

# 1 **Bayesian approaches to epidemiological surveillance: a review and** 2 **introduction for risk-assessors and decision-makers.**

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## 15 **Abstract**

16 Quality decision making in public health and animal health surveillance relies on addressing the challenge of  
17 synthesizing health-related information from disparate sources into actionable information. In the case of  
18 early warning systems for impending outbreaks this challenge is compounded with the need for evidence  
19 generation in real-time, and timely decision-making. The analysts running and interpreting the output from  
20 the epidemiological surveillance algorithms must present those in a format that is appropriate to those who  
21 have responsibility for taking action. We argue that the Bayesian inference framework, which provides a  
22 posterior probability for a given disease state, can be easily combined with a decision theory framework to  
23 support decision-making for disease surveillance and control in a transparent way. We provide a simple  
24 introduction to Bayesian approaches to epidemiological surveillance, with a particular focus on syndromic  
25 surveillance (SyS), that covers: (i) full Bayes (hierarchical) models; (ii) empirical Bayes models; and (iii) semi-  
26 Bayes models that use Bayesian approaches to estimate model parameter distributions but that produce an  
27 output not intended for Bayesian inference. We illustrate the flexibility and robustness of applying Bayesian  
28 probabilistic reasoning with three working examples based on animal SyS data from France and Norway.

29 In more complex SyS scenarios, the main drawback of applying full Bayesian methods resides in the  
30 challenge of setting prior probabilities and the demanding computations, which may necessitate the use of  
31 approximate solutions. As an alternative approach, a framework for communicating SyS results based on the  
32 Bayes factor, i.e. the ratio between the posterior and prior odds that an outbreak is ongoing against an  
33 alternative hypothesis, is presented. Such explicit separation of prior information about a hypothesis and  
34 evidence from the data makes the framework useful for presenting results even when the modelling  
35 approach is not in itself Bayesian.

36 Keywords: Syndromic surveillance, health surveillance, Bayesian modeling, Time-series analysis, Hidden  
37 markov model, outbreak detection

38

## 39 Introduction

40 Health surveillance provides scientific and factual evidence to risk-assessors which are essential to inform  
41 decision-making, and to motivate timely and appropriate action. Increased availability of health-related data  
42 and methodological innovations have fostered new approaches to optimise surveillance systems for early-  
43 detection. One of them is syndromic surveillance (SyS). The public health sector has initiated the use of  
44 “health-related data that precede diagnosis and signal with sufficient probability of a case or an outbreak to  
45 warrant further public health response” (Fricker and Rolka, 2006) for surveillance at the turn of this century,  
46 and has been followed in the last decade by the veterinary health sector (Dórea and Vial, 2016; Dórea et al.,  
47 2011).

48 Risk-assessors are faced with an unprecedented amount of health-related data being passively collected on  
49 national, regional and even individual levels (from flu-related internet searches to antibiotic sales in the pig  
50 industry). Decision-makers must take an increasing number of routine decisions based on these data: which  
51 reports should be part of a formal investigation? Should they wait another day before acting? Answering  
52 such questions is not a trivial task given that passive surveillance data are associated with a higher degree of  
53 uncertainty compared to, for example, data on notifiable diseases (Onisko et al., 2006).

54 Observable data evaluated under different scientific hypotheses (e.g. the null hypothesis  $H^0$ : “no outbreak of  
55 the disease is currently occurring in this region” and the alternative hypothesis  $H$ : “an outbreak of the  
56 disease is currently occurring in this region”) are typically modelled through probability distributions which  
57 depend on unknown quantities called parameters. There are two main approaches to the statistical  
58 inference of parameters and of hypothesis testing. These two classes are known as the *frequentist* and the  
59 *Bayesian* approach. Both classes have existed for centuries but in practice, frequentist methods have  
60 dominated, in large part due to the fact that they include a number of statistical tests that allows  
61 calculations to be performed by hand or using pre-calculated tables. Frequentist approaches assume that  
62 the data are a repeatable random sample (i.e. they can be associated with frequencies) from an infinite  
63 sampling scheme. The underlying parameters are treated as fixed at some unknown value that remains  
64 constant during this repeatable sampling process. In the Bayesian paradigm, the data are treated as  
65 observations from a realised sample (i.e. fixed) and parameters are described probabilistically, reflecting the  
66 uncertainty about their true value. Bayesian methods are very flexible but even moderately complex models  
67 will result in integrals that can only be solved by numerical methods such as Markov chain Monte Carlo  
68 (MCMC) methods. Consequently Bayesian methods did not gain popularity until computational power  
69 become readily available (Madigan, 2005).

70 Ideally, a decision should be made which maximises the expected benefit based on decision theory. We  
71 argue that Bayesian methods applied to health surveillance problems provide an output that is better apt to  
72 support decision-making than the corresponding frequentist approaches. While outputs may support  
73 decision making with transparency, the terminology and technical aspects of the Bayesian inference network  
74 may be daunting and difficult to grasp, hampering communication about the model approaches used in the  
75 surveillance system and the interpretation of statistical outputs. Decision-makers may, as a result, not fully  
76 understand what inference can be drawn from these outputs. The objectives of this paper are three-fold: 1)  
77 to provide a theoretical yet simple introduction to Bayesian methods commonly applied in health  
78 surveillance; 2) to discuss how Bayesian (inference) framework can be used as a general approach for  
79 presenting results from SyS to decision-makers; and 3) to illustrate, through three working examples, how a  
80 Bayesian framework can be applied to outbreak detection scenarios .

## 81 Theoretical overview

82 A literature search aimed at identifying Bayesian methods already used in the field of animal or public health  
83 surveillance was performed in Scopus using the following search string:

84 TITLE-ABS-KEY ( ( bayes\* AND surveillance ) OR ( bayes\* AND syndromic ) )

85 It was outside the scope of this work to provide a systematic literature review. The goal of this scoping  
86 exercise was to identify key references to build the theoretical framework presented, and find relevant  
87 examples to illustrate the use of this framework in practice. Title and abstract were screened for all 3225  
88 resulting documents, and selected abstracts subjected to full-text evaluation. All reports identified which  
89 specifically report the use of Bayesian methods for outbreak detection were included and are cited in the  
90 relevant sections below.

91 A closer look at the articles retrieved from the first search revealed that the terminology used in literature is  
92 not consistent and that a search with fixed keywords would miss significant pieces of work. Thus, the initial  
93 search was followed up by a “snowball approach” in which we looked up the original works cited in books,  
94 reviews and research papers.

## 95 Working examples

96 To illustrate the different approaches to probabilistic reasoning in a Bayesian framework, three surveillance  
97 working examples were constructed:

98 1) Syndromic data on French horses presenting nervous symptoms and respiratory symptoms are evaluated  
99 each week with an empirical Bayesian network to detect incursions of West Nile virus (as in (Mats Gunnar  
100 Andersson et al., 2014)).

101 2) A dynamic empirical Bayesian network is applied to the same data for change point analysis.

102 3) A full Bayes approach to spatio-temporal SyS for bluetongue using on-farm mortality and late abortions  
103 data in Norwegian cattle. More details about this example are given in the Supplementary Material.

104 Although the examples we provide are based on animal health surveillance scenarios, the concepts they  
105 illustrate are very much transferable to public health surveillance systems.

## 106 An introduction to Bayesian inference

107 Important concepts in Bayesian statistics are the prior probability, which is the probability assigned to a  
108 hypothesis or event before the data were observed; and the posterior probability which is the probability for  
109 the same hypothesis given the prior probability and the relevant data (Bernardo and Smith, 1994;  
110 Christensen et al., 2011). The central part of Bayesian statistics is the Bayes’ theorem (equation 1), which  
111 allows us to calculate the posterior probability of a hypothesis of interest  $H$  (e.g. disease present) given data  
112 regarding a chosen indicator event  $E$  (e.g. number of reported clinical cases):

$$113 \quad P(H|E) = \frac{P(E|H)P(H)}{P(E)} = \frac{P(E|H)P(H)}{P(E|H)P(H) + P(E|H^0)P(H^0)}, \quad (1)$$

114  $P(H)$  is the prior probability of the disease within our population and  $P(E|H)$  and  $P(E)$  are the conditional  
115 probability of observing the symptoms in the presence of the disease, and of observing the symptoms  
116 regardless of the disease state of the population respectively.  $H^0$  is the null hypothesis of no disease  
117 outbreak, while the alternative  $H$ , an ongoing outbreak of the disease.

118 A common form of Bayes’ theorem is the odds form (equation 2):

$$119 \quad \frac{P(H|E)}{P(H^0|E)} = \frac{P(E|H)}{P(E|H^0)} \times \frac{P(H)}{P(H^0)} \quad (2)$$

120 It can also be expressed as:

121  $O_{post} = LR \times O_{prior}$  (3)

122 In the form shown in equation (3) it is apparent that the ratio between posterior ( $O_{post}$ ) and prior odds  
123 ( $O_{prior}$ ) equals the likelihood ratio ( $LR$ ) for the observed evidence under the two hypotheses. This form is  
124 extensively used when reporting results from the analysis of forensic evidence where  $LR$  is referred to as  
125 *value of evidence* (Aitken and Taroni, 2004). More generally the ratio of the posterior and the prior odds is  
126 known as the *Bayes factor*.

