Bluetongue Surveillance

Evaluation of Historical Information

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Introduction

The first national surveillance for bluetongue virus in the United Sates was conducted in the winter of 1977/78 (Metcalf *et al.* 1981). This survey was a comprehensive serological survey of slaughter cattle from all 50 States and Puerto Rico and the Virgin Islands. The survey results provided evidence that the prevalence of bluetongue antibody was relatively high in the southwestern US and generally low in the northern States. Serologic surveys conducted in subsequent years have not included all States. Traditionally, the survey has included Connecticut, Delaware, Indiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, New Hampshire, New Jersey, New York, North Dakota, Ohio, Pennsylvania, Rhode Island, Vermont, West Virginia, and Wisconsin. Six States (Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island and Vermont) were tested in combination to form the New England area.

Annual bluetongue surveys were conducted from 1982/83 through 1996/97. Beginning in 1998/99 the surveys were conducted every two years. Based on this protocol, the next serologic survey is planned for the winter of 2004/2005.

The results of bluetongue surveys are used to classify states or regions on the basis of risk. Risk classifications determine export requirements for movement of cattle to Canada. These export requirements are complicated. Besides the prevalence of bluetongue, these requirements also consider the class of cattle, residence status, and seasonal factors. A risk matrix determines how many negative bluetongue tests are required to export cattle from the U.S. to Canada.

States or regions may be classified as low, medium or high incidence states. The low-incidence status is based on an annual bluetongue serologic survey. The prevalence must be two percent or less to qualify for low-incidence status. Any State in the low-incidence category could revert to medium-incidence status in any given year depending on survey results. Medium-incidence states or regions are defined as having prevalence greater than two percent, but such states or regions are characterized as having some period during the year in which they are vector-free. The high-incidence States are those with prevalence levels greater than 2% and which have no vector-free period.

During the vector season (April 1 through October 31), cattle exported to Canada from a low-incidence state are required to have one negative test prior to export. In contrast, cattle exported from medium- or high-incidence states are required to have two negative tests conducted 30-90 days apart prior to export. Similar discrepancies apply to other seasons of the year; cattle producers in low-incidence states have a comparative advantage for exporting cattle to Canada.

The multiple years of surveillance data for bluetongue in cattle provides an opportunity to accumulate data, refine our estimate of the current prevalence of antibodies in the cattle population, and evaluate the sampling intensity necessary to meet international trading requirements.

Bayesian methods provide a framework for accumulating information from a series of sampling surveys. Prior information on prevalence can be updated with new sampling information. In the simplest form, the results of surveillance from a year of surveillance (the posterior distribution) form the prior distribution that is updated with the sampling information from the subsequent year. This method is based on apparent prevalence. A second approach is to produce a posterior distribution that is updated by both the sampling information and the sensitivity and specificity of the test. This approach would provide an estimate of the true prevalence distribution. Both of these methods, however, assume a steady disease state from surveillance period to surveillance period.

The dynamics of infection within populations makes a steady-state assumption somewhat suspect. If the prevalence level of infection among a population was known with certainty for a given year, it is unlikely that prevalence level would be exactly the same the following year because the transmission process would result in fewer, or greater, numbers of infected individuals in the population. In a traditional Susceptible-Infected-Resistant transmission model, steady-state prevalence could theoretically occur if the number of newly infected individuals in the subsequent year exactly equaled the number of infected animals that cleared their infection (thus becoming susceptible to new infection) from the previous year. Prevalence could decline from one year to the next if the rate of transmission in the population resulted in fewer newly infected individuals than those infected during the previous year. Yet, most infectious agents, particularly vector-borne infectious agents like bluetongue virus, are expected to transmit at a rate that increases the number of newly infected individuals in subsequent years.

The dynamics of infection in populations explains why the value of information about the occurrence of infection declines with time. We are more confident about information collected today than we are about information collected previously. More precisely, we are more confident in inferences/conclusions made from more recent evidence than older evidence. The value of information decreases with time because, as time progresses, transmission events can occur that alter our inferences about information.

To account for the time value of sampling information collected for bluetongue virus prevalence, a disease transmission model is needed. This disease transmission model could incorporate a myriad of factors – including vector presence and competence, host density and susceptibility, and environmental conditions (rainfall, temperature) – that influence transmission of bluetongue within a population. Such a model would be complex but it could be use to predict the change in prevalence in a population given biologically plausible parameters. In lieu of a complex model, some reasonable transmission adjustment may be a viable approximation to predict changes in disease prevalence due to transmission of infection. A simple linear equation relating prevalence levels across time represents a very simple disease control/transmission model.

The purpose of this paper is to illustrate and compare inferences from three approaches to accumulating bluetongue virus surveillance information from the New England region of the US. Our goal is to develop a prior distribution for bluetongue prevalence that can be used to assess surveillance requirements for the New England states in 2004. In contrast to sample size calculations based on an uninformed prior, development of an informed prior for prevalence in 2004 could suggest the need for fewer samples in the New England states.

Methods

Three methods are used for accumulating evidence. The simplest method (Method 1) assumes sampling evidence is perfect and simply accumulates from one year to another. The next method (Method 2) is complicated by acknowledging that sampling evidence is imperfect, but, after adjusting the data for the imperfections, the evidence is simply accumulated from one year to another. In contrast to Methods 1 and 2, the most complicated method (Method 3) accumulates imperfect sampling evidence, adjusts the evidence to account for imperfections, and explicitly accounts for the time value of information.

For each method, the decision criterion is assumed to be the confidence (or probability) that bluetongue prevalence among cattle in the New England region is 2% or less. If the cumulative sampling evidence supports the argument that this prevalence is 2% or less, then the region is classified as low-incidence.

Method 1: Accumulating perfect sampling evidence

Conceptually, Method 1 is a straight-forward application of Bayes theorem (Figure 1). An assumption of complete uncertainty about prevalence prior to the first year's survey is reflected in a prior distribution that shows equal confidence, or probability, that prevalence is 0%, 100%, or any value in between. Such an assumption is conservative because it is likely that non-sampling evidence, such as reported diagnoses by veterinary practitioners, would imply a much higher probability for lower prevalence levels (e.g., <50%) than higher prevalence levels. If a prior distribution in year 1 were constructed to reflect such non-sampling evidence, then the posterior distribution derived using Bayes theorem and the perfect sampling evidence collected in year 1 would likely be more certain about lower prevalence levels than it is when a uniform prior is assumed.

