investigation. However, one should also consider the possibility that the real cause of the reduced gains is an inaccurate scale on the feed truck.<sup>16</sup>

### The Diagnostic Process

The purpose of making a diagnosis is to label the patient by state of health, which 1) facilitates communication with the client; 2) explains the clinical findings; and 3) provides a prognosis and plan of action. The veterinarian collects clinical evidence then applies scientific theory, reason, and experience to arrive at a diagnosis. Making a diagnosis requires collection of information about the animal or herd relative to the chief complaint; obtaining a history and examining af-

ected individuals, the herd, and its environment; generating diagnostic possibilities; selecting laboratory aids to diagnosis; and interpreting the results. The methods used to arrive at a diagnosis ranked in order of increasing complexity are: pattern recognition, hypothetic-deductive reasoning; use of algorithms, identifying the key abnormality of function, using exhaustive analysis, or the problem-oriented approach. Experienced clinicians are more likely to rely on the simpler methods such as pattern recognition, whereas novices are more likely to use the more complex methods of diagnosis.<sup>13</sup> This migration over time and experience towards the faster and simpler process of pattern recognition is an example of moving the clinician's thought process from the slower, more critical thinking of System 2 to the more rapid and efficient thinking of System 1 as experience is gained and the clinician becomes more comfortable using heuristics, or rules of thumb.<sup>8</sup> System 1 is especially efficient for making decisions in the heat of battle. However, there are times before the crisis when the critical thinking of System 2 can help one think through anticipated problems<sup>8</sup> – like making a diagnostic error regarding common diseases.

Unfortunately, regardless of experience, there is no foolproof way to make an accurate diagnosis. Studies of physician diagnoses suggest that diagnostic errors are common.<sup>2,5</sup> Diagnostic error occurs when a diagnosis is missed, delayed, or is wrong.<sup>2</sup> Diagnostic errors result from lack of knowledge, cognitive errors, and problems occurring in the diagnostic system. Lack of knowledge may be on the part of the clinician or it may be because of yet undiscovered medical knowledge. Cognitive biases are sometimes subtle, systematic errors in the clinical thought process. Errors in cognitive reasoning are roughly classified as either a faulty assessment of pre-test probability (e.g. either over or underestimating the probability of a disease process), or failing to consider all relevant possibilities (Table 1).<sup>12</sup> There is no clear solution to alleviating cognitive biases because addressing 1 cognitive error

**Table 1.** Some common cognitive errors that lead to misdiagnosis. Over 100 cognitive errors have been described.

Cognitive error	Description
Availability error	Clinician over-estimates the pre-test probability because of recent experience. For example, by remembering a recent dramatic case.
Representation error	Clinician over-estimates pre-test probability because of the appearance of classic signs without considering disease prevalence.
Premature closure	Clinician jumps to a diagnosis, fails to consider other possible diagnoses and stops collecting data.
Anchoring errors	Clinician clings to an initial diagnostic impression even though contradictory evidence is accumulating.
Confirmation bias	Clinician selectively accepts clinical data that supports a pre-conceived notion and ignores data that do not, e.g. cherry-picking
Attribution error	Clinician develops stereotypes about patient or clients that leads them to fail to consider some diagnoses, e.g. "He doesn't feed his cattle well. The only thing wrong with his cattle is malnutrition."
Base-rate neglect	Clinician ignores the low pre-test probability of a disease, e.g. constantly chasing zebras.
Zebra retreat	Clinician backs away from a diagnosis only because it is rare. If you never work up rare diseases, you may be guilty of zebra retreat.

may predispose another. For example, correcting the failure to consider rare diseases may lead to over-consideration of rare diseases which may increase diagnostic costs, lead to a delay in making a diagnosis, or result in an inappropriate plan of therapy. However, it has been suggested that cognitive errors might be reduced by taking a formal pause after collecting history and physical examination data to ask oneself:

- What else could this be if it is *not* the tentative diagnosis?
- What are the worst things it could be?
- Is there evidence that is at odds with the tentative diagnosis?