127 In a continuous sampling space, computation of  $P(E|H)$  involves integration over the unknown model  
128 parameters  $\theta$ :

129 
$$P(E|H) = \int P(E|\theta, H)\pi_y(\theta)d\theta$$
 (4)

130 Where  $\pi_y(\theta)$  is the probability distribution of  $\theta$  based on training data or expert opinion  $y$ . Starting from a  
131 (possibly vague) prior distribution  $\pi(\theta)$ , an updated (posterior) distribution  $\pi_y(\theta)$  given  $y$  may be found via  
132 the general form of Bayes' theorem, see e.g. (Christensen et al., 2011). In other cases, the Bayes factor may  
133 be assessed "directly" as the  $LR$  in equation (2) above, i.e. without any further averaging or integration over  
134 parameters or sub-hypotheses.

135 A natural extension of the Bayesian idea that the values of parameters arise from distributions is the use of  
136 models where parameters arise within hierarchies. In a SyS context, the probability that a disease case with  
137 a syndrome is observed would be a parameter of the distribution of reported cases, and when this  
138 parameter is unknown it may be modelled by a probability distribution. In Bayesian modelling, the  
139 parameters of a prior distribution are referred to as *hyperparameters* and their probability distribution  
140 referred to as *hyperprior distributions*. In the example above the hyperparameter "reporting probability" and  
141 its probability distribution have a real meaning but hyperparameters may also represent unknown statistical  
142 relationships. Using hyperprior distributions in addition to prior distributions is known as *hierarchical Bayes*.  
143 This approach is commonly used for multilevel modelling as it allows us to explicitly incorporate uncertainty  
144 from the multiple levels of the information.

145 For further reading about Bayesian inference see e.g. (Christensen et al., 2011).

## 146 Hierarchical Bayesian models and Bayesian Networks

147 Bayesian models for SyS will typically be based on multiple variables describing different stochastic events in  
148 which the output from one variable is the input for another. A chain of variables may for example describe (i)  
149 the distribution of infected animals; (ii) the number of symptomatic animals given (i); and (iii) the number of  
150 reported animals given (ii). Such models are usually referred to as hierarchical models or *Bayesian networks*  
151 (BN). Other names include Bayesian belief networks, probabilistic graphical models, or probabilistic  
152 independence networks. There is no clear difference between a hierarchical model and a BN and the latter  
153 may be seen as a graphical representation of the joint distribution of a set of variables in the model.

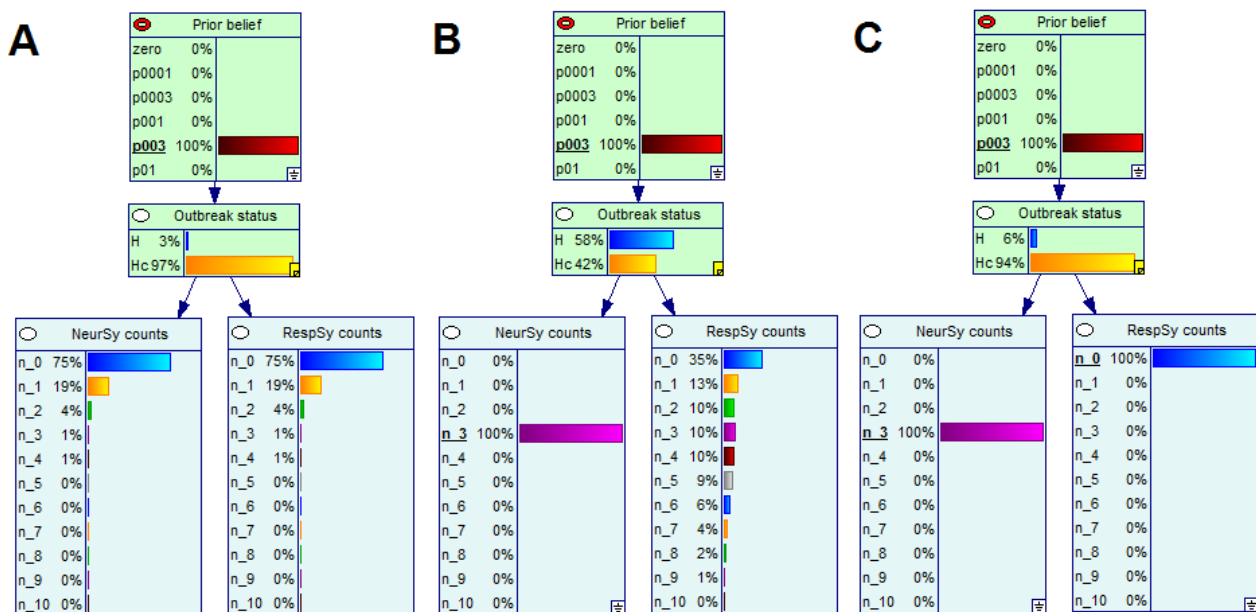
154 The structure of a BN is made up of variables (called *nodes*) which are connected probabilistically (through  
155 *arcs*). The arcs may indicate a direct, functional relationship or an observed statistical relationship where the  
156 cause for the correlation may be outside the model. If the arcs embody direct causal relationships, then the  
157 model is called a *causal BN*. Each node  $X_i$ , represents a function which takes the value of the parental nodes  
158 as input to calculate the probability for each *state* of the node (value of that variable):  $P(X_i|\text{parents}(X_i))$ . If  
159  $X_i$  has no parent, the prior probabilities of its states are specified. Nodes in BN must respect the *Markov*  
160 *condition*, i.e. a node must be independent of its non-descendants, given the state of its parents. This  
161 Markov condition allows us to factor the complete joint distribution of the variables in the model as  
162 following equation (5):

163  $P(X_1, X_2, \dots, X_n) = \prod_{i=1}^n P(X_i | \text{parents}(X_i))$  (5)

164 From equation (5) it then becomes possible to derive the probability of any subset of nodes conditioned on  
 165 the state of another subset of nodes.

166 Figure 1 illustrates how an empirical Bayesian model, where syndromic data are evaluated for each week  
 167 independently, as in (Mats Gunnar Andersson et al., 2014), can be represented as a BN. We used data on  
 168 French horses presenting nervous symptoms (NeurSy) and respiratory symptoms (RespSy) to detect  
 169 incursions of an exotic disease, West Nile virus. The probability distributions of neurological symptoms  
 170 (NeurSy) and respiratory symptoms (RespSy) would typically be estimated by dynamic regression. The  
 171 numbers shown in figure 1 are hypothetical.

172



173

174 **Figure 1:** In this empirical Bayesian model, nodes with a red circle (e.g. “prior Belief”) are decision nodes with  
 175 values set by the user, whereas nodes with a white filled circle are chance nodes. When a chance node  
 176 shows several bars they represent the estimated probability of the node being in that state (e.g. observing 1,  
 177 2, 3,...n syndromic cases). When the chance node has a single bar, 100%, the value of the node is known.  
 178 (e.g. Fig 1b, NeurSy counts). In this case the value of the node is used to recalculate the probability of the  
 179 states of the other nodes in the model.

180

181 BN are quite robust to imperfect prior knowledge and probabilities need not be exact to be useful. This is an  
 182 interesting trait of BN as causal conditional properties are often easier to estimate than the reverse. For  
 183 example, clinicians would find it easier to estimate  $P(\text{NeuroSy} | \text{WNV})$  than  $P(\text{WNV} | \text{NeuroSy})$ .

184 **Bayesian inference and decision theory**

185 Bayes’ theorem can easily be applied *a posteriori* to derive the probability of an outbreak given a statistical  
 186 alarm (signal above threshold: yes/no) derived from frequentist methods (equation 6):

187 
$$p(\text{outbr.} | \text{alarm}) = \frac{p(\text{alarm} | \text{outbr.}) * p(\text{outbr.})}{p(\text{alarm} | \text{outbr.}) * p(\text{outbr.}) + p(\text{alarm} | \text{no outbr.}) * p(\text{no outbr.})}$$
 (6)

188 Risk-assessors will usually have some idea about the prior probability of an outbreak  $P(\text{outbr.})$  and the false  
189 alarm rate of the system  $p(\text{alarm}|\text{no outbr.})$ . Sensitivity  $p(\text{alarm}|\text{outbr.})$  is much harder to quantify as it  
190 will depend on the shape and magnitude of the outbreak. However, it is possible to compute upper and  
191 lower bounds for the posterior probability  $p(\text{outbr.}|\text{alarm})$  by assuming that the sensitivity is, at worst  
192 equal to the false alert rate, and at best equal to 1. In practice, the probability  $p(\text{outbr.}|\text{alarm})$  would  
193 depend on whether the counts are near or very much above a pre-defined threshold (Grossi, 2008).