The first method we used to accumulate the historical surveillance information was based solely on the surveillance results from the New England States from 1991 through 2002. The diagnostic tests used during the period (the immunodiffusion test was used in 1991/92 and 1992/93 and the competitive enzyme-linked immunosorbent assay) were assumed to be perfect in this approach. A Beta distribution has been used to depict prevalence uncertainty from survey results (Schlosser and Ebel 2001). Test results from the first year of surveillance (1991) were used to define a Beta(s+1, n-s+1) distribution where s positives were found in n samples (1996). Results from each subsequent sampling year are used to update the Beta distribution in the following manner:

$$\textbf{(Eqn. 1)}\ Beta\left(\sum_{y=1991}^{y}(s_y)+1,\ \sum_{y=1991}^{y}(n_y-s_y)+1\right)$$

where s_y is the number of successes and n_y is the number of samples in year y. The calculations were implemented on an Excel spreadsheet. The probability of the apparent prevalence exceeding 2.0% was calculated for each sampling using the complement of the cumulative probability function for the Beta distribution in Excel.

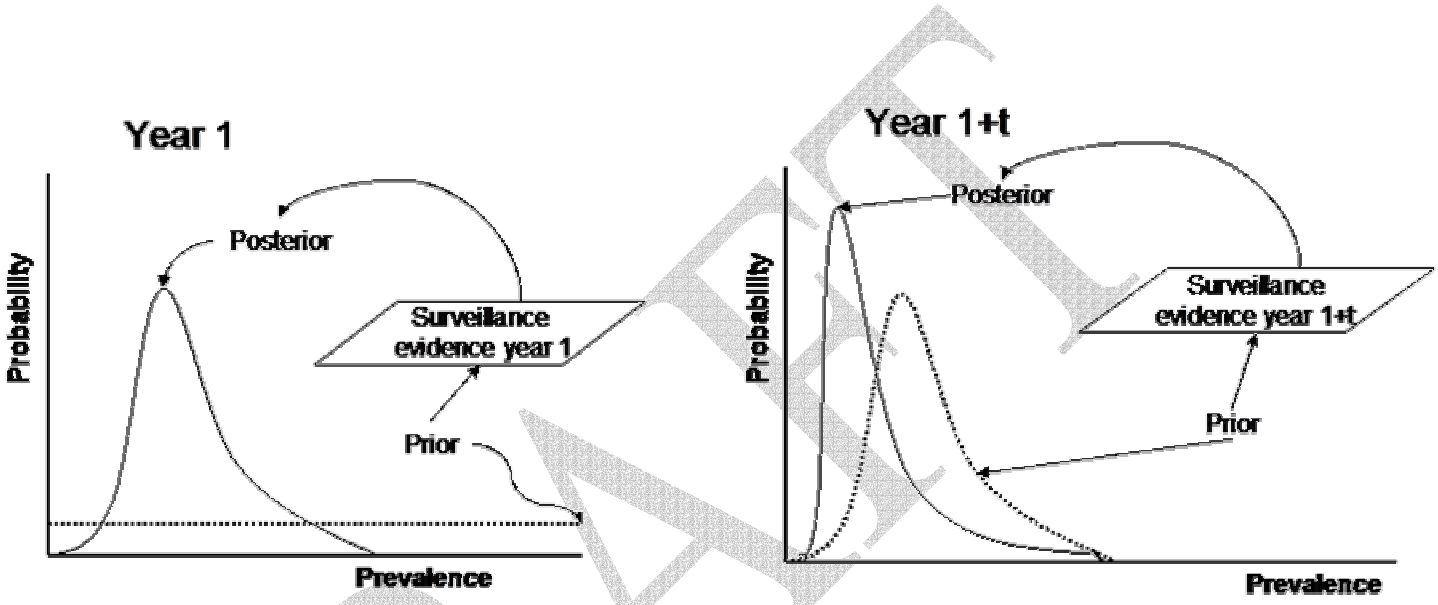

Figure 1: This is a conceptual illustration of accumulating perfect sampling evidence across different years. For a hypothetical year 1, the prior distribution is assumed to be uniform across the range of prevalence. Using Bayes theorem, the perfect sampling evidence collected during year 1 informs this uniform prior distribution to derive the posterior distribution for year 1. For hypothetical year 1+t, the prior distribution is exactly the same as the posterior distribution derived in year 1. Additional sampling evidence collected in year 1+t informs this prior distribution to derive the posterior distribution for year 1+t.

Method 2: Accumulating imperfect sampling evidence

The second method we used for accumulating historical surveillance information adjusted the apparent prevalence for imperfect test characteristics (Figure 2). A Monte Carlo simulation model was implemented in WinBUGS to produce updated estimates for the prevalence, specificity and sensitivity distributions (appendix 1). The WinBUGS algorithm used the observed, or apparent, prevalence to impute the true prevalence by iteratively solving the following equation:

$$\textbf{(Eqn. 2)}\ p_a = (p * Se) + (1-p) * (1-Sp)$$

where p_a=apparent prevalence, p=adjusted (true) prevalence, Se=Sensitivity and Sp=specificity.

The model used the same sampling evidence that were examined in the first model. A uniform prior distribution was assumed for the first year. Using the WinBUGS program, the sampling evidence from the first year was assessed to estimate a posterior distribution. This posterior

distribution was then assumed to be the prior distribution for the second year. This algorithm was repeated until all nine years of evidence were incorporated into the prevalence estimate.

Prior distributions for sensitivity and specificity were approximated based on previous analysis and published field trials (Hoar et al., 2003 and Ward et al., 1996). Sensitivity and specificity were initially assumed to be Beta(98,3) and Beta(99,2) distributions, respectively. These distributions reflect an average sensitivity of 97% and an average specificity of 98%. Nevertheless, the WinBUGS algorithm uses a Gibbs sampling approach to estimate posterior distributions for these inputs after consideration of the testing results from each successive survey.

Each posterior distribution was based on 3000 iterations of the WinBUGS model following a burn in of 1000 observations. The 3000 observations constituted random values from posterior distributions for bluetongue prevalence, test sensitivity and test specificity. The observations were entered into SAS to generate maximum likelihood estimates of parameters for Beta posterior distributions.