By asking these questions, the list of differential diagnoses might be expanded to include things that may have been left out, and prompt the clinician to obtain further necessary evidence, which may include additional clinical and laboratory aids to diagnosis.<sup>12</sup>

#### *The Use of Laboratory Assistance to Aid a Diagnostic Investigation*

A diagnostic test is any procedure used to help the clinician distinguish between different states in a patient's health (e.g. normal and abnormal, or pregnant or not pregnant).<sup>13</sup> Often these are laboratory tests of tissues or fluids (e.g. serological or microbiological assays), but they also include many clinical diagnostic techniques (e.g. radiology or ultrasonography). Unfortunately, clinicians have a tendency to overly rely on diagnostic tests to provide the diagnosis rather than trust their own clinical skills to guide diagnostic reasoning.<sup>4</sup> Reliance on tests over clinical skills has not reduced diagnostic error and in some cases the diagnostic test contributes to the error.<sup>4</sup>

No diagnostic test is perfect. Therefore, some test results can be expected to be in error. Diagnostic test evaluation predicts what errors might occur in either diseased or non-diseased individuals. Diagnostic test interpretation predicts how the errors might be distributed among test positive or negative individuals.<sup>9,10,17</sup> For example, diagnostic test interpretation asks the questions: –is this positive test result likely to be a true-positive or a false-positive? –is this negative result likely to be a true-negative or false-negative? The system 2 answers to these questions could be helpful to predict the effect diagnostic errors might have on a diagnostic plan for an individual or in a population-based health program – essentially test-driving the diagnostic plan on paper, first.

Errors in the diagnostic system include all of the problems that may result in a delayed or incorrect diagnostic test result. These errors include issues associated with human fallibility, as well as issues inherent to the test platform or biological system. For example, the diagnostic sample may have been improperly collected, stored, labeled, transported (e.g. lost or delayed in the mail), or prepared for analysis. The person conducting and interpreting the test may lack experience or reagents may be out of date or contaminated. Even under the best conditions, the test may have inherent

properties, such as cross-reactive antibodies, that result in false-positive or false-negative results. It may be that there is sufficient biological variation in the outcome measure such that it is not possible to distinguish between some normal and abnormal animals.

#### *Understanding the Goal of a Diagnostic Investigation*

Diagnostic tests are used to detect, confirm, document, or exclude a disease. On an individual animal basis, diagnostic tests might help determine the cause of disease, provide a prognosis, direct the course of therapy, or document the effectiveness of therapy. Diagnostic tests are sometimes useful as population-based tools for identifying subclinical reservoirs of disease or infection within a herd, preventing the introduction of infected animals into a herd, assessing or monitoring the level of existing infection within a herd, and determining the effectiveness of biosecurity or biocontainment programs.

#### *Choosing to Use a Test*

Before deciding to use a diagnostic test, the clinician should consider the relative probability of the diseases on the list of differentials, where in the course of disease the patient is, whether the test will help to distinguish the diseases, the diagnostic errors associated with the test(s), if there are any risks associated with using the tests, and whether the results of the tests would alter the treatment plan. It may not be important to know if the calf is scouring due to a rotavirus or coronavirus infection if the diagnosis isn't going to change the fluid therapy plan, anyway. The type of information the test provides is also important. For example, the causal inference that comes from detecting a pathogen present in the tissue of a sick animal is different from discovering serologic evidence that sometime in the animal's life it was exposed to the agent. In addition, the clinician should consider the probability of finding evidence of an infection among healthy and diseased individuals before establishing causal inference. Some infections are widespread in both healthy and diseased individuals, so finding test-evidence of infection in an individual may not be diagnostic. For example, finding serological evidence of bovine leukosis virus (BLV) in a cow with mastitis is not likely to be convincing evidence that BLV is a contributing cause of the mastitis because BLV is highly prevalent in many dairy herds in the US.<sup>1</sup> Sometimes it may be too early or too late in the course of the disease to find evidence of the suspect agent.

### **Diagnostic Test Evaluation**

Diagnostic test performance is evaluated by the parameters sensitivity and specificity.<sup>9,10</sup> Sensitivity and specificity are estimated by testing individuals of known (or suspected) disease (or infection) status. The parameters of sensitivity and specificity for a given test are assumed to be constant for a given stage of infection in a given class of animal.

For example, the performance parameters of a particular ELISA to detect antibodies against *Mycobacterium avium* spp paratuberculosis might differ by age of the animal or stage of disease. Sensitivity (SENS) is a conditional probability describing probability that a diseased individual (D+) will have a positive test result (T+).