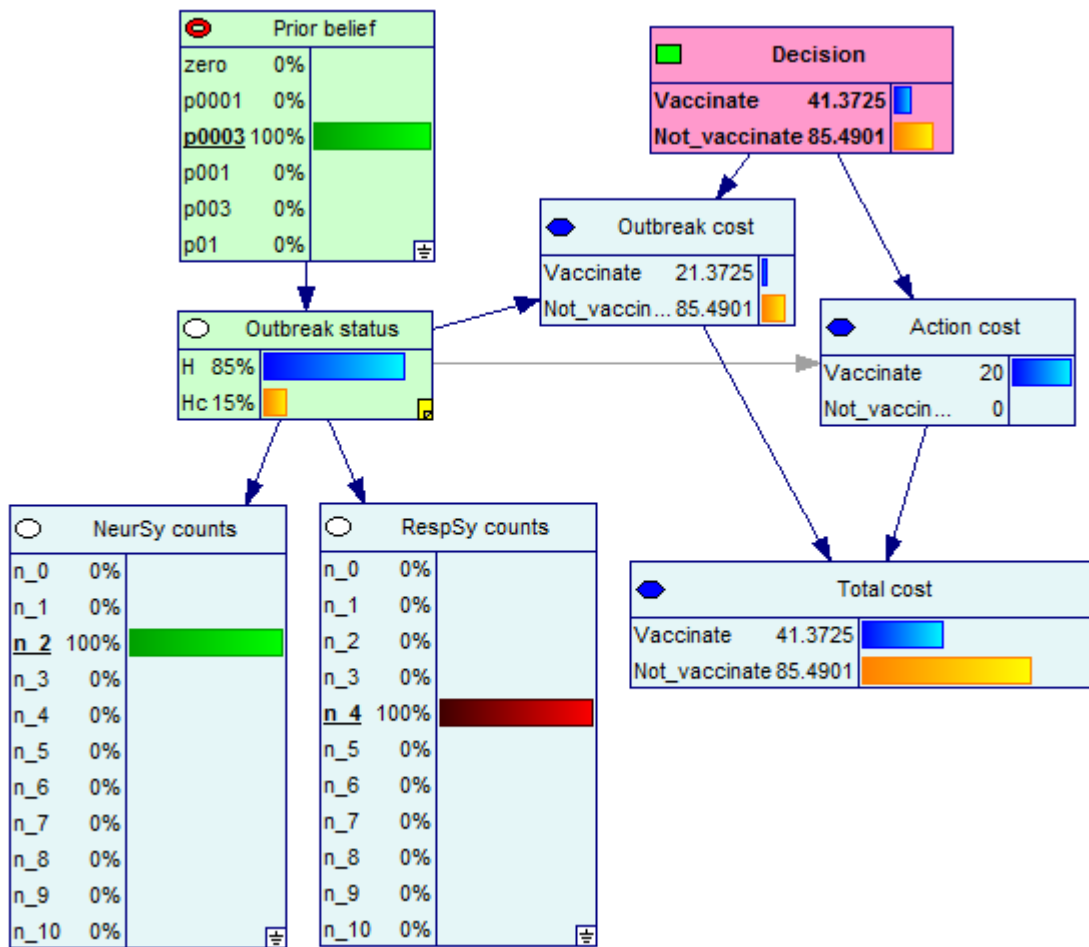
194 Within the Bayesian framework, it is not necessary to define a threshold for the signal (e.g. number of  
195 clinical cases observed). We may instead use the probability densities for the observed signal given an  
196 outbreak  $f(\text{signal}|\text{outbr.})$  or no outbreak  $f(\text{signal}|\text{no outbr.})$ :

$$197 \quad p(\text{outbr.}|\text{signal}) = \frac{f(\text{signal}|\text{outbr.}) * p(\text{outbr.})}{f(\text{signal}|\text{outbr.}) * p(\text{outbr.}) + f(\text{signal}|\text{no outbr.}) * p(\text{no outbr.})} \quad (7)$$

198 and let the threshold be defined for a given posterior probability or expected utility of action (Mats Gunnar  
199 Andersson et al., 2014). The latter is the average amount of clinical cases, or loss of animals, that we expect  
200 to see. Since an unmanaged outbreak as well as actions will result in costs, the expected utility will always be  
201 zero or negative.

202 The Bayesian approach, centered on sequential inference, constitutes a transparent support to risk-  
203 assessors (Heaton et al., 2012) but in some situations, deriving the posterior probability of an outgoing  
204 outbreak may not be enough to take informed mitigation measures (e.g. vaccination, quarantine). The costs  
205 and benefits of the possible actions must be considered in a way that is adaptive, i.e. relies on the latest  
206 collected information. This is particularly important when the surveillance goal of the system is early  
207 detection and decision-makers require an understanding of the explicit trade-offs between waiting another  
208 day for more data and acting today based on the information collected so far.

209 Decision theory is a framework for making optimal decisions given values and uncertainties and is closely  
210 related to game theory. Since Bayesian models for Sys will present as output a posterior probability for each  
211 state, given prior knowledge and evidence, they are easily combined with a decision theory framework as  
212 discussed in (Mats Gunnar Andersson et al., 2014; Onisko et al., 2006) to design a surveillance system that is  
213 optimal, accounting for costs of actions and consequences of outbreaks. Many software for BN, including the  
214 GeNIe modeling environment (“BayesFusion, LLC,” n.d.; Druzdzel, 1999), allows the user to incorporate  
215 functions for calculating utility as extra nodes in BN models. BNs with utility nodes are referred to as  
216 influence diagrams (Figure 2). Decision support models can be built in which a Bayesian model is combined  
217 with a decision theory framework to evaluate the best decision given the evidence or the added value of  
218 “waiting” for more data; or to analyse alternative ways of epidemic control under imperfect information (Lin  
219 and Ludkovski, 2014).



220

221 **Figure 2:** Example of a simple Influence Diagram where the posterior probability of an outbreak is used to  
 222 decide on whether to vaccinate. The evaluation nodes (blue hexagon) takes different values for each  
 223 combination of states of the parental decision and chance nodes. The values shown in the example are  
 224 hypothetical.

225

226 **Dynamic Bayesian Networks (DBN) and Hidden Markov Models HMM (HMM)**

227 If a BN is used to model time-series data, i.e. the arcs flow forward in time, it is known as a *dynamic Bayesian*  
 228 *network* (DBN) or sometimes as temporal BN or two-time slice BN. The DBN represents graphically  
 229 conditional independencies (arcs) between a set of time instances (nodes) with probabilities. The simplest  
 230 DBN for a sequence of observations  $\{Y_1, \dots, Y_t\}$  is the first-order Markov model which only uses  $Y_{t-1}$  to  
 231 derive the value of  $Y_t$ . If the observation  $Y_t$  is generated by some variable which state  $S_t$  is discrete and  
 232 hidden from the observer, the DBN will form a hidden Markov model (HMM). In HMM, both the sequence of  
 233 states and observations follow a first-order Markov order – that is, a given state  $S_t$  is independent of all the  
 234 states prior to  $t - 1$ ; and given  $S_t$ ,  $Y_t$  is independent of the states and observations at all other time indices.

235 A belief propagation algorithm (Pearl, 1988) is used to update the probabilities of all the nodes in the  
 236 network to incorporate new evidence (i.e. new observations). The objective of HMM is to compute the  
 237 optimal estimate of the hidden state (and its uncertainty) given the observed data - the posterior probability  
 238 distribution (or density)  $P(S_t|Y)$  - which can be derived as a recursive form of Bayes' rule. This can be  
 239 computed through a forward filtering and backward smoothing approach (Scott, 2002). Parameter



240 estimation is then performed using methods such as Gibbs sampling (Carter and Kohn, 1994), the  
241 expectation-maximisation algorithm or Markov chain Monte Carlo (MCMC) sampling (Ryden, 2008).

## 242 **Markov switching models & State-space models**

243 Markov switching models (MSM) are an extension of HMM which include lagged observations. The  
244 observable random variables in the MSM depend on their historical values as well as the hidden state  
245 variables.

246 State-space models (SMM) (also known as linear Gaussian state-space models and Kalman filters) are also an  
247 extension of HMM in which the latent variable is continuous and normally distributed (as opposed to  
248 discrete and following a multinomial distribution). A good accessible introduction to HMM, DBN and their  
249 numerous extensions can be found in (Ghahramani, 2001).