Beta posterior distributions were assumed because the Beta distribution was theoretically plausible, flexible, and amenable to use as a prior distribution in the WinBUGS software. The values generated by WinBUGS were calculated using Beta prior distributions for prevalence, sensitivity and specificity. Therefore, it seems plausible that the posterior distributions should be Beta. The Beta distribution is also a plausible distribution for prevalence, sensitivity and specificity because it is constrained to range between 0% and 100%. Because it is a two-parameter distribution, the Beta distribution is also flexible enough to fit complex data.

Once the posterior Beta distributions for each year were estimated, the probability of the prevalence exceeding 2.0% was calculated.

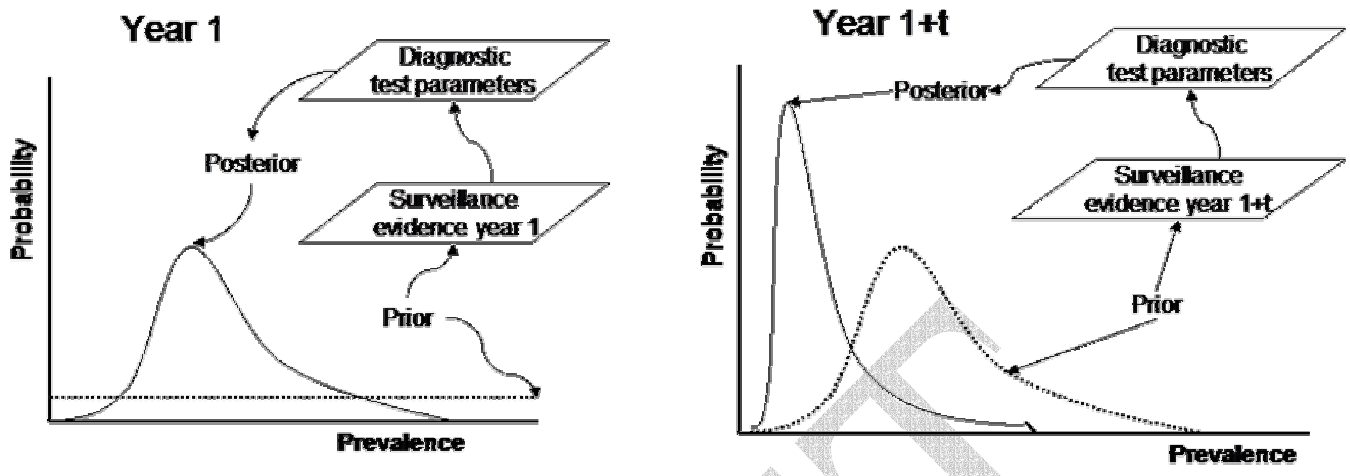

Figure 2: This is a conceptual illustration of accumulating imperfect sampling evidence across different years. Although similar in concept to Figure 1, the posterior distribution derived here for year 1 includes consideration of diagnostic test parameters (i.e., test sensitivity and specificity) that modify inferences about the true prevalence. Nevertheless, like Method 1, the prior distribution for year 1+t is exactly the same as the posterior distribution derived for year 1.

Method 3: Time value of information approach

The third method incorporated the potential for changes in prevalence between surveillance years with the WinBUGS model from the second method (Figure 3). Changes in prevalence between surveillance years are assumed to occur because infection transmits among individual cattle in the New England population. Unfortunately, a transmission model for bluetongue virus that was epidemiologically-based and validated was not readily available for inclusion in this method.

In lieu of an elaborate disease transmission model we assumed that prevalence was correlated in time by some fixed proportion. We developed a Monte Carlo simulation model to multiply the derived posterior distribution of one year by a scalar – but uncertain – coefficient to estimate a prior distribution for the subsequent year.

A transmission coefficient was estimated from the surveillance data collected in states outside of the New England area. This coefficient was the calculated slope of a regression equation where the first year prevalence was treated as the independent variable and the next surveillance period's prevalence treated as the dependent variable. The regression was fit with no intercept, i.e., if prevalence was 0% in year t then prevalence was assumed to be 0% in year t+1.

The regression analysis was simulated in the following manner. All possible pairs of adjacent years were entered into an @Risk program. For example, within a specific state 1991 and 1992 results would be a pair as would 1992 and 1993 results. Uncertainty in these paired observations was modeled using a bootstrap method that defined each member of the pair as a Beta distribution based on its respective surveillance results (i.e., $Beta(s+1, n-s+1)$). For each of 3000 iterations, a set of realizations of the paired data were used to calculate a slope value. If the slope fell below one (implying a decrease in prevalence from year 1 to year 2) we replaced the estimated coefficient with a value of one. This treatment conservatively forced prevalence only to increase or to remain constant from one survey to the next. During each simulation iteration a value selected from the posterior prevalence distribution was multiplied by the slope coefficient. The

product of these two values was one random observation used to form the prior distribution for the subsequent sampling year.

(Eqn. 3) $\text{Prev}_{Y=1+t} = \gamma \times \text{Prev}_{Y=1}$, where γ is the transmission coefficient.

All 3000 replicates from the @Risk model were entered into SAS to generate maximum likelihood estimates of the Beta distribution parameters. The estimated Beta distribution was then inputted to the WinBUGS model as a prior distribution and the algorithm described for Method 2 was followed to estimate a posterior distribution for the subsequent surveillance year.

Surveillance prior to 1996 occurred on an annual basis. After 1996 the surveillance became biennial. Transmission coefficients were calculated separately by fitting regression lines for the different time frames. There were 169 pairs available to estimate the one-year transmission coefficients applicable through 1996. There were 23 pairs available to estimate the two-year transmission coefficients applicable after 1996. Similar to the first two methods, the probability of the adjusted prevalence exceeding 2.0% was calculated.