$SENS = P(T+ | D+)$  -This notation is read as the probability of being test positive *given that the individual has the disease*.

Specificity (SPEC) is the conditional probability that a non-diseased (D-) individual will test negative (T-). The probability only applies to the population of individuals without disease.

$$SPEC = P(T- | D-)$$

### Diagnostic Test Interpretation

Failure to understand the concepts of diagnostic test interpretation have led many clinicians down preventable paths of incorrect diagnoses and inappropriate treatment decisions. Poor diagnostic interpretation applied to population-based decision making can lead to devastating and costly errors. Blind application of a diagnostic formula is not a substitute for clinical judgment, but neither is clinical judgment sufficient in the absence of quantitative thinking. Quantitative diagnostic interpretation complements clinical judgment to enhance the decision making process. The formulae and concepts presented here are easily applied with common computer spreadsheet functions (Figures 1

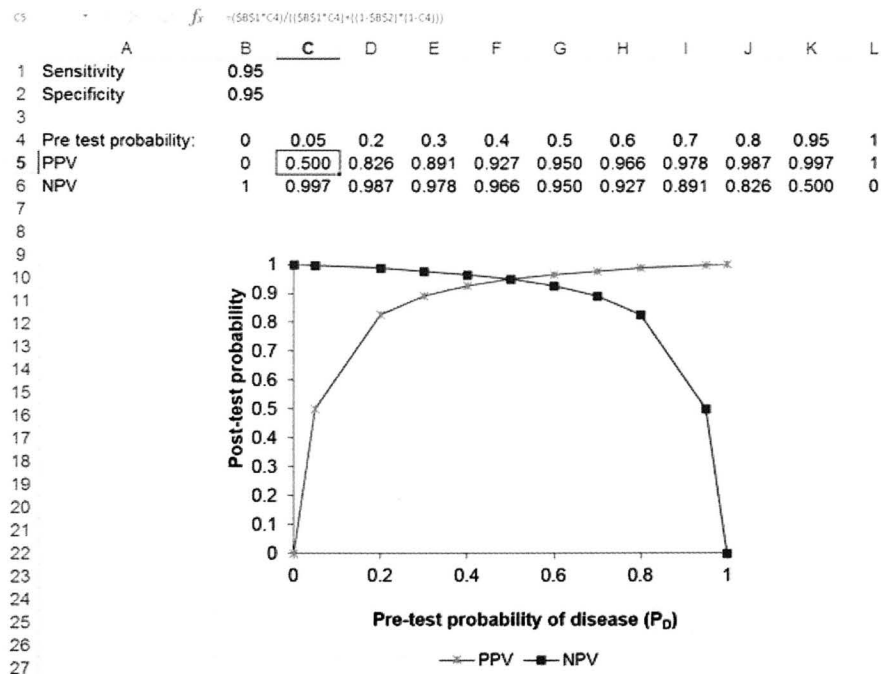
and 2). Computer spreadsheet software is sufficiently user friendly so that quantitative analysis is within the grasp of anyone with interest.

Sensitivity and specificity values by themselves are not useful for test interpretation because, of course, clinicians do not know the true disease status of the animals they test. Clinicians are most interested in the probability that the test result represents the true infection status of the individual. This probability is called the post-test probability or predictive value.<sup>9,10</sup> Positive predictive value (PPV) is the conditional probability that an individual with a positive test result is truly infected. Restated: given a positive test result, what is the probability this animal is truly infected? Negative predictive value (NPV) is the conditional probability that an individual with a negative test result is truly not infected. Restated: given a negative test result, what is the probability this animal is truly not infected?