## 250 **Not one but several Bayesian approaches**

251 The general term Bayesian may be applied to “any method that seeks to approximate the posterior  
252 (probability) distribution for some variable(s) or parameter(s) of interest” (definition attributed to (Bernardo  
253 and Smith, 1994)). Generally, three types of Bayesian models can be considered:

254 I. Models in which data are used to obtain posterior probability distributions for parameters which are then  
255 used for inference. Such hierarchical models, that include hyperparameters and hyperpriors, are referred to  
256 as **full Bayes** (Lawson and Kleinman, 2005). Some publications use the term “full likelihood method” for  
257 these models (Frisén and Andersson, 2009). A full Bayes approach entails formulating subjective prior  
258 probabilities to express pre-existing information; carefully modelling the data structure; checking and  
259 allowing for uncertainty in model assumptions; and possibly formulating a set of possible decisions and a  
260 utility function for the value or cost for correct and incorrect decisions.

261 II. Methods that seek to estimate the posterior probability of a variable of interest, but do not build full  
262 Bayes models are collectively named **empirical Bayes** (Lawson and Kleinman, 2005). In this case, point  
263 estimates for (some) input parameters are used (e.g. based on maximum likelihood or linear regression)  
264 rather than applying a parameter distribution.

265 III: Models that use Bayesian approaches to estimate model parameter distributions but that produce an  
266 output in a format not intended for Bayesian inference. These can be referred to as **semi-Bayes**.

267 From a decision- maker’s perspective the semi-Bayes approach (III) is indistinguishable from the traditional  
268 frequentist approach. Bayesian models may be used to estimate parameters of a regression model for time  
269 series analysis, as shown in Jung et al.(Jung et al., 2006), but the resulting model is used to compute  
270 confidence intervals for the syndromes of interest and define action thresholds just as in a traditional SyS.  
271 These were not often reported in the SyS literature and will not be discussed further.

272 Our literature informed discussion presented below will focus on the first two cases, full Bayes and empirical  
273 Bayes models. Within each of these classes, the models developed may differ significantly in their  
274 mathematical representation and technical implementation. In many cases, the naming of the methods and  
275 the technical description (e.g. using discrete distributions for small counts but approximating data with  
276 continuous distributions for large counts) may mask the fact that the models are, at a more fundamental  
277 level, very similar.



## 278 Bayesian framework as applied to SyS

### 279 1. One region-one time unit

280 The simplest situation is a surveillance system that, as in working example 1, is implemented for a region as  
281 a whole, looking at data for one time unit at a time. Observation  $Y$  (e.g. number of clinical cases for a  
282 syndrome) at time  $t$  is generated by some process (health/disease status of the population under  
283 surveillance) whose state  $S_t$  is hidden from the observer. The standard frequentist solution to this scenario is  
284 the Shewhart method which compares a daily sample statistic against an upper control limit typically set to  
285 be a multiple of the standard deviation of the mean (Shewhart, 1939). While most efficient in detecting  
286 spike-type outbreaks, the Shewhart method does not perform well when the increase in the mean of the  
287 process is slow.

#### 288 I. Full Bayes

289 Schmidt and Pereira (Schmidt and Pereira, 2011) reviewed generalized dynamic models commonly used for  
290 modeling time series of count data, and demonstrated how the parameters of interest could be estimated  
291 using a full Bayes approach. In particular, the authors demonstrated how a Bayesian framework could be  
292 used to estimate the probability of disease (in their case dengue fever) given the absence of reported  
293 positive cases. The “one region – one time unit” is the simplest biosurveillance scenario we can consider, and  
294 most examples found in the literature using a full Bayesian approach addressed the more complex scenarios  
295 of multiple time points and/or multi-dimensional surveillance data, as presented in the next sections.

#### 296 II. Empirical Bayes

297 Andersson et al. (Mats Gunnar Andersson et al., 2014) developed an Empirical Bayes model for syndromic  
298 surveillance of WNV and Equine Influenza using syndromic data as described in the working example 1. In  
299 this approach, where only one time unit is considered, the distributions of reported cases are modelled using  
300 linear regression models fitted by maximum likelihood. This allows calculation of ratio of the likelihood of  
301 observing  $n$  cases given an ongoing outbreak, over the likelihood of observing  $n$  cases given no outbreak.  
302 This ratio, mentioned above as the value of evidence ( $V$ ) can then be multiplied by the prior odds of an  
303 ongoing outbreak to obtain the posterior odds.

304 The approach may be extended to handle multiple data streams by assuming that they are conditionally  
305 independent given any of the hypotheses the likelihood ratios from the two data streams can be combined  
306 by multiplication:

$$307 LR = \frac{P(E_1, E_2 | H_1)}{P(E_1, E_2 | H_2)} = \frac{P(E_1 | H_1)}{P(E_1 | H_2)} \times \frac{P(E_2 | H_1)}{P(E_2 | H_2)} \quad (8)$$

308 where  $E_1$  is the evidence from syndrome 1 and  $E_2$  is the evidence from syndrome 2. This equation is  
309 equivalent to the simple BN in working example 1.

310

### 311 2. One region-multiple time units

312 A more advanced surveillance scenario would be to look at data from one region accumulated over several  
313 time units at a time. This is exemplified by extending working example 1 into working example 2.

314 We use the term *change point analysis* (CPA) for methods that seek to detect subtle change(s) in incidence  
315 and to characterise the direction of the change in a time series between change points. Knowing the time at  
316 which process parameters have started to shift, the so-called change point, makes it easier to initiate a  
317 search to identify and eliminate the source of variation. Frequentist statistical process control charts are

318 used to detect shifts in a process parameter by distinguishing between assignable cause variation (i.e. new  
319 emergent properties) and common causes of the process variation (i.e. variation that is predictable  
320 probabilistically). They may incorporate the cumulative sums of the deviations of the sample values from the  
321 target values (CUSUM) (Lucas, 1985) or may use a weighted average of the sample statistics with  
322 exponentially decaying weights (termed exponentially weighted moving average chart or EWMA) (Holt,  
323 2004; Winters, 1960). These methods and others are reviewed in (Unkel et al., 2012), and more recently in  
324 (Yuan et al., 2019).

325 Application of the Bayesian framework to the change point estimation problem allows us to draw inferences  
326 based on posterior distributions for the time and the magnitude of a change (Barry and Hartigan, 1993).  
327 Kass-Hout et al. (Kass-Hout et al., 2012), for example, applied the CUSUM CPA method to detect changes in  
328 emergency admission trends that can indicate influenza illness in USA. The authors showed that the use of  
329 CPA, in comparison to single-point detection, allowed decision-makers to make a more informed decision on  
330 which alarms warranted response, prioritizing time-series changes depending on whether they represented  
331 decreasing, stable or increasing trends. However, the authors brought attention to the inherent assumption  
332 of a normal distribution for the time-series data, an issue that Texier et al. (2016) (Texier et al., 2016) later  
333 suggested could be the reason for a more accurate and less biased performance of frequentist methods in  
334 their particular evaluation using simulated data.

### 335 *I. Full Bayes*

336 Full Bayes approaches for CPA are often based on HMM. Le Strat and Carrat (1999) (Le Strat and Carrat,  
337 1999) pioneered the use of HMM in biosurveillance which many biostatisticians have built upon. The  
338 recursive nature of HMM allows us to easily run them in real time as only the present observation(s) and the  
339 previously estimated state and uncertainty matrix are required, i.e. no additional past data are needed.  
340 Unkel et al. (Unkel et al., 2012) provided a comprehensive review of statistical methods used for prospective  
341 detection of infectious disease outbreaks, and pointed HMM among the class of methods that can explicitly  
342 account for the correlation structure among observations in a time-series.

343 HMM and MSM can be used in a purely temporal setting, where the transition from non-outbreak to  
344 outbreak scenarios is seen as a Markovian process. That is, disease outbreak states are modeled as hidden  
345 state variables which control the observed time series. The process was evaluated for the detection of  
346 simulated anthrax outbreaks in a time-series or clinic visits collected from a metropolitan area (Lu et al.,  
347 2010, 2008). The authors showed higher sensitivity compared to traditional deterministic SyS methods. They  
348 also pointed out that the method was less sensitive to extreme values than traditional approaches, as a jump  
349 component could be introduced to absorb sporadic extreme values. This is expected to reduce the number  
350 of false alarms and increase robustness to variations in the data, which is the result reported by other  
351 authors applying HMM to determine the epidemic and non-epidemic periods from influenza surveillance  
352 data (Conesa et al., 2015; Martínez-Beneito et al., 2008; Rath et al., 2003). Amorós et al. (Amorós et al.,  
353 2020) later extended the temporal model presented by Martínez-Beneito et al. (2008)(Martínez-Beneito et  
354 al., 2008) to model specifically the differentiated incidence rates between equally spaced time points,  
355 improving detection in earlier stages of the epidemic, when incidence rates are low.

356 Influenza monitoring was also used as the test case for a framework that used Bayesian networks both to  
357 estimate the probability of an individual patient having the specific disease, based on its electronic medical  
358 records, and then the probability of an outbreak in the population (Cooper et al., 2015). The population  
359 component is based on a SEIR compartmental spread disease model (Susceptible-Exposed-Infected-  
360 Recovered). In this framework, which is unique in its integrated approach to combining patient and  
361 population outbreak detection and characterization, counts are not the only source of evidence. The  
362 population probabilities of an ongoing outbreak also become more informative with more and better  
363 information about the individual clinical cases.

