

Connectivity-based risk ranking of infectious salmon anaemia virus (ISAv) outbreaks for targeted surveillance planning in Canada and the USA

R. Gautam^a, D. Price^b, C.W. Revie^{b*}, I.A. Gardner^b, R. Vanderstichel^b, L. Gustafson^c, K. Klotins^d, M. Beattie^e

^aAnimal Health Science Directorate, Canadian Food Inspection Agency 1400 Merivale Road, Ottawa ON, K1A 0Y9, Canada.

^bDepartment of Health Management, University of Prince Edward Island, Atlantic Veterinary College, 550 University Avenue, Charlottetown, PEI, C1A 4P3, Canada.

^cUSDA APHIS VS Centers for Epidemiology and Animal Health, Surveillance Design and Analysis, 2150 Centre Ave, Fort Collins, CO 80526-8117, United States.

^dAnimal Health Directorate, Canadian Food Inspection Agency, 59 Camelot Drive, Ottawa, ON, K1A 0Y9, Canada.

^eGIS Gas Infusion Systems Inc., 40 Dante Road, St. Andrews, New Brunswick, E5V 3B9, Canada.

*Current address: Department of Computer and Information Sciences, University of Strathclyde, Glasgow G1 1QE, UK.

Corresponding author: Raju Gautam, Email: raju.gautam@canada.ca

ABSTRACT

Infectious salmon anaemia (ISA) can be a serious viral disease of farmed Atlantic salmon (*Salmo salar*). A tool to rank susceptible farms based on the risk of ISA virus (ISAv) infection spread from infectious farms after initial incursion or re-occurrence in an endemic area, can help guide monitoring and surveillance activities. Such a tool could also support the response strategy to contain virus spread, given available resources. We developed a tool to rank ISAv infection risks using seaway distance and hydrodynamic information separately and combined. The models were validated using 2002-2004 ISAv outbreak data for 30 farms (24 in New Brunswick, Canada and 6 in Maine, United States). Time sequence of infection spread was determined from the outbreak data that included monthly infection status of the cages on these farms. The first infected farm was considered as the index site for potential spread of ISAv to all other farms. To assess the risk of ISAv spreading to susceptible farms, the second and subsequent infected farms were identified using the farm status in the given time period and all infected farms from the previous time periods. Using the three models (hydrodynamic only, seaway-distance, and combined hydrodynamic-seaway-distance based models), we ranked susceptible farms within each time interval by adding the transmission risks from surrounding infected farms and sorting them from highest to lowest. To explore the potential efficiency of targeted sampling, we converted rankings to percentiles and assessed the model's predictive performance by comparing farms identified as high risk based on the rank with those that were infected during the next time interval as observed in the outbreak data. The overall predictive ability of the models was compared using area under the ROC curve (AUC). Farms that become infected in the next period were always within the top 65% of the rank predicted by our models. The overall predictive ability of the combined (hydrodynamic-seaway-distance based model) model (AUC = 0.833) was similar to the model that only used seaway distance (AUC = 0.827). Such models can aid in effective surveillance planning by balancing coverage (number of farms included in surveillance) against the desired level of confidence of including all farms that become infected in the next time period. Our results suggest that 100% of the farms that become infected in the next time period could be targeted in a surveillance program, although at a significant cost of including many false positives.

Keywords: infectious salmon anaemia virus, disease spread, risk ranking, risk of infection, surveillance planning.

1. Introduction

Infectious salmon anemia virus (ISAv; genus *Isavirus*, family Orthomyxoviridae), is a globally-important pathogen of farmed Atlantic salmon (*Salmo salar*) and is currently listed by the World Organisation for Animal Health (OIE, 2017) and the governments of Canada and the United States (USA) for disease control purposes. ISAv and clinical outbreaks of ISA are detected sporadically in Atlantic Canada with a few outbreaks almost every year (Gagné & LeBlanc, 2017) but wild salmon and salmon farms along the west Canadian (CFIA 2017a) and Washington state coasts are considered ISAv free (Gustafson et al., 2017). When ISAv is detected, efficient responses by industry and disease regulatory agencies can help contain viral spread from an index-case farm site to neighboring farm sites (Mardones et al., 2014). An effective response and management also reduces economic impact and may increase public confidence about health and wellbeing of both farmed and wild fish.