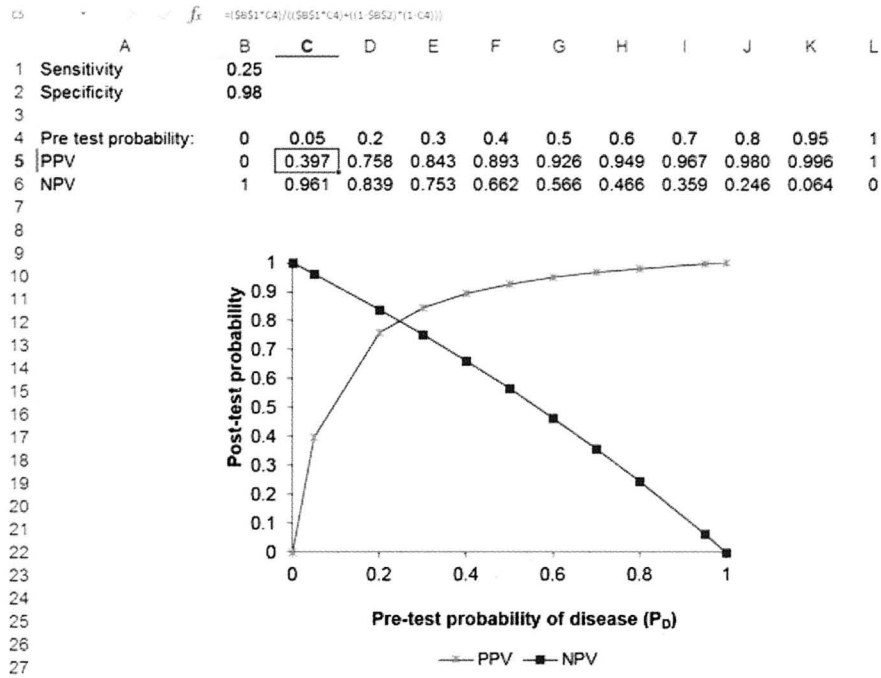
$$PPV = P(D+ | T+)$$

$$NPV = P(D- | T-)$$

Experienced clinicians know intuitively that clinical judgment is necessary to interpret diagnostic test results. The importance of clinical judgment to test interpretation can be shown in quantitative models. Post-test probability is calculated by using information about test sensitivity and specificity as well as information called pre-test probability. Pre-test probability is the probability of the individual truly being diseased ( $P_D$ ) before considering test results. One could think of  $P_D$  as the proportion of animals actually having the specific disease from an imaginary population of animals all



**Figure 1.** Spreadsheet calculations of positive (PPV) and negative predictive value (NPV) over the entire range of pre-test probability of disease for a diagnostic test with 95% sensitivity and 95% specificity. Both PPV and NPV exceed 90% when the pre-test probability of disease is 40% to 60%. However, in situations where the disease is less likely, as when screening healthy populations, the PPV decreases. In situations where the clinical judgement is that the disease is likely, the NPV decreases.



**Figure 2.** Spreadsheet calculations of positive (PPV) and negative predictive value (NPV) over the entire range of pre-test probability of disease for a diagnostic test with 25% sensitivity and 98% specificity. This is the expected performance of a Johne’s disease ELISA when used to test healthy adult cattle. If this test was used to pre-purchase test cattle from a population with an expected 5% prevalence of infection a positive test result would be wrong 60% of the time (PPV = 0.4) and a negative test result would be correct 96% of the time (NPV = 0.96). Notice the nearly straight curve for NPV. This indicates that a negative test result provides little additional information over pre-test probability. Purchasing only test-negative cattle would result in a purchased population with 4% prevalence of infection instead of 5% prior to testing. This is an inefficient testing strategy.

with the same clinical presentation and history. We estimate  $P_D$  using what we know from review of the literature (e.g. from surveys reporting prevalence), other epidemiologic knowledge, history and physical examination, or previous experience. The formulas for PPV and NPV in terms of SENS, SPEC, and  $P_D$  are:<sup>9</sup>

$$PPV = \frac{SENS \times P_D}{(SENS \times P_D) + (1 - SPEC) \times (1 - P_D)}$$

$$NPV = \frac{SPEC \times (1 - P_D)}{SPEC \times (1 - P_D) + (1 - SENS) \times P_D}$$

**Multiple Test Strategies**

Sometimes, more than 1 test is used to strategically aid diagnostic interpretation, because the combination of tests either improves test sensitivity, at the cost of specificity, or improves test specificity at the cost of sensitivity.