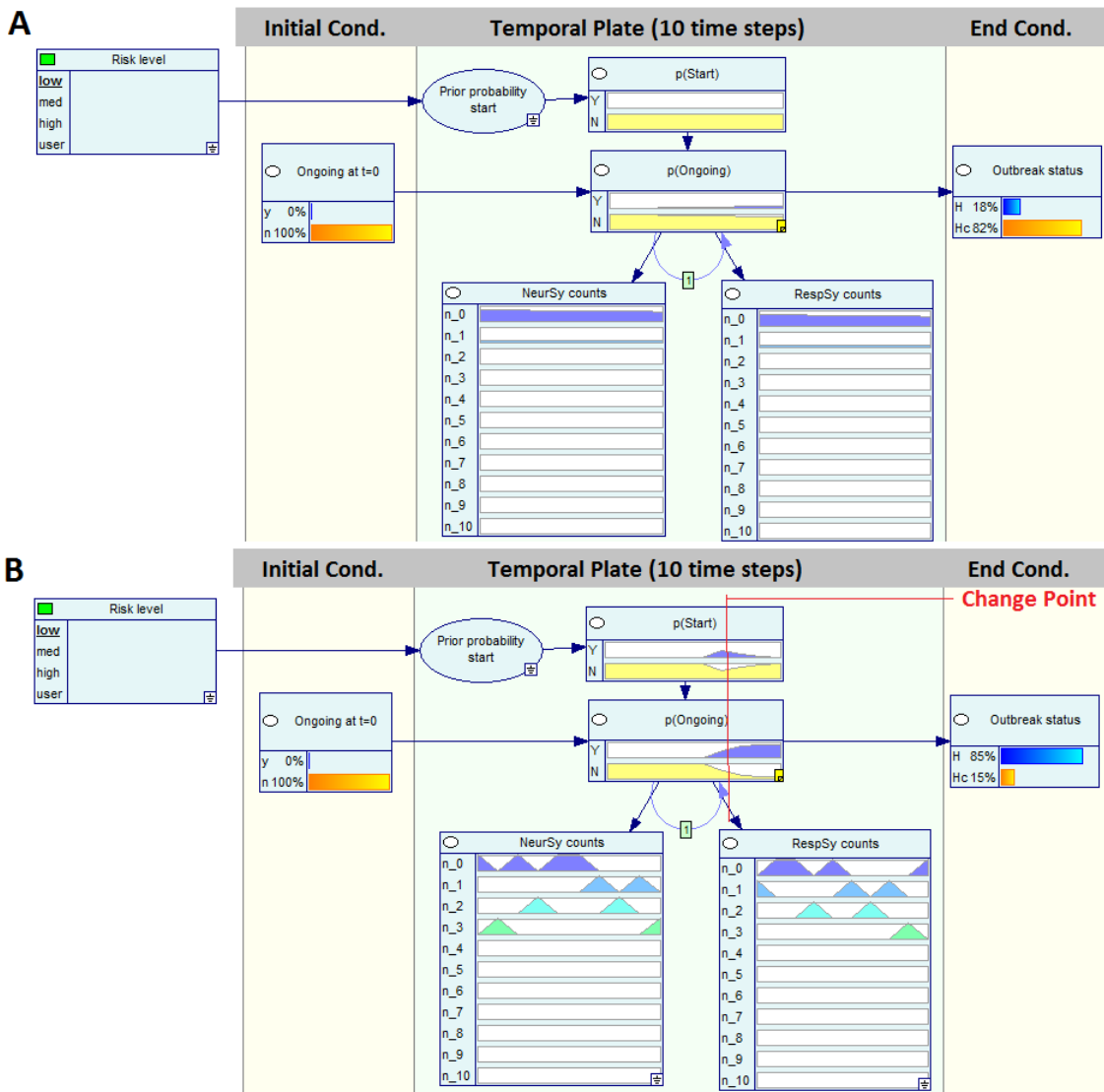
364 Dawson et al. (2015)(Dawson et al., 2015) used a similar Bayesian network methodology, informed by  
365 individual medical records and a spread model, but improved by incorporating a particle filter. In the words  
366 of the authors, “[t]his inclusion allows the system to track the fraction of the population sick as a continuous  
367 parameters, rather than as a few coarse discrete states, which is especially important when the number of  
368 cases are small”. The gain in timeliness and specificity comes at the cost of a high parametrisation burden,  
369 which can be particularly disadvantageous for detection of unknown diseases or rare diseases used as  
370 biological weapons.

371 Watkins et al. (Watkins et al., 2009) used reported case counts of hepatitis A, superimposed with simulated  
372 outbreaks, to evaluate the suitability of HMM as a surveillance methods for use in sparse small area count  
373 data, with limited availability of baseline data. At false alarm rates around 0.05, the Bayesian method did not  
374 outperform traditional CUSUM methods, but at 0.01 false alarm rates the HMM had both greater sensitivity  
375 and shorter timeliness for detection.

376 Höhle et al. (Höhle and An Der Heiden, 2014) used a hierarchical Bayesian model to account for reporting  
377 delay during an outbreak of Shiga toxin-producing *Escherichia coli*. The authors explicitly modelled the delay  
378 distribution (discrete time survival regression) in parallel to the epidemic curve, allowing for changes in the  
379 reporting delay as intervention measures are implemented, and an effective “nowcasting” of the epidemic  
380 burden in order to inform control strategies. The approach was also used for surveillance of foodborne  
381 disease in China (Wang et al., 2018), and dengue fever in Brazil (Bastos et al., 2009) and Thailand  
382 (Rotejanaprasert et al., 2020). A Bayesian nowcasting model which accounts for reporting delay while  
383 explicitly modeling the temporal relationship between cases – to accurately model reporting delay  
384 accounting for the fact that future cases are intrinsically linked to past reported cases – was recently  
385 introduced and made available as the R package {nobBS} (McGough et al., 2020). Liu et al. (Liu et al., 2020)  
386 used a Bayesian model to learn from individuals reporting behaviour in online participatory health  
387 surveillance systems, and estimating their probability of reporting every week. The model was applied to ILLI  
388 prevalence estimation in Australia to demonstrate how the framework can be used to correct inconsistent  
389 participation and sampling bias in prevalence estimations.

## 390 *II. Empirical Bayes*

391 Working example 2 illustrates a simple empirical DBN (Figure 3). Such absorbing state model is only  
392 appropriate when the goal of the surveillance system is the early detection of emerging diseases for  
393 example, but it is not suitable for the monitoring of recurrent seasonal diseases such as influenza.



394

395 **Figure 3:** In this Dynamic Bayesian Network, the probability distributions for respiratory and neurological  
 396 syndromes are the same as in Figure 1 and assumed to be dependent only on the state of node p(Ongoing).  
 397 The nodes in the “dynamic” part of the network, however, take one value for each time-step. The node  
 398 P(ongoing) takes the values “yes” or “no”. The state may change from “no” to “yes” with a probability  
 399 defined in node P(onset). Once the node is in state “yes” (outbreak started), it cannot switch back. Such  
 400 models are referred to as “absorbing state models” (Heaton et al., 2012).

401

402 The DBN in Figure 3 is a first order Markov model since the state of each time-instance is only dependent on  
 403 the state of the previous time-instance (represented by the circular arc at node “Ongoing”). A DBN may be  
 404 extended to allow higher order (>1) interactions between time instances such as an  $n^{th}$  order DBN allows  
 405 arcs from  $\{Y_{T-n}, \dots, Y_{T-1}\}$  to  $Y_T$ .

406 While the approach above uses the Bayesian decision framework to weight in the likelihood of being in an  
 407 epidemic versus non epidemic state based on the number of observed cases, García et al. (2015) (García et  
 408 al., 2015) proposed a method based on the shape of the distribution for the number of cases, which they  
 409 tested for detection of influenza-like illness (ILI). Their method is based on the rationale that the number of  
 410 reported cases, which follows an autoregressive dynamic in the absence of an outbreak, will change to

411 exponential growth during the early phase of the outbreak. The authors noted that the method, which could  
412 be implemented in a straightforward algorithm, relies only on training based on historical data, without the  
413 need to tune free parameters. Furthermore, it allows quantitative estimations of epidemic parameters.  
414 Polyakov et al. (Polyakov and Breban, 2016) also explored the idea of a breakpoint change, but in this case  
415 the authors looked for a statistically significant change in the epidemic's basic reproduction number,  $R_0$ .

416 Brooks et al. (Brooks et al., 2015) proposed a framework for monitoring ILI seasonal epidemic in which the  
417 prior for an upcoming seasonal curve is calculated considering sets of transformations of past seasons'  
418 curves. As the season progresses and data becomes available, the likelihood of being in any of these curves  
419 are weighted based on actual observed data. These weights are used to generate distributions – rather than  
420 point values – for forecasts of specific epidemic targets, such as peak and duration.