Under current federal management in Canada, if ISA is confirmed in a farm the Canadian Food Inspection Agency (CFIA) initiates disease response activities. These activities aim to eradicate the disease in areas that were previously free of ISA and control the spread in areas that have a history of previous occurrence of the disease. Although, location of index cases of ISA cannot be predicted due to limited understanding about the factors leading to emergence of the virus at a farm, effective ISA management, operating within the constraints of the available resources by federal and provincial governments and industry, can minimize the size of an outbreak. The current federal standard for identifying a high-risk farm is seaway distance proximity to any infected site of ≤ 5 km if mortalities can be removed on a regular basis (depending on the mortality rate and environmental conditions) and ≤ 15 km if mortalities cannot be removed regularly (personal communication with Dr. Kim Klotins, CFIA, 2017). The level of available resources provided by the government and industry, such as trained personnel and infrastructure to carry out site investigations, is an important factor that determines the ability to respond to an outbreak situation. A tool that can identify farm sites at greater risk of disease introduction given the location of the index site would help focus monitoring and surveillance activities during disease response.

To facilitate understanding of disease spread in aquaculture settings within the marine environment, disease spread models have been proposed using outbreak data (Scheel et al. 2007, Aldrin et al. 2010, Aldrin et al. 2011), including ISAv spread in Norway and Chile (Aldrin et al. 2011, Mardones et al. 2013). While these models have provided insights into ISAv transmission parameters and improved understanding of potential pathways of disease spread, there is a need for a tool that can facilitate surveillance planning by identifying and ranking farms that are likely to become infected following an outbreak of ISAv on an index farm. An important putative risk factor for the spread of disease between farm sites is proximity to an infected farm. The risk of disease transmission is reported to decrease as the seaway distance increases between farm sites

(Mardones et al., 2014). Furthermore, because transmission of most pathogens between farms in the marine system is likely waterborne after controls of movement of finfish and fomites are imposed, further adaptation using hydrodynamic information from particle dispersal models may improve the accuracy of model predictions for transmission events. Hydrodynamic models have been used to assess ISA_v spread in the Quoddy region of Canada and Maine (Gustafson et al., 2007); and recent advances in hydrodynamic and ocean circulation models have estimated pathogen dispersal, which has been applied to spread of infectious hematopoietic necrosis virus (IHNV) between salmon farms in British Columbia (B.C.), Canada (Foreman et al. 2015).

The overarching goal was to develop a practical modelling framework of potential disease transmission, applied in a resource-constrained setting to rank aquaculture farm sites at risk of ISA_v infection using seaway distance and hydrodynamic information as indicators of transmission risk between salmon farm sites. The objectives of the present study were to: 1) compare and rank ISA_v risk of infection among farm sites using seaway distance, hydrodynamic information, and combined seaway distance and hydrodynamic information-based models; and 2) validate the models using historical ISA_v outbreak data.

2. Methods

2.1. Model structure

At any outbreak time period t , we considered that active farm sites could be in one of the two states: susceptible or infectious, depending on the infection status during the time period. Once ISA_v was detected in a cage of a farm, we considered the farm site infectious until all fish in the farm site were harvested. A cage was considered infected if and two fish from the cage tested positive by any two of the three ISA diagnostic tests: indirect fluorescent-antibody test, RT-PCR or virus isolation (Gustafson et al. 2007). The assumption was considered relevant because infected cages in the farm are depopulated after a positive ISA_v test result, but fish in all other cages continue to be raised if mortality is within normal limits and monthly screening tests remain negative. Therefore, remaining cages could harbour the virus in the farm (McClure et al., 2004) and multiple-cage outbreaks could be detected periodically within the same farm site similar to that reported by Mardones et al., (2013). We further elaborate on the implication of this assumption in the Discussion section.

For each time period, t that one or more farm sites became infected, an overall ISA_v infection risk score (IR_i) was calculated for each susceptible farm site S_i , based on the transmission risk from all infected farm sites during the time period, and assuming that transmission risks from each infected site are independent. The risk scores were estimated in three different ways: (i) based on the seaway distance between farm sites, (ii) based on hydrological currents (hydrodynamics) connecting sites, and (iii) based on both seaway distance and weighted

hydrodynamic information. A seaway distance based infection risk score, IR_i^d for susceptible farm site S_i is estimated using equation (1), modified from Aldrin et al., (2011). This score assumes that the likelihood of infection decreases as the distance between infectious and susceptible farms increases.