Testing in parallel is the concurrent use of 2 or more separate diagnostic tests for the same disease. Animals are considered to have the disease if they test positive to any of the tests. Parallel testing increases test sensitivity, but decreases test specificity. This means that parallel testing results in fewer false-negative results, but more false-positive

results. Therefore, parallel testing is used when the consequence of missing a disease has greater importance than having false positives. In a sense, the animal must “prove” it is healthy by testing negative multiple times. Parallel testing helps to rule out a disease. The mnemonic “sNout” is used to indicate that negative results from very sensitive test strategies can be used to rule out a disease.<sup>14</sup>

For 2 independent tests:

$$SENS_P = 1 - [(1 - SENS_A) \times (1 - SENS_B)]$$

$$SPEC_P = SPEC_A \times SPEC_B$$

Testing in series is the sequential use of 2 or more tests based on a positive result on the previous test, such that subjects that test positive on the first test are tested again, usually with a much more specific diagnostic test. Animals that test positive on all tests are considered to have the disease. Testing in series increases test specificity, but decreases sensitivity. This means that testing in series results in fewer false-positive results but more false-negative results. Therefore, series testing is used when the consequence of a false positive is great. For example, serial testing is often employed in herd testing schemes where a single positive test result might classify the herd as having a disease. In a sense, the animal must “prove” that it has the disease. Serial

testing helps rule in a disease. The mnemonic “sPin” is used to indicate that positive test results from very specific test strategies can be used to rule in a disease.<sup>14</sup>

For 2 independent tests:

$$SENS_S = SENS_A \times SENS_B$$

$$SPEC_S = 1 - [(1-SPEC_A) \times (1-SPEC_B)]$$

#### Apparent Prevalence

Apparent prevalence (AP) is the percentage of animals determined to be diseased (infected) based on diagnostic test results.<sup>10</sup> Apparent prevalence may differ from true prevalence because of test error. If the parameters of test performance are known then AP can be predicted over a range of values for true prevalence ( $P_D$ ):

$$AP = SENS \times P_D + (1-SPEC) \times (1-P_D)$$

#### True Prevalence

The true prevalence of disease can be calculated from the apparent prevalence obtained by population testing if the parameters of test performance are known:

$$TV = \frac{AP + SPEC - 1}{SENS + SPEC - 1}$$

#### Diagnostic Efficiency

Tests may be in error as false-positive or false-negative results. False-negative (FN) results are a function of SENS (FN = 1-SENS), and false-positive (FP) results are a function of SPEC (FP = 1-SPEC). Diagnostic efficiency (EFFIC) describes the proportion of individuals correctly classified by the test results. Diagnostic efficiency depends on the parameters of test performance and  $P_D$ .<sup>17</sup>

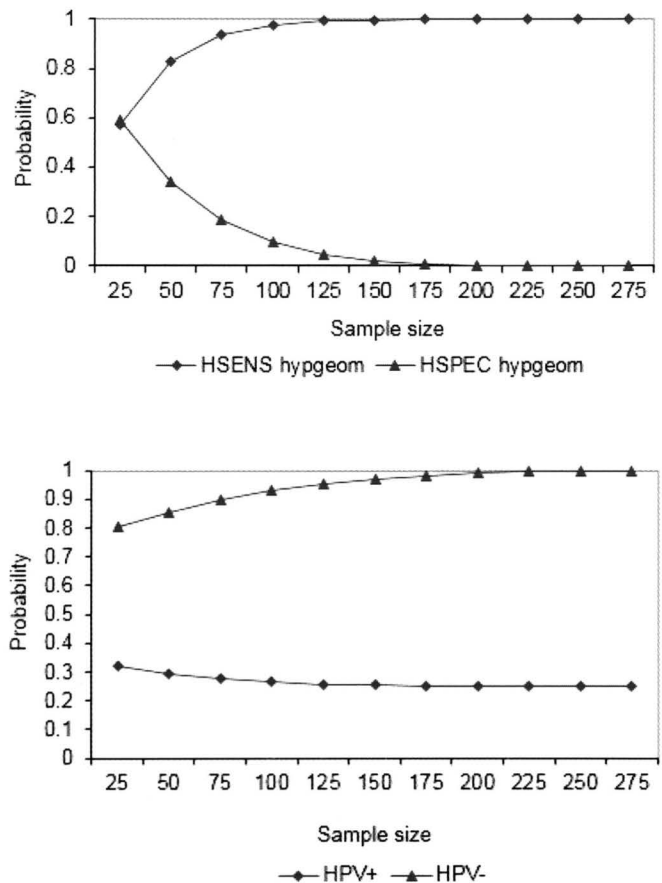
$$EFFIC = SENS \times P_D + SPEC \times (1-P_D)$$