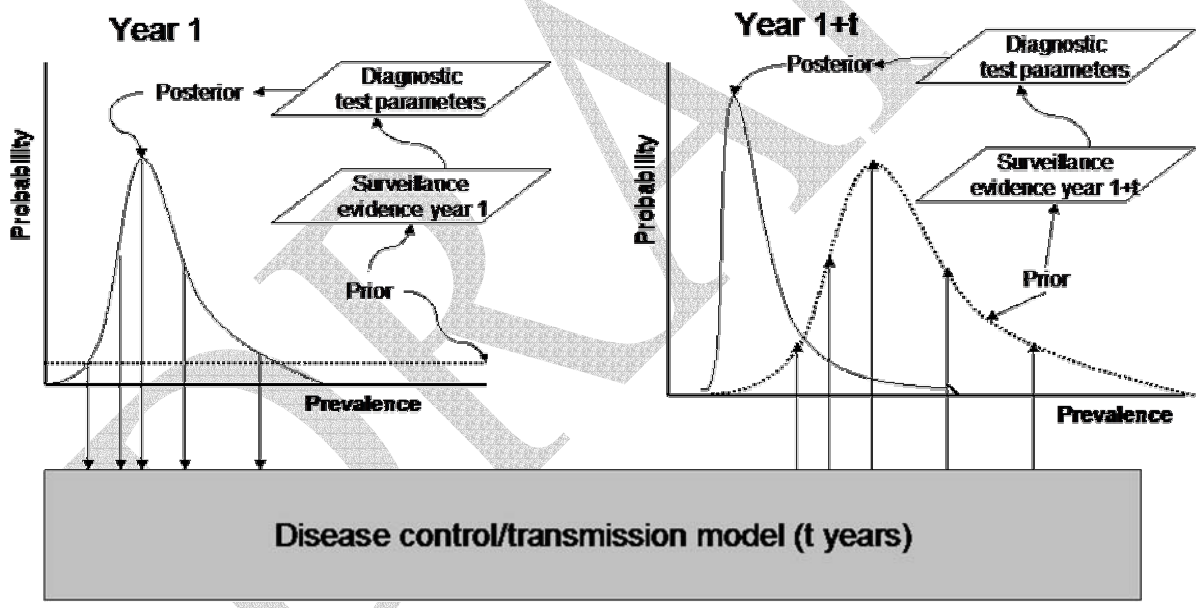

Figure 3: This is an illustration of accumulating sampling evidence while explicitly accounting for time in the valuation of previous evidence. The posterior distribution derived for year 1 serves as an input to a disease control/transmission model. The output of that transmission model is a predicted distribution for prevalence in year 1+t prior to consideration of the sampling evidence collected in year 1+t and the diagnostic test parameters. Therefore, the prior distribution for prevalence in year 1+t is some function of – but not exactly the same as – the posterior distribution derived in year 1.

Determining sample size needed

The final output of all three methods was a prior distribution for bluetongue prevalence in 2004. The results from Method 3 were chosen to demonstrate an approach for determining sample size for surveillance in 2004 because that prior distribution implied a higher prevalence compared to the other methods.

The basic approach to sample size determination was to use the prior distribution for 2004 and update it with alternative sample sizes (iteratively) to determine a posterior distribution that would allow for a 99% probability that the prevalence is less than 2%. We chose the 99% level because the prior distribution for 2004 already demonstrated that the probability that the prevalence was less than 2% was greater than 95% which indicates that no samples are needed.

The sample size determination was performed using @Risk software. A sample size was chosen for simulation. For each of the simulated iterations a prevalence level was randomly selected from the 2004 prior distribution. This prevalence was then used as an input into a binomial distribution to randomly select the number of positive results among the chosen sample size. The resulting number of "successes" (diseased animals detected) and sample size were used to update the parameters of the prior distribution as follows;

$$\textbf{(Eqn. 4)}\ Beta\left[\alpha_{prior} + s_{iteration}, \beta_{prior} + n - s_{iteration})\right]$$

where α_{prior} and β_{prior} are the parameters for the 2004 prior distribution, $s_{iteration}$ is the number of successes predicted in the 2004 survey and n is the sample size for the 2004 survey. This simulated Beta distribution represents a predictive posterior distribution for 2004.

The prevalence associated with the 99th percentile of the posterior distribution was calculated. The process was repeated 10,000 times at each potential sample size. The sample size which resulted in the mean of the 99th percentile prevalences being 2% or less was determined to be a reasonable sample size for the 2004 survey.

Results

Method 1

Across 12 years of surveillance for bluetongue antibodies in New England, a total of 7853 samples were taken and 25 positive results were reported from nine surveys (Table 1). In each surveillance year, the probability of the apparent prevalence being >2% was always 0.004 or less. The mean prevalence based on a Beta distribution varied annually from 0.16% to 0.78%. For the cumulative surveillance approach, the probability of the apparent prevalence being >2% was always <0.001 and the mean prevalence ranged from 0.17% to 0.40%. The Beta mean for the cumulative method tended to decrease over time except for the first year when the annual and cumulative prevalence were the same.

Table 1: Posterior distributions for annual and cumulative surveillance from Method 1.

Year	Annual				Cumulative			
	Number tested	Number positive	Beta mean (%)	Prob >2%	Number tested	Number positive	Beta mean (%)	Probability >2%
1991	1786	2	0.17	<0.001	1786	2	0.17	<0.001
1992	1424	10	0.77	<0.001	3210	12	0.40	<0.001
1993	712	1	0.28	<0.001	3922	13	0.36	<0.001
1994	745	2	0.40	<0.001	4667	15	0.34	<0.001
1995	380	1	0.52	0.004	5047	16	0.34	<0.001
1996	887	5	0.67	<0.001	5934	21	0.34	<0.001
1998	641	0	0.16	<0.001	6575	21	0.33	<0.001
2000	635	0	0.16	<0.001	7210	21	0.31	<0.001
2002	643	4	0.78	0.004	7853	25	0.33	<0.001

Accumulating evidence across time using Method 1 causes the resulting posterior prevalence distributions to shift (Figure 4). The central tendencies of the posterior distributions can shift dramatically. For example, the distribution with the smallest median (50^{th} percentile) value is the posterior distribution for 1991 while the distribution with the largest median value is the posterior for 1992. Nevertheless, a progressive reduction in distribution variance is evident as the sampling data is accumulated across time. For example, the 10^{th} and 90^{th} percentiles for the 1991 posterior distribution are 0.06% and 0.3%, respectively; a range of 0.24%. In contrast, the 10^{th} and 90^{th} percentiles for the 2002 posterior distribution are 0.25% and 0.41%, respectively; a range of 0.16%. Similarly, the standard deviations for the 1991 and 2002 posterior distributions are 0.1% and 0.06%, respectively.