$$IR_i^d = \sum_{j=1}^n TR_{ij}^d \quad (1)$$

where TR_{ij}^d is the seaway distance dependent transmission risk score to a given susceptible site, S_i , the superscript (d) indicates that the infection risk score is estimated based on seaway distance between the susceptible farm S_i and $j = 1, 2, \dots, n$ active farm sites. Mathematical representation of this transmission risk score for each susceptible site, S_i is given by:

$$TR_{ij}^d = \exp(-\varphi \cdot d_{ij}) \cdot I_j \quad (2)$$

where d_{ij} is the seaway distance in kilometers between susceptible site, S_i and farm site j ; φ is a scaling parameter representing the decrease in transmission risk as the distance between the infected and susceptible farm sites increases for each kilometer; and I_j is an indicator variable that takes the value of 1 when site j is infected and 0 otherwise. The transmission risk, TR_{ij}^d (equation (2)) can be modified to account for other factors that are known to influence the spread of the disease (e.g. local contact network, and variability in infectiousness of farms and host susceptibility). However, accounting for factors other than seaway distance and hydrodynamic information is beyond the scope of this study and therefore was not considered herein. The parameter φ , estimated to be 0.42 for ISA_v by Aldrin et al., (2010), was used in our analysis because it allows for a small but positive infection risk (0.0018) at a distance of 15km, which is used as the upper limit for classifying high-risk farm sites in Canada. However, as explained later in the discussion section the value of this parameter does not affect the infection risk score in our study. We also used this framework to assess the effect of Euclidean distance between farm sites over seaway distance.

The infection risk score based on hydrodynamic information (IR_i^h) can be estimated for each susceptible farm site by simple modification of Equation 1 that sums over the number of infectious farm sites to which it is hydrologically connected (i.e. infectious farm site is upstream of susceptible farm sites). A farm site is defined as upstream if it is the site of particle release and all farm sites receiving the particles are downstream relative to the releasing site. This score assumes that transmission of disease can only occur between farms that are hydrologically connected (i.e. no transmission via wild fish acting as biological vectors between farms for example), and that transmission is independent of the distance between hydrologically-connected farms.

$$IR_i^h = \sum_{j=1}^n I_j \cdot H_{ij} \quad (3)$$

In Equation 3, I_j is the same indicator variable as in equation 2, and H_{ij} is the indicator variable that takes the value of 1 if the farm site, j is hydrologically connected to the susceptible farm site, S_i downstream and 0 otherwise. Hydrodynamic connectivity between farms was determined from published particle-track outputs from a finite-volume coastal ocean model (FVCOM) available in southwestern New Brunswick (Chang et al. 2007), as also presented in a series of government documents in the early 2000s (Chang et al. 2005a, Chang et al. 2005b, Chang et al. 2006a, Chang et al. 2006b, Page et al. 2004, Page et al. 2005). A hydrodynamic connectivity matrix consisting of 0s, indicating no connection and 1s, indicating presence of virus particles released from one farm site tracked to another farm site within a single 12.4 hour tidal cycle was generated from hydrodynamics models (Chang et al., 2007 and references therein). Details of the hydrodynamic models and the basis used to determine hydrodynamically-linked farm sites have been described previously (Gustafson et al., 2007)

Similarly, an infection risk score based on both seaway distance and weighted hydrodynamic information (IR_i^{dh}) can be estimated by summing over the weighted TR_{ij}^d , with the weight being determined based on hydrological connectivity. This score assumes that some transmission can occur between farm that are not hydrologically connected, and that the likelihood of infection decreases as the distance between susceptible and infected farms increase.

$$IR_i^{dh} = \sum_{j=1}^n TR_{ij}^d \cdot Hw_{ij} \quad (4)$$

where, Hw_{ij} is the weight, which is 1 if farm site j is hydrologically connected to susceptible farm site, S_i and 0.1 if farm site j is not connected hydrologically to susceptible farm site. Weighting by 1:10 ratio was chosen to give greater preference for waterborne transmission between hydrologically-connected farm sites, while still being able to capture residual transmission from other possible pathways represented by seaway distance (e.g. biological vectors such predatory fish or simply because of proximity). Sensitivity of the model to Hw_{ij} was performed by increasing and decreasing the weight by 50% and 100% (i.e. using Hw_{ij} = 0.01, 0.05, 0.15 and 0.2).

2.2. Location of salmon farms and historical outbreak data

The aquaculture region in the Bay of Fundy, New Brunswick (N.B.), is divided into several Bay Management Areas (BMAs) with farms on both sides of the Canada-USA border. The Bay of Fundy has about 93 licenced net-pen sites for grow out of salmon smolts for 18 to 24 months to a market weight of approximately 5kg. However, only 30% - 40% of licensed farms are active at

any one time. Farms are fallowed for at least 3-6 months before repopulation and BMAs typically have a single age class. Farm sites considered in this study were located in BMA 1 and BMA 6 in the Bay of Fundy together with 6 neighbouring farms in the Quoddy region of Maine, USA (Figure 1).