421 Izadi et al. (Izadi et al., 2009) presented innovative work using BN to evaluate the performance of SyS  
422 algorithms. The authors evaluated algorithms both intended for the one-time unit evaluation problem, as  
423 well as options that consider multiple time-points. Their work is mentioned in this section because as for  
424 other work that we have classified as empirical Bayes, detection is based on frequentist statistical  
425 approaches, but a Bayesian framework is used to deal with uncertainty in the process, and aid decision  
426 making – in this case decision about algorithm choice and parameterization. Ebel et al. (Ebel et al., 2017) used  
427 an empirical Bayes approach to account for the variability and uncertainty associated with reporting of  
428 foodborne illness cases, and estimate the actual power of outbreak detection through surveillance.

### 429 **3. Multi-dimensional surveillance data**

430 Multivariate SyS systems, which concurrently monitor several health-related data streams, have greater  
431 sensitivity and are more reliable than univariate systems (Rolka et al., 2007). This is because no single data  
432 source captures data from all the individuals involved in an outbreak. Some diseases will cause a wide  
433 variety of clinical symptoms in different people or animals (e.g. diarrhoea in some, fever in others) and/or  
434 will affect different strata of the population (e.g. different age or production groups). Since there is generally  
435 different information contained in observations from different data sources, SyS systems should seek to  
436 simultaneously evaluate various combinations of multiple data sets using multivariate approaches –  
437 overviews are provided in (Frisén, 2010; Sonesson and Frisé, 2005).

438 Many information systems will also record some sort of spatial information related to a syndromic case (e.g.  
439 postal code of patient, geographic coordinates of a farm). Including this extra layer of information in the  
440 analytical methods can allow detection of localised outbreaks of a disease or identify variations in regional  
441 patterns. Spatial and spatio-temporal frequentist aberration-detection algorithms have been developed,  
442 ranging from spatial CUSUM (Dassanayaka, 2015) to space-time scan statistics (Kulldorff, 2001) and spatio-  
443 temporal regression methods (Kleinman et al., 2004). For a comprehensive review of methods for space-  
444 time disease surveillance, readers are referred to (Robertson et al., 2010).

445 The application of Bayesian alternatives to multi-dimensional surveillance in general, and spatial-temporal  
446 monitoring in particular, are reviewed below with examples.

#### 447 **I. Full Bayes**

448 Dynamic Bayesian Networks can be used to discover the interplay among multiple data sources monitored  
449 for health surveillance. Such method was applied by Sebastiani et al. (Sebastiani et al., 2006) to jointly  
450 monitor four data sources employed for influenza surveillance. The joint model can be used to forecast the  
451 beginning of epidemics, as well as the peaks of epidemics, and in their work showed that paediatric patients  
452 were infected with respiratory viruses before the rest of the population.

453 Later coining this as “Bayesian Information Fusion Networks”, a series of papers demonstrated the  
454 enhancement of disease surveillance systems by this method's advantages of combining multiple data

455 sources and providing Bayesian decision support capabilities. Mnatsakanyan et al. (2009) (Mnatsakanyan et  
456 al., 2009) described a system for detection of influenza-like events combining chief complaints from  
457 emergency department (ED) visits, International Classification of Diseases Revision 9 (ICD-9) codes from  
458 records of outpatient visits to civilian and military facilities, and influenza surveillance data from state health  
459 departments. The system showed results high sensitivity and specificity for timely detection compared to  
460 confirmed laboratory cases. Burkom et al. (Burkom et al., 2011) “fused” environmental data with public  
461 health data, including water quality data in the surveillance and early detection of waterborne disease  
462 outbreaks. The fusion networks method was later refined to improve sensitivity while reducing false alarm  
463 rate (Burkom et al., 2013). The refined method considers the inclusion of many different sources of data,  
464 which are then tested individually for their inclusion in a process of hierarchical training of the Bayesian  
465 networks. Hierarchical model selection was also used by (Ertem et al., 2018) to enable combination of  
466 multiple predictors into the previously referenced model developed in (Brooks et al., 2015).

467 Morrison et al. (2016) (Morrison et al., 2016) applied the hierarchical Bayesian framework to improve  
468 environmental health models, which usually focus only on monitoring health outcomes, with the explicit  
469 modeling of environmental exposure (risk factors) as a latent process. The authors implemented the  
470 computation efficiently by using integrated nested Laplace approximations, and demonstrated the  
471 superiority of the method compared to univariate models.

472 A causal Bayesian network to model an entire population of people (not just those seeking treatment) was  
473 introduced by Cooper et al. (Cooper et al., 2004) to monitor emergency department chief complaint data.  
474 The so called Population-wide Anomaly Detection and Assessment (PANDA) algorithm was later extended to  
475 simultaneously monitor two data sources of different granularity: aggregated regional counts for OTC sales  
476 and multivariate ED records for individual patients (W.-K. Wong et al., 2005). The latter work used the  
477 extended PANDA for detection of anthrax release, but the authors pointed out that the algorithm could be  
478 used even to model the effects of noncontagious disease outbreaks. Later, the population-wide Bayesian  
479 network model idea was applied again to emergency department data for detecting both specific and non-  
480 specific disease outbreaks (Shen and Cooper, 2009). This hybrid approach can jointly model known diseases  
481 (e.g., influenza and anthrax) by using informative prior probabilities, and unknown diseases (e.g., a new,  
482 highly contagious respiratory virus that has never been seen before) by using relatively non-informative prior  
483 probabilities.

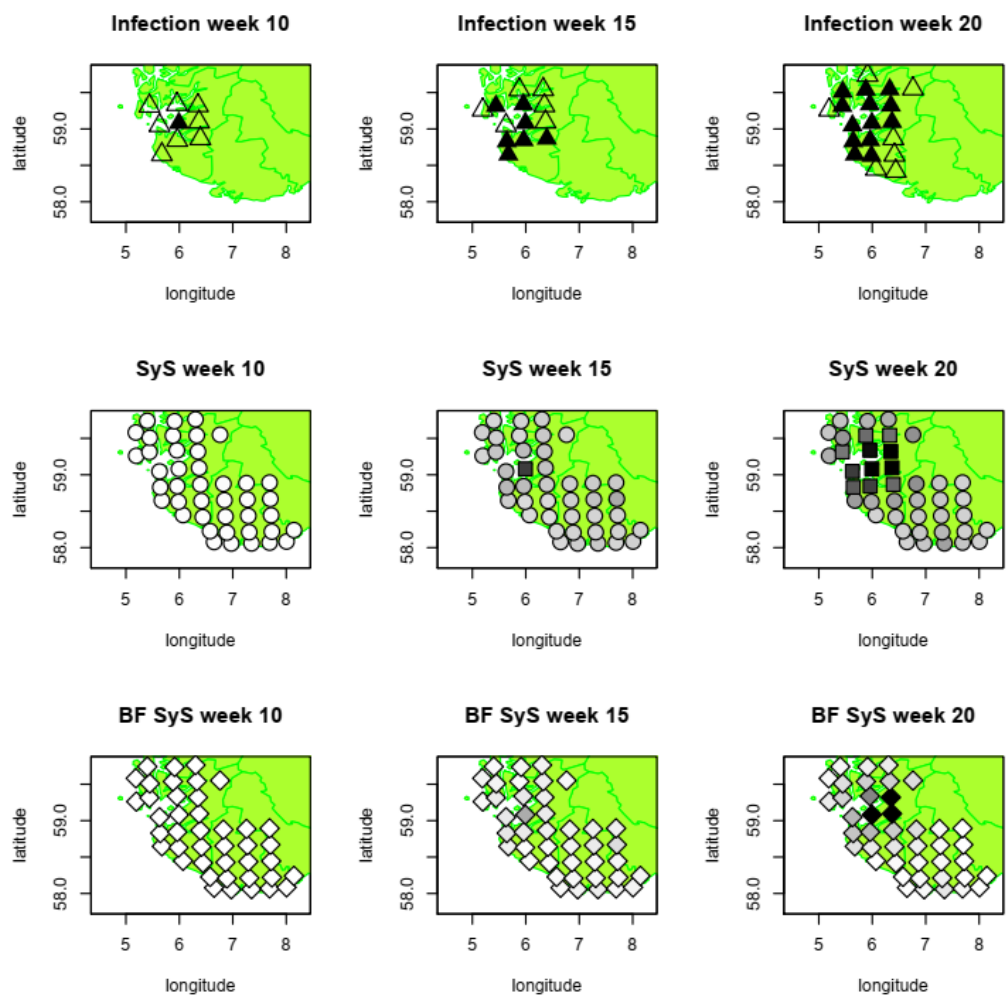
484 Multi-dimensional surveillance data also emerges when the spatial dimension is explicitly taken into account.  
485 The Bayesian-network-based spatial scan statistic (BNetScan), similarly to the temporal approaches  
486 described above, is an entity-based BN that models the underlying state and observable variables for each  
487 individual in a population. This network is then used to determine the posterior probability of each sub-  
488 region containing a cluster. It has been applied to simulated outbreaks of influenza and cryptosporidiosis  
489 injected into Emergency Department data (Jiang et al., 2010).