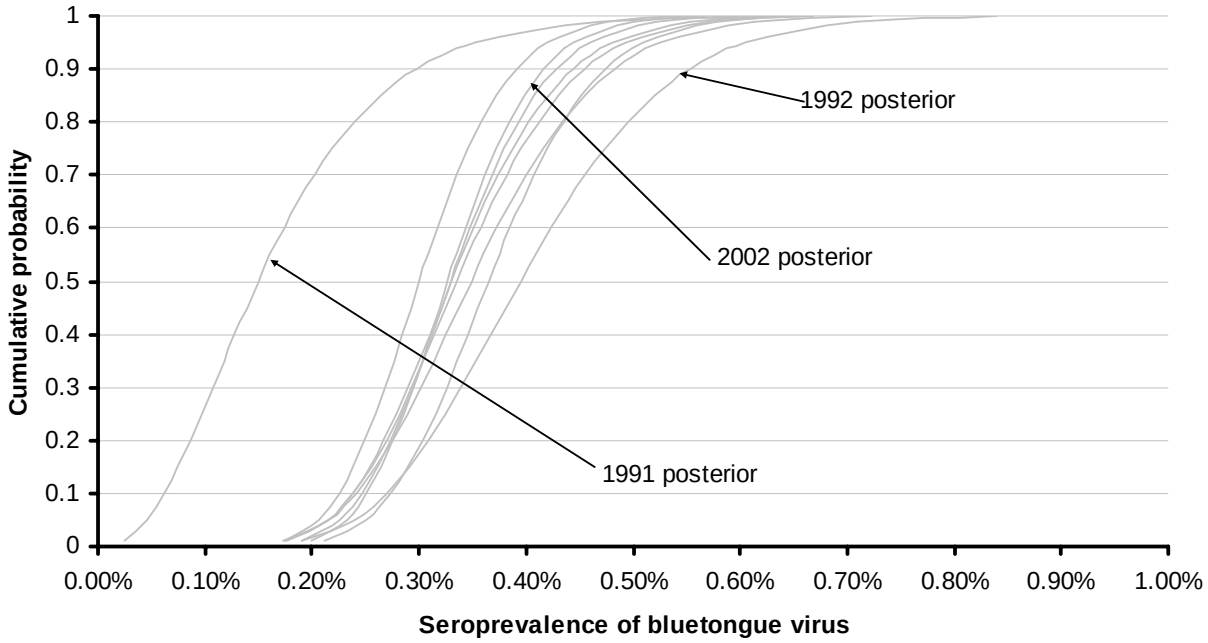

Figure 4: **This graph illustrates the nine posterior distributions estimated using Method 1. Although the central tendencies of the distributions can shift, there is a progressive reduction in distribution variance as more sampling evidence is accumulated across time.**

Method 2

Method 2 provides estimates for true bluetongue prevalence, sensitivity and specificity (Table 2). The estimated mean prevalence only varied between 0.07% and 0.2%. The probability of the adjusted prevalence exceeding 2.0% was always <0.0001. Specificity was very high and stable (~99.8%). Sensitivity fell between 96.5% and 93.6%.

The mean prevalence estimated following the 2002 survey (0.09%) is lower than the mean prevalence estimated for the same year using Method 1 (0.31%). Such a result can be approximated using Eqn. 2 and the estimated prevalence, sensitivity and specificity from Method 2 for the 2002 survey. This result suggests that despite the relatively high specificity of the serologic test for bluetongue virus, the true prevalence is less than the apparent prevalence (i.e., positive results are more likely to be false positive than negative results are to be false negative).

Table 2: Cumulative results for adjusted prevalence and test characteristics (sensitivity and specificity) using Method 2. The probability of prevalence exceeding 2% was <0.0001 for all posterior distributions.

Year	Posterior Prevalence			Sensitivity			Specificity		
	Alpha	Beta	Mean (%)	Alpha	Beta	Mean (%)	Alpha	Beta	Mean (%)
1991	1.17	1201	0.1	42.5	1.56	96.5	1429	2.54	99.8
1992	1.54	829	0.2	31.1	1.22	96.2	1316	4.15	99.7
1993	1.64	1336	0.1	24.3	1.05	95.9	1849	4.37	99.8
1994	1.82	1662	0.1	19.1	0.91	95.4	2030	4.61	99.8
1995	1.87	1787	0.1	14.6	0.79	94.9	2302	5.04	99.8
1996	2.08	1592	0.1	13.0	0.76	94.5	1913	5.3	99.7
1998	2.10	2218	0.09	11.2	0.71	94.0	2346	5.14	99.8
2000	2.07	2820	0.07	10.1	0.68	93.7	2477	4.33	99.8
2002	2.17	2362	0.09	9.71	0.66	93.6	2474	5.82	99.8

The shifts in posterior prevalence distributions for Method 2 are less dramatic than observed for Method 1. The 1992 posterior has the largest mean and standard deviation of the nine distributions estimated (Figure 5). Because it is informed by the 1998 and 2000 surveys in which no positive samples were found, the 2000 posterior has the smallest mean and standard deviation. Nevertheless, because four positives were found in 643 samples in the 2002 survey, the 2002 posterior distribution is shifted higher relative to the 2000 posterior distribution.