The ISA_v outbreak data in the Bay of Fundy, N.B. and Quoddy region of Maine, between May 2002 and August 2004, were obtained from coauthors (LG, MB) and are described in detail in Gustafson et al. (2007). Briefly, the data included outbreak information (including georeferenced locations of study farm sites; month and year in which each 2002 year-class (YC) farm site was stocked, directional (releasing and receiving farm) hydrodynamic connectivity information based on particle tracking model that was classified as present or absent; date of ISA_v detection on the farm by month, number of cages on the farm holding fish by month, and estimated month and year in which harvest was completed at the farm site for 26 N.B. farm sites and 6 USA farm sites. Two farms in N.B. had identification issues and were removed from the analysis, which used the remaining 30 farms. Hydrodynamic information was available for all of the study farm sites in 2004. It was assumed that all farms were infected with the same strain of ISA_v as strain typing information was not described for any farm. Also, it was assumed that infectious effect of an infected farm site was not influenced by the number of infected cages and/or fish in the farm.

2.3. Analysis and risk ranking of farm sites for ISA_v spread

Seaway distances between farm sites were calculated using their point locations as the centroid to generate a matrix of seaway distances. Distances were calculated using the ‘gdistance’ package (Van Etten, 2017) in R (R Development Core Team, 2017), to produce a matrix of seaway distances between pairs of farm sites. Using the outbreak data (here defined as the laboratory confirmed detections of ISA_v in different months in previously disease-free farms), the chronological order of ISA outbreaks on the 30 farms was generated and the number of farms detected as infected in 8 sequential outbreaks over a period of 15 months was determined (Table 1). Subsequent outbreak periods were not used for further calculation of infection risk because there were fewer susceptible farms than infectious farms. The time sequence of the spread of infection was determined from the outbreak data that contained the monthly infection status of the cages in the farms. Once a farm was infected during the outbreak, it was considered infected in subsequent time periods until all fish were harvested on the farm. The first infected farm site was considered as the index site location for estimating a transmission risk score for ISA_v to all other active susceptible farm sites in the subsequent time interval. For second and subsequent time periods all the farms that were infected and active at the beginning of the time period were considered infectious for determining the transmission risk of ISA_v to remaining active susceptible farm sites in the next time interval. Infection risk scores based on seaway distance (IR_i^d), hydrodynamic information (IR_i^h), and both seaway distance and weighted hydrodynamic

information (IR_i^{dh}) were calculated by solving Equations 1, 3, and 4, respectively. Using these scores, all susceptible farms were ranked for ISAv infection risk from highest to lowest across all 8 outbreak time periods.

2.4. Predictive accuracy of models based on historical ISAv data

To evaluate the predictive performance of the three methods (*i. e.*, IR_i^d , IR_i^h , IR_i^{dh}) for identifying the farms to be targeted for surveillance, we first computed the infection risk scores for each susceptible farm at each of the 8 time periods of the chronological order of ISAv outbreaks according to the available data. Various levels of surveillance coverage (proportion of the susceptible farms targeted for surveillance) were evaluated by changing the number of farms to be sampled, from a single farm to all susceptible farms. To achieve this, we converted the infection risk scores of all susceptible farms within a particular period to percentiles, ensuring that the percentile scores associated with the farms increased with decreasing risk score. This ensured that farms were always sampled from highest risk score to lowest risk score at any level of surveillance coverage considered. For each level of surveillance coverage, susceptible farms were classified as true positives if they were predicted for sampling based on the risk score and became infected during the next time period, false positives if they were predicted for sampling but did not become infected, true negatives if they were not predicted for sampling and did not become infected, and false negatives if they were not predicted for sampling but became infected. The sensitivity (ability of the model to target the farms that became infected during the next time period) and specificity (ability of the model to not target farms that did not become infected) were calculated for the three methods at all (0 to 100%) levels of surveillance coverage. A measure of overall predictive ability for each method was obtained by calculating the area under the ROC curve (AUC), using the cumulative sensitivity and specificity across all 8 outbreak time periods and levels of surveillance coverage (*i.e.* between 0 and 100%). We chose to assess model performance against the level of surveillance coverage because it gives an indication of required resources in terms of number of farms to sample.

Analysis was performed using R (R Development Core Team, 2017), and QGIS (QGIS Development Team, Lyon) was used to create maps.

3. Results

The first ISAv outbreak site among the 12 active sites of 2002 year-class was detected in May 2002. Table 1 shows the chronological order of outbreak dates along with the summary of the number of infected and susceptible farm sites. Figure 2 shows the index farm site and all the active and inactive susceptible farm sites at the start of the study in May 2002.