490 Spatio-temporal data are also the most common use case for HMMs. The transition probabilities of the  
491 Markov chain can be allowed to vary over space and time, in the fashion of conditional autoregressive  
492 modeling (CAR) models in which spatial correlation in the disease data is modelled by a set of random  
493 effects. Several extensions to HMM (such as beyond normality (Rolka et al., 2007), beyond two hidden  
494 states, multivariate extensions and random observation time (Pearl, 1988)) are available. More recent  
495 advances go further. The spatio-temporal conditional autoregressive HMM with an absorbing state proposed  
496 in (Heaton et al., 2012) combines good sensitivity and specificity, use of covariate information, inclusion of  
497 spatio-temporal dynamics, and transparent support to decision-makers.

498 Working example 3 illustrates a full Bayes approach applied to a spatio-temporal SyS for bluetongue disease  
499 using two data-streams: increased mortality, and late abortions in the Norwegian cattle population. A HMM  
500 model with an absorbing state was implemented, similar to Heaton et al. (2012) (Heaton et al., 2012) but  
501 with some changes. For example, our model includes time delays between infection and resulting observed



502 data. An overview is given in Figure 4, and a detailed description of the model is given in the Supplementary  
 503 Material. The model for the baseline rates (i.e. number of deaths and late abortions without an outbreak)  
 504 was fitted to actual historical data from 2006. Data on the individual level were aggregated on a grid of 25  
 505 km x 25 km cells, with a total of 42 grid points covering the south-west region of Norway from which the  
 506 data originate. A model for the bluetongue outbreak signal was fitted using simulated outbreak data  
 507 (Szmaragd et al., 2009), and this signal was then added to the observed baseline cases. Another simulated  
 508 outbreak of bluetongue in the same region was used for the SyS with infections status unknown for the  
 509 whole county. The main parameter of interest is the infections status (infected or not infected with the  
 510 disease) of each grid point for each week. The first simulated infection occurs five weeks after the start of  
 511 the syndromic surveillance, but the increase of deaths and late abortions does not pick up speed until week  
 512 14. Detection is set to occur when the estimated probability of infection is above 50%, which occurs at week  
 513 15. Approximate posterior distributions of model parameters were obtained using MCMC simulation using  
 514 OpenBUGS version 3.2.3 (Thomas et al., 2006). A similar framework was applied to the monitoring of  
 515 nervous symptoms in horses, showing how spatio-temporal monitoring can be applied simultaneously for  
 516 detection of a specific disease (in this case West Nile Virus) and a more general class of diseases related to  
 517 the syndromic manifestation (Hedell et al., 2019).



518  
 519 **Figure 4:** A full Bayes approach to spatio-temporal surveillance for bluetongue in Norwegian cattle. The first  
 520 row shows the grid points infected at various times in the simulation, with open triangles indicating infection  
 521 but not yet any additional deaths or late abortions. The second and third rows illustrate the ability of the SyS  
 522 model to predict the infection status. The second row shows the posterior probability that each region is  
 523 infected, while the third row shows the Bayes factor.



524

525 (Zamiri et al., 2015) modelled influenza spread within populations using SIR compartment models  
526 (Susceptible-Infected-Recovered). Individual sets of SIR parameters are used to model the epidemic  
527 dynamics within each area, and spatial spread and information are then explicitly modelled by adding a set  
528 of transition probabilities between every pair of monitored geographical areas. The optimal Bayesian  
529 predictor for the unknown number of ongoing epidemics is an extension of previous formulations of  
530 nonlinear multitarget filtering to account explicitly for spatial spread of disease, and be able to process  
531 multiple syndromic data streams representing the reports from multiple geographical areas. While the full  
532 Bayesian optimal solution is computationally intractable, the authors implemented an estimation algorithm  
533 based on a probability hypothesis density (PHD) filter with particle systems (known as particle-PHD or  
534 sequential Monte Carlo (SMC) PHD filter in tracking literature (Jégat et al., 2008). While the framework was  
535 shown to be useful in providing timely prediction of the epidemic peak and duration, the authors highlight  
536 that this is rather a conceptual solution, and implementation in practice requires further research.

537 (Zou et al., 2018) also used a hybrid hierarchical Bayesian framework in which a spatial explicit model is  
538 coupled with a particle filter, which the authors highlight allows for online updating of streaming data.”

539 A Bayesian model that outperformed SaTScan was introduced by Li et al. (Li et al., 2012). BaySTDetect is a  
540 mixture of a component that describes the background effect of the disease in a study region as a whole,  
541 accounting for spatial and temporal autocorrelations, and a second component that estimates the time  
542 trend for each area. Bouliერი et al. (Bouliერი et al., 2020) later extended the model by addressing important  
543 limitations, such as allowing for the mixing parameter which designates areas as following a usual or unusual  
544 trend to vary in time. It is important to note that the framework has only been applied in the surveillance of  
545 non-communicable, non-infectious conditions. These have not been extensively explored in this article. For a  
546 recent review of spatiotemporal models for non-communicable disease surveillance readers are referred to  
547 Blangiardo et al. (Blangiardo et al., 2020)

## 548 *II. Empirical Bayes*

549 The main challenge to multi-dimensional monitoring is handling the complex correlation structure among  
550 the data sources monitored, which cannot be easily addressed without the help of Bayesian networks, as  
551 described in the full Bayes approaches listed above. While less common, empirical Bayes frameworks have  
552 also been constructed to handle the spatial dimension or the combination of multiple sources of data.

553 One example is the Bayesian spatial scan statistic proposed by Neil et al. (Neil et al., 2006). The (original)  
554 Kulldorff scan statistic (Kulldorff, 1997), which is based on the concept of likelihood ratios, “preludes”  
555 Bayesian models but lacks a Bayesian interpretation. Since it is possible to estimate, by simulation, the  
556 probability of obtaining a particular value of a scan spatial or spatiotemporal statistic under baseline and  
557 outbreak conditions (Lawson and Kleinman, 2005), it is also possible to apply the continuous form of Bayes  
558 Theorem to estimate the Bayes ratio between H and  $H_A$  and thus make inference on the posterior  
559 probability of H.

560 The framework for syndromic surveillance based on the value of evidence presented in examples 1 and 2  
561 (Struchen et al., 2017) has been extended to monitor multiple syndromes (Faverjon et al., 2016), and  
562 account for reporting delays (Struchen et al., 2017).

563 Manitz et al. (2013) (Manitz and Höhle, 2013) extended the widely used Farrington aberration detection  
564 based on generalized linear models (GLM) algorithm (Farrington et al., 1996; Noufaily et al., 2013), to a  
565 Bayesian generalized additive model (GAM). This extends the original algorithm by allowing adjusting for  
566 concurrent processes influencing the case counts. The authors demonstrated this by incorporating the  
567 influence of absolute humidity when modeling weekly reports of campylobacteriosis cases in Germany. Fast  
568 and efficient integrated nested Laplace approximations allowed the method to be made available through an

569 easily accessible implementation in the R (statistical programming environment R (R Core Team and Team,  
570 2016)) package {surveillance} (Höhle, 2007; Salmon et al., n.d.). Salmon et al. (Salmon et al., 2015) later built  
571 further into this framework by including an adjustment to account for reporting delays. Vial et al. (F Vial et  
572 al., 2016) applied the framework to multivariate time series surveillance in animal health. While the authors  
573 highlighted challenges such as defining the expected covariance structure among series in the presence and  
574 absence of an outbreak, they also demonstrated such as the ability to include known covariates.

## 575 Discussion

576 As the number of health data sources grows in volume and complexity, so does the number of approaches  
577 developed to continuously monitoring these data and provide decision-makers with information to support  
578 surveillance. Making this information actionable requires being able to incorporate the outputs of the data  
579 analyses into surveillance practice in a transparent way. In this scoping review we have focused specifically  
580 on the surveillance goal of early disease detection, and reviewed the use of Bayesian frameworks in  
581 syndromic surveillance systems.

582 We set claim already in the introduction that Bayesian inference can support decision-making in transparent  
583 ways by providing a posterior probability of being in specific disease occurrence states, and doing so by  
584 incorporating many sources of data, as well as prior knowledge of disease dynamics. As Moss et al. (2016)  
585 (Moss et al., 2016) pointed out, the ongoing challenge of integrating data analytics into surveillance practice  
586 “requires close collaboration between modellers, epidemiologists, and public health staff”. Many of the  
587 challenges lifted by the authors – such as underestimation of the true number of cases and inherent biases  
588 in reporting-based data – were addressed with Bayesian frameworks in the examples presented and  
589 discussed here. These examples further highlighted the flexibility and robustness of the Bayesian framework,  
590 while also pointing our challenges such as complex implementation.