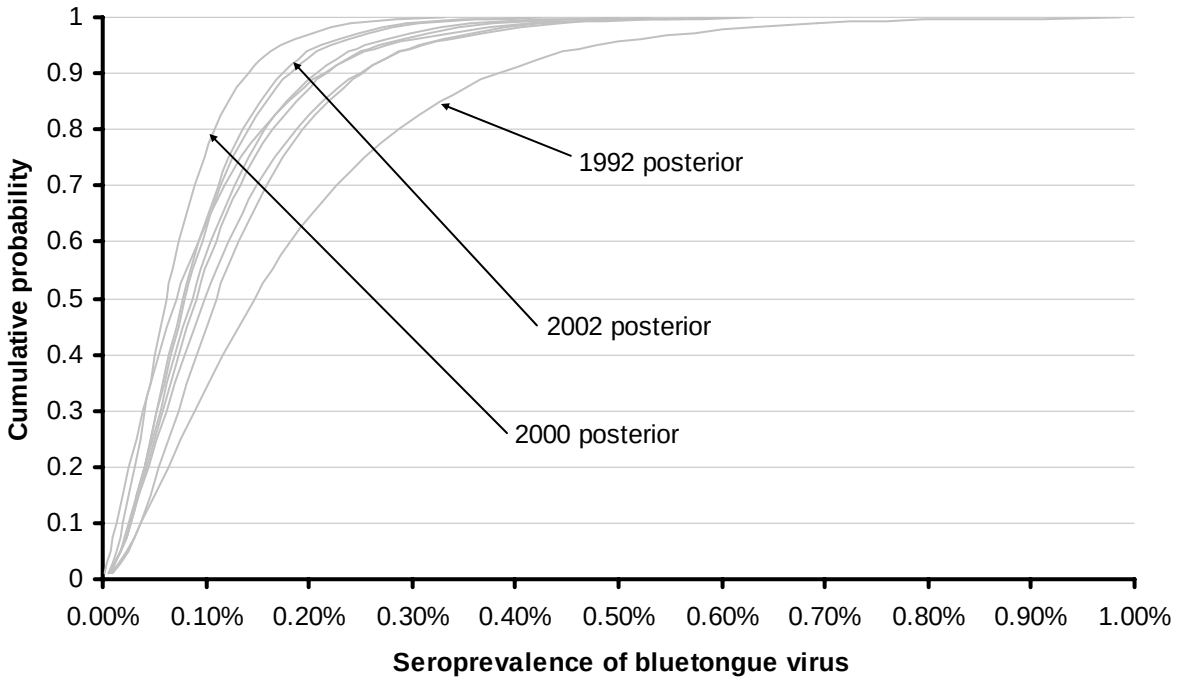

Figure 5: This graph illustrates the nine posterior distributions estimated using Method 2.

Method 3

This method required estimation of a transmission coefficient to model the change in prevalence across time. The one-year incremental transmission coefficient had a mean of 1.00 and a standard deviation of approximately 0.02; its 99th percentile was 1.08. Therefore, the prior distribution for a given year was essentially the same as the posterior distribution of the preceding survey year if that preceding survey was conducted just one year previously. Nevertheless, for surveys separated by two years, the transmission coefficient's mean was 2.03 and its distribution always exceeded 1.00 (Figure 6).

Method 3 estimates bluetongue prevalence, sensitivity and specificity while explicitly accounting for transmission dynamics across survey years (Table 3). The estimated mean prevalence varied more widely than did the other cumulative methods (0.1% to 0.7%). In contrast to the other methods, however, the results presented are actually prior distributions for the survey year. In other words, the prior distribution estimated for 2004 incorporates the sampling evidence from 2002 and the effect of the transmission coefficient on the 2002 posterior distribution.

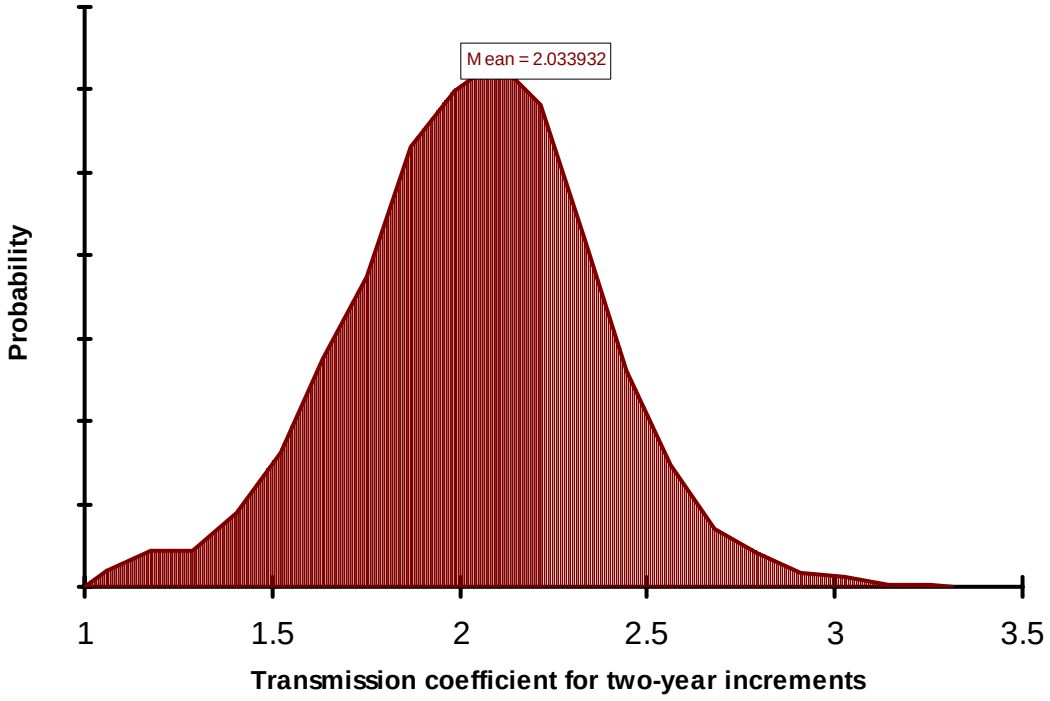

Figure 6: This graph shows the transmission coefficient probability distribution estimated from data pairs when surveys were conducted two years apart.

The mean prevalence was fairly stable during the first part of the surveillance period. After 1995, however, the mean prevalence increased and peaked in 2004. The probability of the adjusted prevalence exceeding 2.0% remained <0.0001 until 2004, when the probability was calculated to be 0.012. Sensitivity and specificity values were consistent with results from Method 2.

Table 3: Cumulative results for adjusted prevalence and test characteristics (sensitivity and specificity) with the transition scalar incorporated (model 3).

Year	Prior Prevalence				Sensitivity			Specificity		
	Alpha	Beta	Mean (%)	Prob >2%	Alpha	Beta	Mean (%)	Alpha	Beta	Mean (%)
1992	1.22	1238	0.1	<0.001	42.5	1.56	96.5	1429	2.54	99.8
1993	1.67	875	0.2	<0.001	28.7	1.18	96.1	1292	4.11	99.7
1994	1.76	1385	0.13	<0.001	22.4	1.01	95.7	1917	4.58	99.8
1995	1.87	1721	0.11	<0.001	17.8	0.88	95.3	1841	4.21	99.8
1996	1.9	1839	0.1	<0.001	15.0	0.81	94.9	1868	5.31	99.7
1998	2.0	788	0.25	<0.001	13.8	0.76	94.6	1868	5.31	99.7
2000	1.77	619	0.29	<0.001	11.4	0.73	94.0	2166	4.65	99.8
2002	1.66	549	0.3	<0.001	10.0	0.71	93.4	1222	2.31	99.8
2004	2.62	374	0.7	0.012	9.16	0.64	93.5	1139	2.46	99.8

In contrast to Methods 1 and 2, the prior prevalence distributions for Method 3 tend to increase in variance as sampling evidence is accumulated across time (Figure 7). Such a trend is predictable given that the posterior distributions are multiplied by the random variable γ. Because γ is most substantial for the two-year increments, the effect is most dramatic between the prior distributions of 2002 and 2004. In this case, the mean and standard deviation for 2004 is more than twice the mean and standard deviation for 2002. This effect is mostly the result of γ, but also reflects the four positive samples found in the 2002 survey.