Overall accuracy averaged over the 8 time intervals was assessed using the AUC of the respective models (Figure 3a). For the seaway distance-based model, overall accuracy was 83%, for the hydrodynamic-based model it was 32% and for the combined seaway distance and hydrodynamic-based model it was 83%. Both models that included a seaway distance component were able to correctly identify 100% of the farms sites becoming infected in the next time interval when surveillance coverage was 65% or more. This was however; achieved with a false positive rate of 67% (i.e. 67% of the susceptible farms included in the surveillance did not become infected in the next time period). Figure 3b shows the increase in sensitivity of the model prediction against the proportion of the susceptible farm sites considered for surveillance (surveillance coverage). Using Euclidean distance instead of seaway distance decreased the AUC and 100% predictive sensitivity could only be achieved at 100% surveillance coverage as opposed seaway distance.

Sensitivity analysis of the hydrological weighting parameter Hw_j had minimal effect on the predictive performance (i.e. AUC) of the model for the combined method.

4. Discussion

We developed a model framework to rank the risk of marine salmon sites using seaway distance and hydrodynamic information given an ISA_v infection is detected at one or more farm sites. This ranking can be used to target farms at higher risk of ISA_v infection for surveillance. Predictive performance of the model based on combined seaway distance and hydrodynamic information was comparable to the seaway distance-based model. The model based on hydrodynamic information alone was inferior to the model based only on seaway distance. In the following sections, we discuss potential explanations for these findings in the context of available information and consider important implications, strengths and limitations of the study.

Previously, Gustafson et al. (2007) reported that hydrodynamic connectivity between farms predicted spatiotemporal spread of ISA_v in the Quoddy study region, though with limited strength. This is consistent with our finding that hydrodynamic information alone did not perform as well as seaway distance alone or the weighted combined model in terms of predicting higher risk farm sites (Figure 3a). There are several potential reasons for this finding. The hydrodynamic information, produced in the early 2000s from the FVCOM, was based on a single tidal excursion run for a short period of time (12.4 h), and may not have accurately represented pathogen dispersal between farms. The FVCOM model outputs are computationally demanding to produce, and as such were included in this study from the literature. We speculate that although one high-low tide cycle may be too short of a time period, it could potentially offer a biologically meaningful option to investigate risk of spread during the early stages of an outbreak (within hours). It may also be useful to estimate viral load, where the maximum ISA_v dose could

be correlated with FVCOM particle tracks, based entirely on modeled water movement. Seasonal variability from one-tide cycle is an additional challenge, where hydrodynamic information is known to vary across seasons due to changes in atmospheric circulation (Olivares et al., 2015). Although ISA_v survival can be constrained by both the biological activity of natural seawater and ultraviolet light radiation, it is likely to exceed 12.4 h; therefore, the full reach of the waterborne ISA_v may not have been captured in the hydrodynamic information. A recent study has estimated the survival of ISA_v in natural seawater to be less than 24 hours (Vike et al., 2014). Hydrodynamic information based on a longer period of time (e.g. running the model for 24 hours or 2 high-low tidal cycles) with a seasonal influence included in the model could provide more complete information on hydrodynamic connections among farm sites in the absence of complete knowledge regarding ISA_v survival in marine waters during an outbreak.

It is also possible that hydrodynamic information reflected the true potential of viral spread via natural connectivity through water, however, other transmission factors were not considered in our model. Such factors include fish movement between sites (Murray et al., 2002) and lack of biosecurity practices involving shared equipment and personnel (Murray & Peeler, 2005) that could have contributed to some of the unexplained ISA_v transmissions (i.e. farms predicted as low risk that became infected) between farm sites. Further, spatiotemporal cage-level analyses suggested a waning in the predictive significance of ISA_v events on sites connected hydrographically after just one month (Gustafson et al., 2007), which may challenge our assumption that sites remain infectious long after affected cages have been removed. Multiple outbreaks involving different cages in many of the infected farm sites was observed in the study data, which is why we considered the farm to remain infectious unless all fish were harvested.

However, early detection and early removal of affected cages is demonstrated as a successful control strategy for ISA_v (Ellis, 2006), and may substantively limit the potential for protracted waterborne spread. Extending analyses beyond the index cage to all cages on affected sites may help answer this question. Future studies may also verify whether the strong performance of seaway distance indicators is in part due to confounding effect of other factors beyond waterborne spread. It should be recognised that although, seaway distance is the most important among the identified risk factors, it only explained about 20% - 45% of the ISA_v outbreaks in Norway, and most of the outbreaks were attributed to unknown factors (Aldrin et al., 2010, 2011).