#### Aggregative Testing Strategies - Sampling to Detect Disease in a Population

Sometimes it is important to determine if a disease is present or absent within an aggregate of individuals, for example a litter, pen, barn, flock or herd (the term “herd” will be used to designate any such group of animals).<sup>15</sup> The probability of detecting evidence of disease or infection in a diseased herd is termed herd-level sensitivity (HSENS). If the disease status of a herd is determined by testing individuals, then HSENS is a function of SENS, SPEC,  $P_D$ , the number of reactors used to classify the herd as infected, the size of the herd, and the number of animals tested within the herd.<sup>4,5</sup> If there is an expected minimum value for  $P_D$  within infected herds and test performance has been evaluated, then the number of animals to test can be determined to assure a given value for HSENS. This is the number of animals that must be tested to detect the presence of infection with a probability equal to HSENS.<sup>11</sup>

Herds could be classified based on different cut-point values for the numbers of reactors (R) used to classify the herd as diseased. HSENS can be estimated using the binomial probability distribution given the probability of a given number of reactors being present in a sample of size n from the herd. The probability of a reactor is the sum of the probability of a true-positive reactor ( $SENS \times P_D$ ) plus the probability of a false-positive reactor ( $(1-SPEC) \times (1-P_D)$ ); note, this is the apparent prevalence (AP), as previously defined.

Except for the rare circumstance when a test of individuals is perfectly specific (SPEC = 1) it is possible for false-positive reactors (FP = 1-SPEC) to result in a false-positive



**Figure 3.** The probability of correctly classifying Johne’s disease infected herds (HSENS) with 5% prevalence and non-infected herds (HSPEC) by testing various numbers of animals from herds of 400 animals using an ELISA that is 25% sensitive and 98% specific (as in Figure 2), assuming a single positive test classifies the herd as test-positive, and that 25% of herds have Johne’s disease. As the sample size increases HSENS increases, but HSPEC decreases towards zero (i.e. all truly negative herds will be falsely classified as infected). Because of false-positive herd classifications, the apparent proportion of affected herds will approach 100% as sample size increases, and only the truly infected herds will be classified correctly. Because of false-positive test results, this test by itself is not useful for differentiating infected herds from non-infected herds, regardless of sample size. A spreadsheet file for these calculations is available from the author.

herd classification. Therefore, consideration must also be given to herd-level specificity (HSPEC), the probability that a non-diseased herd would be correctly classified.<sup>11</sup> Even a small probability for a false-positive result becomes magnified as many individuals with a herd are tested, reducing HSPEC (Figure 3). Most often, when classifying herds by disease status using tests of individuals, it is desirable to maximize test specificity, even at the cost of test sensitivity to avoid low herd-level positive predictive value (HPV+; Figure 4). Herd-level negative predictive value (HPV-) increases as the number of animals sampled increases (Figures 3 and 4).

Often the sample size (n) is large relative to the herd size (N) (n/N > 0.05) and usually herd sampling is conducted

without replacement (i.e. once tested, the animal is removed from the pool for selection). In these circumstances the hypergeometric distribution function is more appropriate for calculating HSENS and HSPEC.<sup>6</sup> Calculation of the hypergeometric function requires inputs for R, n, N, and the number of infected animals in the herd (S).

$$\begin{aligned} \text{HSENS} &= 1 - P(x < R | n, p = \text{AP in a diseased herd}) \\ &\quad \text{(Binomial distribution)} \\ &= 1 - P(x < R | n, S = (N \times \text{AP}), N) \\ &\quad \text{(Hypergeometric distribution)} \end{aligned}$$