591 The Bayesian approach can easily incorporate different sources of data (W. Wong et al., 2005), while  
592 accounting for both the uncertainties in the estimations, and the stochasticity of the model (Salmon et al.,  
593 2015). Bayesian models are flexible enough to deal with trends, seasonality and other covariates, and  
594 different distributions (e.g. Poisson, Gamma). The ability to incorporate prior knowledge about the  
595 distribution of parameters can also help hone inference (e.g. through the narrowing of credible intervals) for  
596 highly-dimensional models which may result from the scaling of BN to millions of nodes (e.g. modelling of an  
597 entire population) for real-time surveillance applications. Traditionally, a strength of Bayesian methods has  
598 been the ability to monitor for specific diseases, based on their known characteristics; while frequentist  
599 methods, being non-specific, were better apt at monitoring for unknown diseases. However, recent  
600 methodological developments have proved successful in applying BN to detect known diseases by using  
601 informative prior probabilities, and unknown diseases by using relatively non-informative prior probabilities  
602 (Shen and Cooper, 2007). Examples reviewed – both full and empirical Bayes – demonstrated that BN are  
603 suited to model the underlying epidemiological process, but can also be applied to models that rely on the  
604 observed data alone to both predict and detect epidemic curves (Brooks et al., 2015).

605 A full Bayesian model where all parameters retain their probability density distribution is robust to  
606 overfitting and may handle complex data-streams with correlated data. Such approach is considered by  
607 some to be the “gold standard” and fulfil important optimality criteria. This is, at least in theory, an  
608 advantage over the empirical approaches that include shortcuts (e.g. using maximum likelihood or  
609 expectation maximisation to estimate parameters) and simplified assumptions regarding dependency which  
610 may both serve to propagate errors. Under particular scenarios (in particular when sampling size is low),  
611 Bayesian credible interval estimates obtained from MCMC, such as those generated through Gibbs sampling,  
612 will be narrower than confidence intervals calculated on the basis of large sample approximations (Salameh  
613 et al., 2014).

614 Despite the flexibility and robustness gained with the inclusion of prior probabilities into Bayesian based  
615 monitoring models, their specification can be challenging. This is particularly the case when dealing with  
616 multiple sources of evidence. While Bayesian models allow the incorporation of many sources of data, and  
617 provide robustness in the estimation of their probability distributions (Morrison et al., 2016), deciding on the  
618 structure of covariance among data streams, both in the absence and presence of an outbreak, is not a trivial  
619 task (Flavie Vial et al., 2016). A combination of expert opinion and previous data are often required to find  
620 suitable informative prior distributions. In many cases, weakly informative priors are used; weakly in the  
621 sense that the final results (posterior distributions) are mainly influenced by data rather than the priors.  
622 When the amount of data is scarce the choice of prior distribution may have a large influence on the final  
623 results. Therefore, investigating the sensitivity of the results for different priors may be important. LeStrat  
624 and Carrat (Le Strat and Carrat, 1999) proposed to detect outbreak and non-outbreak phases of influenza  
625 with HMMs using Gaussian distributed priors while Rath et al. (Rath et al., 2003) later demonstrated better  
626 detection accuracy using a mixture of Gaussian and exponential distributions. However, it is important to  
627 remember that in frequentist SyS, implicit priors are used. The sensitivity and specificity of the system are  
628 calculated based on outbreaks simulated from a probability distribution hence making the performance  
629 parameters conditional on these prior assumptions.

630 Irrespectively whether the analysis is based on frequentist or Bayesian approaches, the existence of multiple  
631 hypotheses is a major challenge for interpretation and communication. In the examples above the  
632 hypotheses of main concern (H) would be that there is an outbreak of the disease (or disease group) of  
633 interest and the null hypothesis (H0) that everything is normal. Bayes rule is used to estimate the posterior  
634 probability that an outbreak is ongoing under the assumption that the set of hypotheses is exhaustive, that  
635 is  $P(H) + P(H_0) = 1$ . When we deal with a finite number of hypotheses (H1, ..., Hn) we may assign a prior  
636 probability to each hypothesis and apply Bayes rule. In many cases, it is impossible to include all hypotheses  
637 in the model. There may be other possible explanations for a peak in a data-stream which is not covered by  
638 any model hypothesis and in such instances, it is not possible to calculate the posterior probability of H. The  
639 same problem applies when, for example, estimating the specificity of a detection algorithm. In the Bayesian  
640 decision framework, however, we can still use likelihood ratios to calculate the odds ratio between two  
641 hypotheses included in the decision framework, for instance outbreak presence over non-outbreak (Taroni  
642 et al., 2010).

643 Thus, presenting the result as a posterior probability of a specific disease may be dangerous. One option is to  
644 make the set of hypotheses exhaustive by explicitly defining H as “an outbreak of disease X or another  
645 disease displaying similar symptoms” and assuming all other scenarios explaining the results are covered by  
646 H0. Another possibility is to present the results as the likelihood ratio or the Bayes factor between each pair  
647 of hypotheses that are part of the model.

648 The main drawback of applying full Bayesian approaches to real-life SyS scenarios resides in the resulting  
649 computations, which can be quite complex and necessitate the use of approximate solutions. For example,  
650 models based on both continuous and discrete distributions may be handled in a MCMC framework  
651 (typically Gibbs sampling as in WinBUGS/OpenBUGS/JAGS). In some cases, it is possible to find a solution in  
652 “closed form”, i.e. the integrals have an algebraic solution, circumventing the need for finding distributions  
653 for parameters by simulation and thereby speeding up calculations. To overcome the long computational  
654 time associated with most MCMC-based models, approximate solutions to BN, including integrated nested  
655 Laplace approximations (Schrödle et al., 2011) have been developed. In the most complex cases,  
656 implementation of the full Bayes method may be theoretically too demanding and computationally too  
657 difficult and thus, in practice, the simpler empirical methods will still have a part to play (Lawson and  
658 Kleinman, 2005).

## 659 **Conclusion**

660 One of the main advantages of Bayesian approaches to epidemiological surveillance is their conceptual  
661 simplicity and the fact that their fundamental principles are based on relatively few concepts. Studies have  
662 linked the easiness of explanation of medical decision-support systems to user perception of the system and  
663 the accuracy of decision-making) (Suermondt and Cooper, 1992). The Bayesian framework where results are  
664 presented as posterior probabilities (and strength of evidence as LR's or Bayes factors) has been found to be  
665 analogous to intuitive human reasoning and thus useful for presenting and interpreting results. They have  
666 been adopted, for example, as the golden standard for presenting forensic evidence in many countries  
667 (Aitken and Taroni, 2004). Nonetheless, the posterior probability for a given node will depend on several  
668 factors that may need explaining to the decision-makers: the evidence (itself possibly arising from multiple  
669 data streams), the BN structure (nodes and arcs), and the BN parameters (local conditional probabilities).  
670 Thankfully, methods (e.g. the hierarchical explanation method) do exist for selecting and organising  
671 information to explain BN inference in the context of outbreak detection (Madigan et al., 1997; Šutovský and  
672 Cooper, 2008). The Bayesian approach fits nicely in a decision theoretic framework. If utility functions and  
673 the posterior probabilities of the hypotheses are provided, it is possible to find the best action for the  
674 decision-making problem at hand.

675 A common objection to Bayesian methods is that the posterior probabilities can be strongly influenced by  
676 the priors. As an alternative approach (M G Andersson et al., 2014), it is proposed a framework for  
677 communicating SyS based on explicit separation of prior information about an hypothesis and evidence from  
678 data. In this framework the results from SyS would be presented as the Bayes factor, i.e. the ratio between  
679 the posterior and prior odds that an outbreak is ongoing against an alternative hypothesis. A specific  
680 advantage of this approach is that is it logical for communicating results also when the set of hypotheses is  
681 not exhaustive. Furthermore, it is analogous with scale of evidence adopted at many forensic institutes  
682 (Nordgaard et al., 2012). From that perspective the proposed framework is useful for presenting results even  
683 when the modelling approach is not in itself Bayesian.

684

## 685 **List of abbreviations**

686 BN: Bayesian network

687 CPA: change point analysis

688 CUSUM: cumulative sum control chart

689 DBN: dynamic Bayesian network

690 EWMA: exponentially weighted moving average chart

691 HMM: hidden Markov models

692 ID: influence diagrams

693 LR: likelihood ratio

694 MCMC: Markov chain Monte Carlo

695 SMM: state-space models

696 SyS: syndromic surveillance

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## 698 **Competing interests**

699 The authors declare that they have no competing interests.

700

## 701 **Authors' contributions**

702 MGA, FV, PH, AL and JG conceived the concept and framework developed in this manuscript. MGA and RH  
703 analysed the data presented in the working examples. FV, FCD GMA and RH contributed to the literature  
704 review and wrote the paper. PH, AL and JG commented on various versions of the manuscript. All authors  
705 read and approved the final manuscript.

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