A possible limitation of this study was the lack of ISA_v genotype information for each infected farm. Since the outbreak happened over a long period of time, the possibility of several different unrelated genotypes of ISA_v involved in the outbreak of 2002-2003 cannot be ruled out (Krossoy et al., 2001; Gagné and Leblanc, 2017), which may account for some of the unexplained virus transmissions (Krossoy et al., 2001). There were 3 other non-2002 YC farm sites that were

infected during the beginning of the study period, but we restricted the study to 2002 YC farm sites only. However, we performed the analysis to assess the effect of those three farm sites by including them as exposure sources for the 2002 YC sites, and their inclusion had only a small effect on the measure of predictive performance of the three methods in terms of the AUC. The AUC for hydrodynamic only based model increased slightly from 32% to 42%, whereas for seaway distance and combined seaway-hydrodynamic based models there was $\leq 5\%$ decrease in the AUC. We assumed that the farm remained infectious, although the infected cage was depopulated. However, in the outbreak data many of the infected farms experienced outbreaks in other cages in the subsequent time periods, similar to that reported by Mardones et al., 2013; we believe that our assumption was reasonable.

Although, among the identified risk factors, seaway distance has been demonstrated to be a major risk factor compared to most other pathways of disease transmission (Aldrin et al. 2010, Aldrin et al. 2011), its importance has not been compared with hydrodynamic information. The addition of hydrodynamic connectivity information to the seaway distance only slightly improved the predictive performance of the model. The limited hydrodynamic information based only on a short tidal cycle and ignoring effect of seasonal variation used within this study does not adequately support a detailed comparison of performance between seaway distance-based and hydrodynamic-based models. However, it may be that using seaway distance alone allows for the capture of transmission attributable to other factors, such as farmed fish movement, equipment, use of common vessels and personnel sharing. Farm sites operated by the same company are more likely to be closer together and to share equipment and personnel, establishing a local contact network among farms. If recommended biosecurity practices to prevent viral spread are adhered to more strictly, there may not be strong relevance for including these factors as transmission pathways in the model. An advantage of a model based on seaway distance is that desired sensitivity for correctly predicting farm sites for infection can be obtained even at relatively low surveillance coverage. For example, at a surveillance coverage of 22% of the susceptible farms at risk, the sensitivity was 70% (Figure 3b). Increasing the surveillance coverage to 30% increased the sensitivity to almost 85%. All the farm sites that become infected are correctly identified at a surveillance coverage of 65%, although this came at the expense of many false positives. The parameter estimate for the rate of decline of transmission risk with increasing distance was obtained from Aldrin et al. (2010). However, it should be noted that for risk ranking with only seaway distance as the pathway of transmission in the model, the choice of parameter value does not make any difference on the overall risk ranking of the farms and consequently the predictive ability of the model. This is because when distance is the only factor in the model, infection risk will decrease with increasing distance no matter what parameter value is chosen. However, choosing a correct parameter estimate will become important if the model is modified to include other potential pathways of virus transmission.

If ISAv is detected in a farm site, it will trigger a series of control and monitoring activities. The purpose of the study was to help guide such activities by identifying higher risk farm sites and tailor surveillance program to achieve desired confidence, while accounting for the available resources. Therefore, the performance of the model was based on evaluating whether a farm site that became infected in the subsequent time period was among the ones predicted by the model at a desired surveillance coverage or not, given the amount of resources available (percent of susceptible farms monitored). Because ISAv is subject to a control program, our model can serve as a decision tool to determine appropriate level of surveillance coverage (number of farms needed for surveillance) for achieving a desired level of confidence in targeting farms potentially at risk of infection. The trade-off between correctly identified farm sites and false positives can be approximated from Figure 3a.

5. Conclusions

Previously, separate ISAv spread models have been developed using seaway distance or hydrodynamic information (Gustafson et al., 2007, Aldrin et al., 2011). In this study, we provide a method to combine the effects of seaway distance and hydrodynamic information for ranking farm sites at risk of ISAv infection following outbreak in an index farm. The stronger performing indicator of risk (seaway distance) was also the simplest and most rapid to conduct, which is an important characteristic for tools designed to support emergency response. The proposed method can also be used to combine these two effects for simulation modelling of disease spread. Furthermore, the model can be easily extended to include other risk factors and can be adapted for targeted surveillance of other aquatic animal diseases.

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Table 1: Number of study farm sites that were susceptible or infected of all active farms by outbreak date.