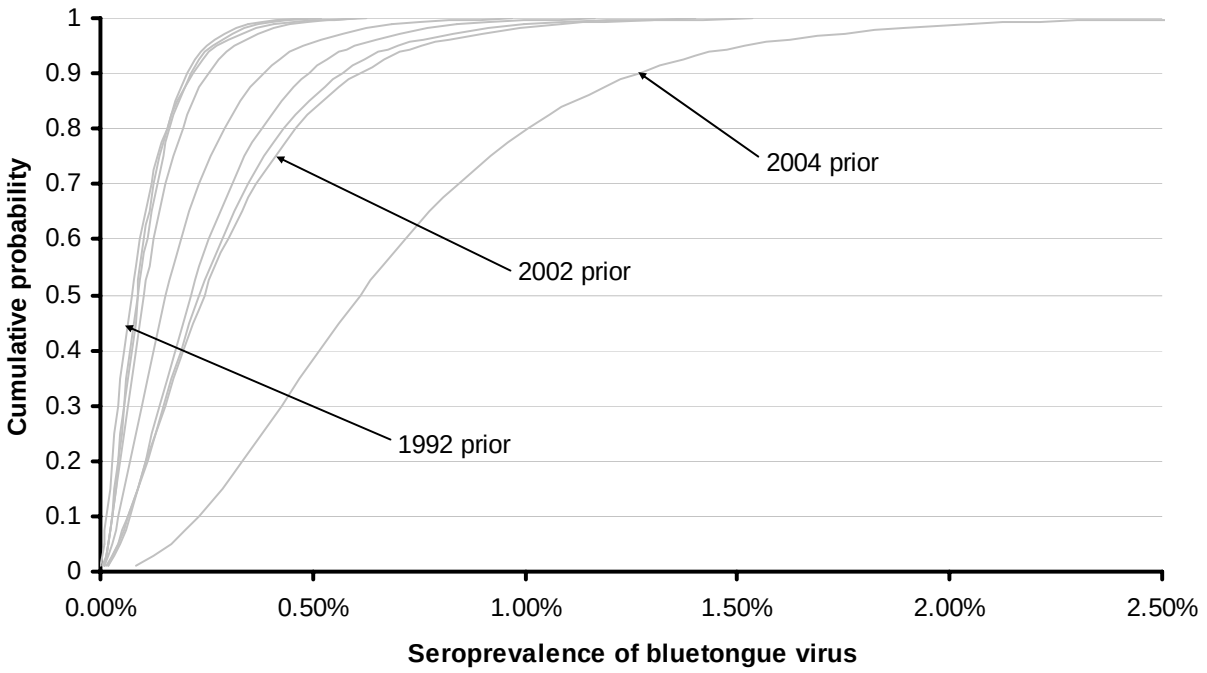

Figure 7: **This graph illustrates the nine prior distributions estimated using Method 3.**

Comparison of methods

The prior prevalence distribution for 2004 estimated by Method 3 suggests a larger mean and variance than the 2002 posterior distributions using Methods 1 or 2 (Figure 8). Because the time value of sampling information is not incorporated into Methods 1 and 2, the 2002 posterior distributions estimated by those methods are equivalent to the 2004 prior distributions.

If Methods 1 or 2 were used to estimate uncertainty about bluetongue prevalence in the New England states, there would be little doubt that the virus occurred among less than 2% of the cattle population. Such a conclusion suggests there is no need for further sampling in 2004. The effect of such sampling will be to redundantly support the prior evidence that bluetongue virus occurs at prevalence well below 2%.

The incorporation of a transmission coefficient to account for the time value of sampling evidence in Method 3 results in a higher probability that bluetongue prevalence is greater than 2%. There is a 1.2% probability that prevalence might exceed 2% and a 98.8% probability that prevalence is less than or equal to 2%. Nevertheless, the current guidelines for bluetongue surveillance only require a 95% probability that prevalence is less than, or equal to, 2%. Therefore, the results from Method 3 support classifying the New England states as minimal incidence without any further sampling in 2004.

