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Is between-farm water-borne pathogen dissemination an important driver in the epidemiology of salmonid rickettsial septicaemia in Chile?

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ABSTRACT

Although the bacterium *Piscirickettsia salmonis* has been detected in many salmon-producing countries around the world, losses caused by salmonid rickettsial septicaemia (SRS) are mostly occurring in the Chilean aquaculture industry. Horizontal transmission of SRS between salmonid farms was suggested, based on the existence of spatiotemporal correlation in the level of disease between neighbouring sea farms. However, it remains unclear to which extent between-farm water-borne pathogen dissemination is important in the epidemiology of SRS in Chile. Such information is critical to assess the level of risk of transmission of SRS from one farm to another at different mortality incidence levels and to apply appropriate and cost-effective mitigation measures. In this study, we used weekly SRS mortality data from all salmonid farms in the Los Lagos region between January 2012 and September 2018 to model the spatiotemporal autocorrelation in the SRS-attributed mortality in the study area. A generalized additive regression modelling framework was adopted, using a linear functional component to model the influence of other farms on the target farm. Several nested statistical models were built to compare the significance of different covariates. Predicted values of SRS mortality on the target farm, conditional on different distance, time lag and mortality values from the source farms were estimated from the best model. The results showed that there was a statistically significant association between the weekly mortality incidence at source farms and the mortality incidence at target farms during the same week and during the previous weeks. This study did not provide evidence that the spatiotemporal correlation observed in SRS mortality may be due to water-borne pathogen dissemination between farms and alternative explanatory mechanisms should be investigated. It remains possible that the patterns of lagged correlation observed between source and target farm mortality may be due to a model artefact. In addition, there was no evidence of a threshold effect above which farms pose a substantially larger health risk to their neighbours. Stronger evidence for or against between-farm transmission of *P. salmonis* may be obtained by different methods.

1. Introduction

Salmonid rickettsial septicaemia (SRS[1]) is an infectious disease caused by the bacterium *Piscirickettsia salmonis*. The disease was first identified in Chile in coho salmon farms in 1989 (Bravo and Campos, 1989), and has since caused substantial losses to the industry in all salmonid species. Although smolt stocks are disease-free at sea entry, a previous study of regulatory data showed that about 80% of production batches will be diagnosed with SRS during the sea production phase (Hillman et al., 2020). The occurrence of horizontal transmission between farms has been suggested in Chile for SRS and other pathogens, as well as for ectoparasites such as sea lice (Rees et al., 2014; Kristoffersen et al., 2013; Price et al., 2017; Arriagada et al., 2017). These suggestions were based on detecting spatiotemporal correlation in the level of disease or infestation between neighbouring sea farms, a phenomenon also called 'infection pressure' by some authors. However,

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[1] AIC: Akaike information criterion; CI: confidence interval; Sernapesca: Servicio Nacional de Pesca y Acuicultura (Chilean National Fisheries and Aquaculture Service); SIFA: Sistema de Información para la Fiscalización de Acuicultura (National Aquaculture Information System); SRS: salmonid rickettsial septicaemia;

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the distances between sites and the site densities for which this correlation poses a substantial health risk have not been characterized. In addition, it remains unclear whether the available evidence of spatiotemporal correlation between farms is due to direct horizontal transmission between farms or to infection by a common environmental reservoir of *P. salmonis*. In the latter case, the SRS mortality on neighbouring farms would be correlated due to such farms sharing similar environmental and spatial characteristics. Under the hypothesis of horizontal transmission between farms, the pathogen circulation could be mediated by a vector or occur via bacteria suspended in the flowing saltwater column. The latter would be possible given the extended survival time of *P. salmonis* in salt water, which can be up to 50 days (Olivares and Marshall, 2010). In addition, the role of wildlife reservoirs is unclear as *P. salmonis* has been identified in native fish species in Chile (Contreras-Lynch et al., 2015).

Comprehensive management of SRS outbreaks requires direct application of control measures in affected farms to limit the local transmission of SRS and hence reduce mortality within a farm. Moreover, control measures should effectively mitigate the risk of SRS spreading from one farm to other farms. The Chilean National Fisheries and Aquaculture Service (Servicio Nacional de Pesca y Acuicultura, Sernapesca) sets regulatory thresholds for SRS mortality incidence rates that, if exceeded, trigger mandatory responses to control outbreaks of SRS and hence reduce the risk of transmission to nearby farms. These regulations rely on the assumption that the infectivity of a farm for neighbouring farms is correlated with the mortality incidence on the infected farm. However, the level of risk of transmission of SRS from one farm to another at different mortality incidence thresholds is yet to be characterized for the Chilean salmon farming industry.

This study was the fifth in a series of epidemiological studies to examine risk factors for SRS and evaluate the effectiveness of interventions to control the disease (Happold et al., 2020a, 2020b; Hillman et al., 2020; Meyer et al., 2019). This work aimed to generate information that supports Sernapesca in evaluating the current regulatory threshold for on-farm interventions (Sernapesca, 2012). Our specific objective in this work was to examine the plausibility of the hypothesis that spatiotemporal correlation of SRS mortality between farms in Chile is caused by water-borne pathogen dissemination between farms.

2. Material and methods

2.1. Study population

The study population comprised all seawater farms and farm-level production cycles included in the data provided by Sernapesca between January, 2012 and September 2018, in the Los Lagos region of Chile where a large proportion of the saltwater rearing of salmonids occurs (Sernapesca, personal communication). The unit of analysis was the farm-level weekly observation, hereafter referred to as 'farm-week'.