Outbreak date	Number of farm sites		
	Active (Susceptible + Infected)	Susceptible	Infected
May, 2002*	12	11	1
July, 2002	30	28	2
Sep., 2002	30	26	4
Oct., 2002	30	23	7
Nov., 2002	30	22	8
March, 2003	29	22	7
May, 2003	25	17	8
June, 2003**	25	12	13

* Date of index-case farm site detection.

**Subsequent periods not used for further calculations because there were too few susceptible farm sites compared to infected farm sites.

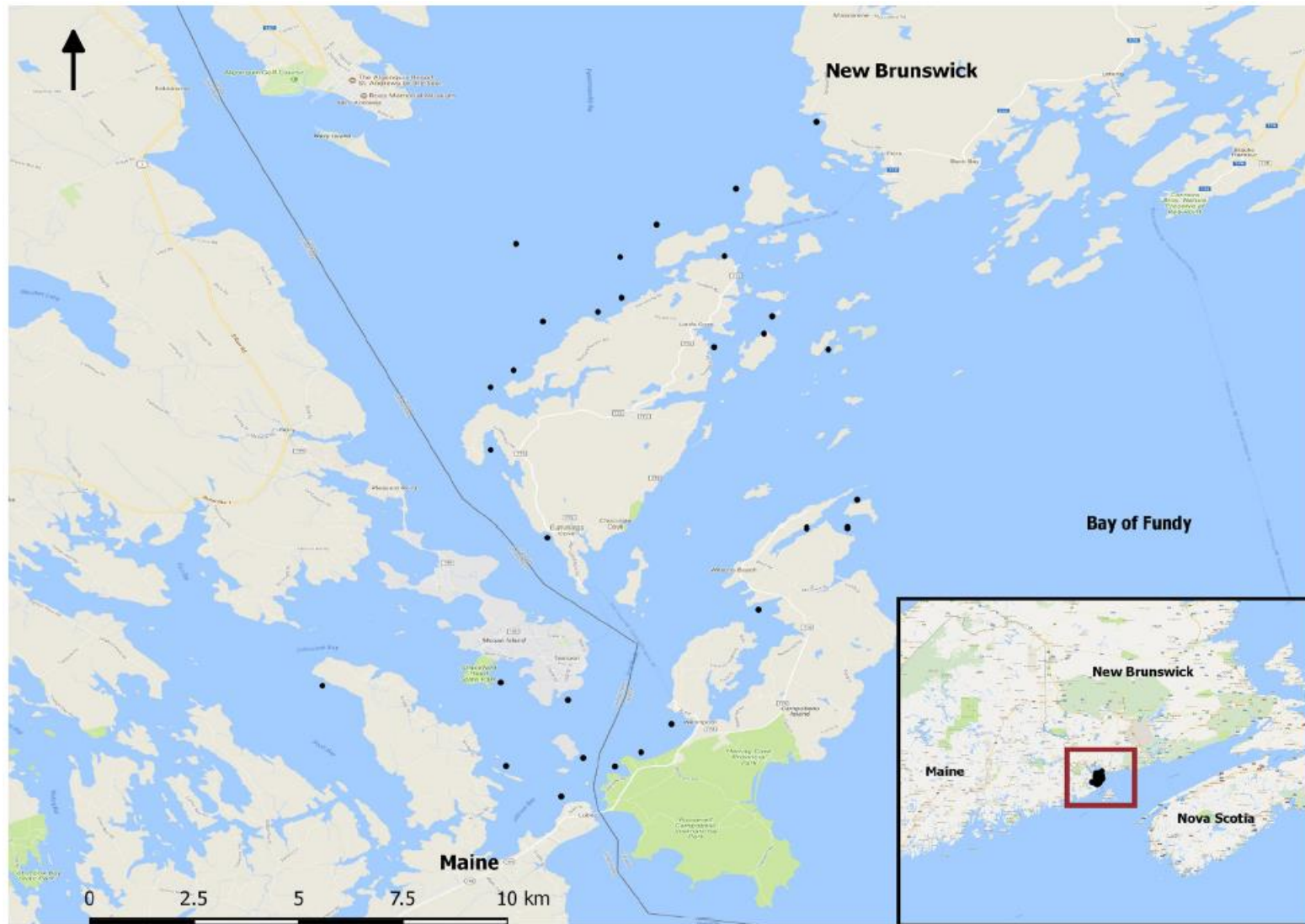


Figure 1. Location of salmon farms (black dots) in the Bay of Fundy in New Brunswick, Canada and Quoddy region of Maine, USA.