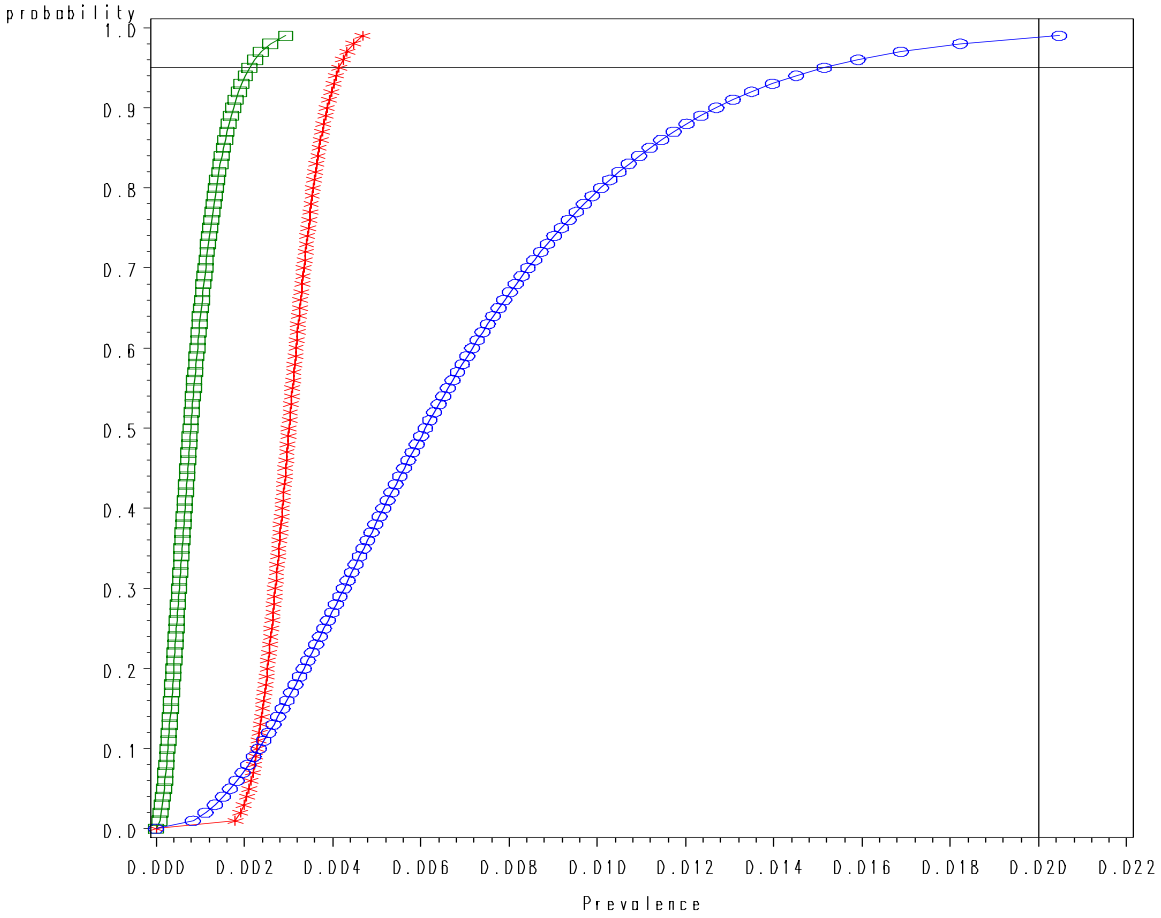

Figure 8: Comparison of the cumulative distributions for the prior distributions for 2004 from the three models (red=model 1; green=model 2; blue=model 3)

Sample size determination

In 2004 there is a 98.2% probability that prevalence is less than, or equal to, 2% using Method 3. If there was a requirement of 99% probability at the 2% prevalence level to achieve the minimal incidence classification, we can determine the approximate number of additional New England samples that would be required in 2004. Sample sizes were iteratively examined to identify a level that would return a 99th percentile value of 0.02 or less for the posterior distribution. The targeted posterior distribution was attained with a sample size of approximately 20 samples (Table 4). If 25 samples were taken then the mean percentile drops slightly below the 0.02 target.

Table 4: Simulated posterior distributions for sampling in 2004 based on potential sampling efforts.

Sample size	2004 Predicted Posterior Beta Distribution (means)		99th percentile (mean)
	Alpha	Beta	
10	2.69	383.9	0.0202
20	2.75	393.9	0.0200
25	2.79	398.8	0.0199

Discussion

Bluetongue surveillance has been ongoing in the northeastern United States since the early 1980's. During that time period the sample size has decreased from a high value of 3332 (in 1983) to about one-fifth of that level in recent years. Additionally, since 1996 the surveillance has shifted from being implemented annually to being conducted biennially. The decrease in sampling effort is in contrast to the usual requirement that surveillance based on the absence of prior information will require increasingly large sample sizes as prevalence gets small regardless of whether the objective is to detect or estimate disease. We believe the alteration in sampling protocol over time is an intuitive acknowledgement of the value of historical surveillance information.

The three methods we used to accumulate historical information quantitatively demonstrated the intuition behind these protocol changes. The value of each method is related to the assumptions that are necessary for their implementation. The first method essentially accumulates the samples from year to year and assumes a steady disease state and a single population which is being tested with a perfect test. The second method relaxes the perfect test assumption but no transmission of infection is assumed to occur from year to year. The third method accounts for transmission of infection from year to year. Although more detailed transmission models can be constructed, we believe the third method is a sufficiently conservative method for accumulating information.

The objective of bluetongue surveillance has been to document that specific areas have prevalence of less than 2% with 95% confidence. The Bayesian approach used here allows us to make a probabilistic statement based on the accumulated information. The prior distributions for 2004 from all three methods indicate that this probability is greater than 95%. These results suggest that no sampling is required in the northeastern area to meet Canadian import criteria. If bluetongue surveillance is not implemented in the northeast this year then the third method would have to be extended to allow for additional uncertainty in the prevalence distribution in years following 2004.

In contrast, neither Methods 1 nor 2 would incorporate additional uncertainty due to skipping a surveillance year.

We demonstrated the method for estimating sample size with Method 3 by assuming we raised the probability of the prevalence being less than 2% from 95% to 99%. The sample size required when the historical information is available is substantially less than the current surveillance level. In the past, a sample of 600 animals was collected for each state or region during each survey. Such a sample was consistent with detecting a prevalence of 0.5% or greater with 95% probability. Using the informed prior distribution, however, a sample of about 20-25 would be sufficient to demonstrate prevalence less than 2% with 99% confidence. More sophisticated methods, such a value of information analysis that considers the costs or benefits of misclassifying states, could be used to derive an optimal sample size. Yet, these advanced methods would require substantially more information than the prior distribution we used to determine the necessary sample size. Furthermore, such methods would be more appropriately applied by the importing country because, ultimately, decisions about confidence in prevalence levels are made by the importer.

Method 3 has the potential for incorporation of more complex transmission models to more accurately describe changes in disease over time. For an arbovirus, a transmission model could include vector density and competence, weather patterns, circulating virus levels. Ultimately, we would expect that surveillance would not be restricted to serologic testing of cattle but could include field collection of vector species.

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Appendix 1

The WinBUGS model below was used to concurrently estimate an adjusted prevalence (pi), sensitivity (se) and specificity (sp). This model is for the first sampling year where the prior distributions for se and sp were determined from the literature and the adjusted pi was assigned an uninformed prior.

```
#Year one (1991) model
model
{
s~dbin(p,n)
p <- (pi*se + (1-pi)* (1-sp))

pi~dbeta(1,1)
se ~ dbeta(98,3)
sp ~ dbeta(99,2)

}

'Data
list(n=1786, s=2)

'inits
list(sp=0.95, se=0.95, pi=0.1)
```