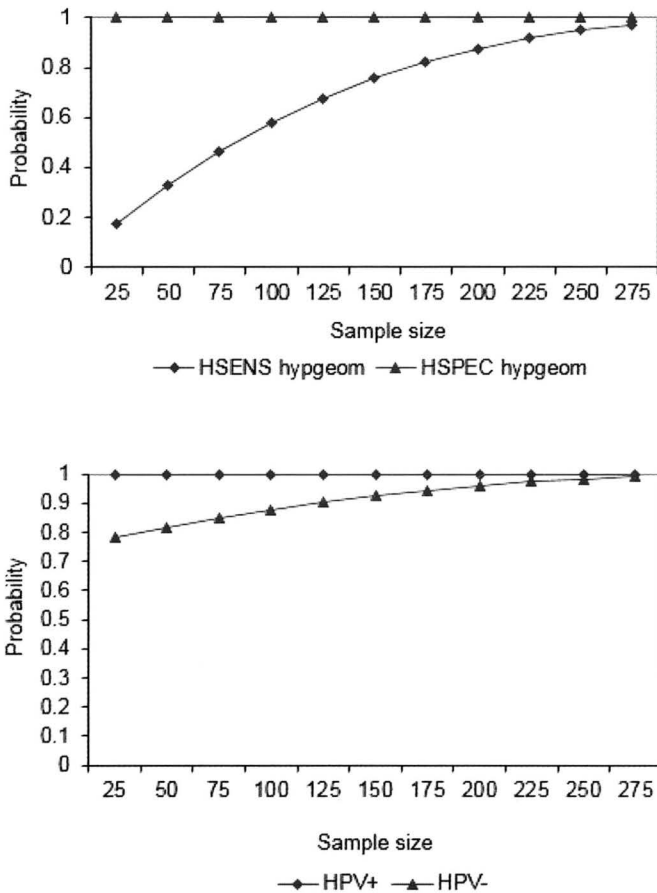
$$\begin{aligned} \text{HSPEC} &= P(x < R | \text{sample size} = n, p = (1 - \text{SPEC})) \\ &\quad \text{(Binomial distribution)} \\ &= P(x < R | n, S = (N \times (1 - \text{SPEC})), N) \\ &\quad \text{(Hypergeometric distribution)} \end{aligned}$$

Models for herd-level predictive value (HPV+, HPV-), apparent prevalence (HAP), and diagnostic efficiency (HEFFIC) can be developed by substituting HSENS for SENS, HSPEC for SPEC, and the proportion of herds containing infected individuals (HP<sub>d</sub>) for P<sub>d</sub>. into the appropriate formulas.<sup>11</sup> Simulation models for herd-level test performance have also been described.<sup>7</sup>

The choice of sample size has important implications for herd surveillance and survey research. The outcome of surveys to detect diseased herds may be biased if sample size estimates failed to consider the effect of imperfect test performance, herd size, and clustering of disease in sub-populations.<sup>11</sup> Sample size estimates are often obtained from software that use formulas assuming perfect test performance; however, serious errors in sample size estimation can result if test performance is not considered. Further, for a given sample size the accuracy of the herd's disease classification will differ in different sized herds and in sub-populations where disease is expected to cluster differently.<sup>11,15</sup>

### Conclusion

Veterinarians, by definition, provide service to their clients by providing accurate, functional diagnoses which lead to effective therapeutic decisions as well as appropriate plans for biosecurity and biocontainment. There is an unspoken contract with clients that veterinary diagnoses are accurate and reliable. "Eye-ball" or "gut-feeling" decisions are difficult to justify, as is blind faith trust in a diagnostic test result. However, it is possible to make appropriate diagnostic decisions, or at least to understand how reliable the diagnostic results are likely to be, by applying sound causal logic and clinical judgment to the quantitative principles of diagnostic interpretation. Population-based diagnostic decisions are usually of high economic consequence to veterinary clients, making adherence to these principles even more important when the diagnosis affects a population. Diagnostic testing, in the hands of a clinician with an appreciation for physical examination and history taking, aware of their own cognitive



**Figure 4.** The probability to correctly classify Johne's disease infected herds (HSENS) with 5% prevalence and non-infected herds (HSPEC) by testing various numbers of animals from herds of 400 animals using a serial testing scheme of ELISA testing followed by fecal culture of ELISA-positive cattle (resulting in an overall lower sensitivity and higher specificity than ELISA alone), assuming a single positive test classifies the herd as test-positive and that 25% of such herds have Johne's disease. Because of the high test specificity of fecal culture, the herd-level specificity (HSPEC) remains high as the sample size increases and herd-level sensitivity (HSENS) increases. By following this diagnostic scheme, testing approximately 275 adult cattle in a herd of 400 results in high herd-level positive (HPV+) and negative (HPV-) predictive value—almost all herds would be classified correctly.

biases, and understanding the importance of the predictive value of the test, becomes a powerful tool for helping clients improve the health of their cattle.

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