Figure 2. Index farm site along with all active and inactive susceptible farm sites at the beginning of the study period, May 2002. The inactive farm sites became active in the subsequent months, i.e. in June and July of 2002.

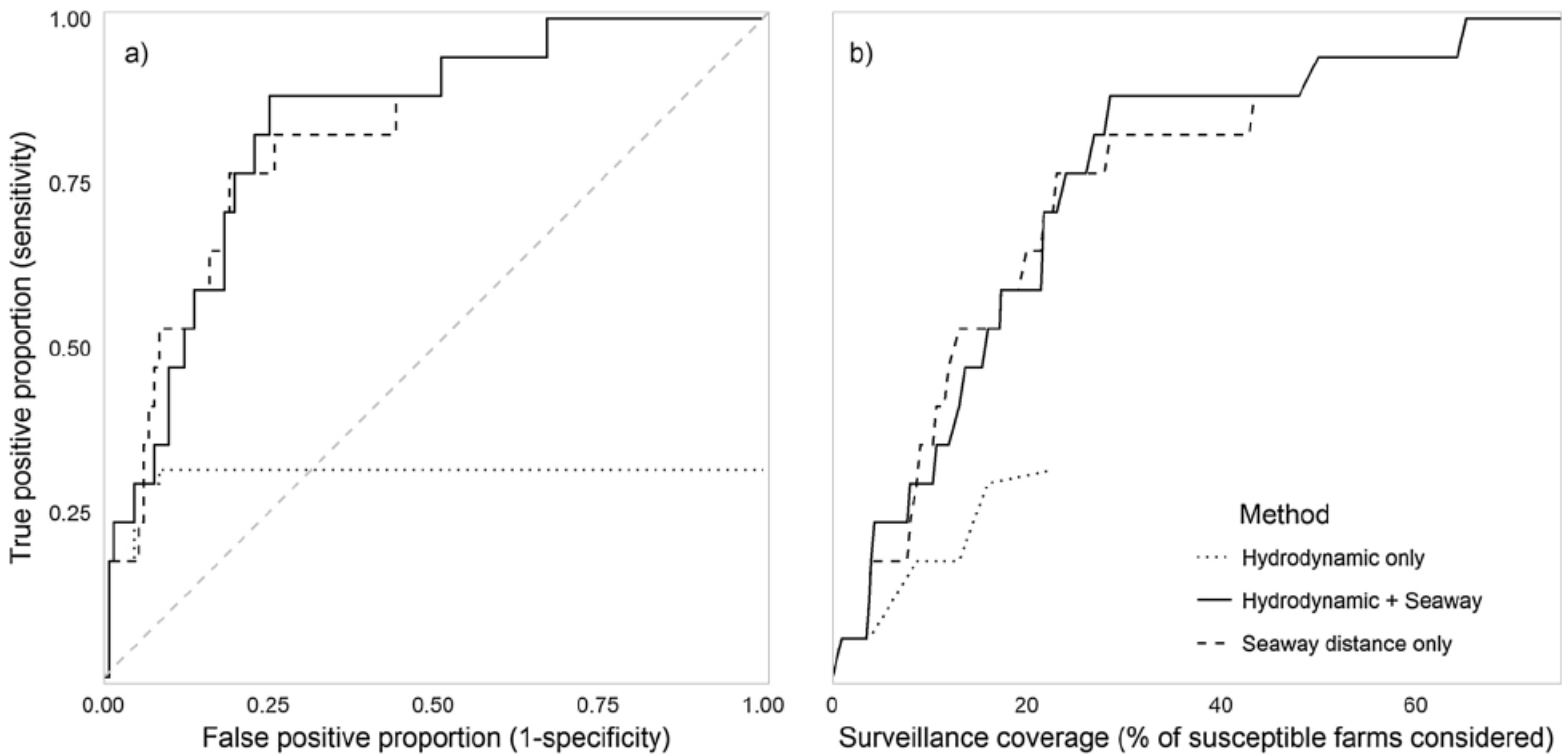


Figure 3. (a) Receiver operating characteristic (ROC) curves for seaway distance-based model (dashed), combined hydrodynamic information and seaway distance model (solid), and hydrodynamic only based model (dotted). The area under the curve (AUC) for models based on seaway distance, combined and hydrodynamic only were 0.83, 0.83 and 0.32, respectively; (b) sensitivity of the model based on the three methods by surveillance coverage (i.e. the % of susceptible farms considered for surveillance). Note, that the curve for hydrodynamic based model terminates abruptly because model predictive performance was calculated only if susceptible sites were hydrologically connected to infected sites and ignored otherwise.