2.2. Data sources

Weekly, farm-level mortality reports were obtained from the Sistema de Información para la Fiscalización de Acuicultura (SIFA) database. The SIFA database was deployed at the end of 2010 and contains complete data since January, 2012 based on mandatory mortality reporting by all salmonid production companies. The mortality data used in this study were based on mortality categories as reported in the SIFA database, rather than laboratory-confirmed disease cases.

2.3. Statistical regression model

2.3.1. Primary outcome

The outcome variable was the SRS-attributed mortality count for each farm-week observation in the study area. Here we considered the mortality incidence in a given region as a single variable. The spatiotemporal autocorrelation of this variable was considered as the primary exposure. More specifically, we included two separate model terms to account for autocorrelation: the SRS-attributed mortality incidence on other farms at different distances and time lags (primary exposure) and the temporal autocorrelation at the same farm.

2.3.2. Primary exposure variable

The primary exposure variable was the SRS-attributed mortality incidence on the 50 closest active farms ('source farms') around the farm on which the mortality was measured ('target farm'), during a window of time prior to the week of interest. This variable effectively modelled the spatially and temporally lagged autocorrelation of the outcome variable.

In a previous study on SRS in Chile where authors investigated several between-farm distances up to 20 km, the model with the lowest Akaike information criterion (AIC) included spatial influence between farms distant by up to 10 km (Rees et al., 2014). Here, the source farms were located at distances up to 150 km, allowing the model to reveal any spatiotemporal autocorrelation, regardless of the underlying mechanism of such correlation. The source farms were limited to the 50 closest farms for computational reasons.

In this work, we used a varying coefficient model (Hastie and Tibshirani, 1993) that allowed mortality on a given farm to vary as a smooth function of mortality located at different distances and temporal lags from this farm. The influence of the source farms on the SRS-attributed mortality count at target farm i during week t was modelled using a linear functional (Ramsay and Silverman, 2006; Wood, 2017) of the following form:

$$\sum_{j \neq i,k} F(d_{i,j}, k, mort_{j,t-k})$$

with j the indices of the active farms within a 300-km radius of farm i, $d_{i,j}$ the sea-way distance between farms i and j, k between 0 and 10 weeks, $mort_{j,t-k}$ the mortality at farm j during week t-k, and F a spline function estimated from the data. The mortality at farm j during week t-k was measured as an incidence rate in the full model, i.e., as the mortality incidence count during that week divided by the number of fish present at the beginning of the week. In an alternative model (see explanations below), the mortality at farm j during week t-k was measured as an incidence count. In addition to the linear functional term, the model was risk-adjusted for the other risk factors observed at each farm and within-farm autocorrelation, as described below.

2.3.3. Other explanatory variables

The autocorrelation model was adjusted for other risk factors, given the large variability between different farms and different production cycles, and in order to account for possible confounding. Seven risk factors identified as important from previous studies conducted by the authors or published results from other research groups were included in the models.

The fish-level factors included in the model were the fish species, the time since sea entry in degree-days, and the mortality from other infectious causes during the week of observation. Two predictors were included to capture temporal trends: the number of days since the first observation in the dataset (January 2nd, 2012) to account for broad scale temporal trends such as variations between years, and the day of the year was included to account for potential seasonal trends. Lastly, we included the average sea water temperature during the week of observation, which was the only available variable related to environmental conditions with low rates of missing data. The farm latitude was included to account for other unmeasured environmental and spatial variations.

2.3.4. Statistical methods

The weekly SRS-attributed mortality incidence count data was

Table 1
Characteristics of each statistical model.

Statistical model identifier	Model characteristics
1 (null model)	No spatiotemporal autocorrelation term.
2 (full model)	Spatiotemporal autocorrelation estimated with a lag between 0 and 10 weeks.
3	Farm and company effects not included.
4	Spatiotemporal autocorrelation estimated with a lag up to 15 weeks rather than 10 weeks.
5	Spatiotemporal autocorrelation estimated with a lag up to 4 weeks rather than 10 weeks.
6	Spatiotemporal autocorrelation estimated using Euclidean distances rather than sea-way distances.
7	Latitude effect not included.
8	Mortality on source farms estimated as an incidence count rather than an incidence rate.

treated as a negative binomial response to account for overdispersion in the counts. These counts were offset by the natural logarithm of the number of fish present at the beginning of the week. A generalized additive regression modelling framework was adopted, and implemented through the *mgcv* package (Wood, 2017) available within the R statistical computing environment (R Development Core Team, 2019).

The linear functional component of the model that included time lag, distance and SRS-attributed mortality incidence observed at other farms was modelled via a tensor product smooth (Wood, 2017). Other explanatory variables were included either as linear effects or as spline smooth effects (thin plate regression splines) (Wood, 2017), based on initial data exploration. Continuously valued explanatory variables were centred and scaled.

Clustering of the farm-week records within company, farm and production cycle was considered when building the models. Different methods for including random effects for company, farm and production cycle, and a stricter temporal within-farm autoregression structure, were trialled but were not computationally feasible to implement given the large size of the dataset ($\approx$ 49,000 farm-week records). Ultimately, the random effects were included in the model as spline smooth effects, which are treated as penalized regression terms, an estimation method equivalent to that of conventional random effects (Wood, 2004). In short, the coefficients associated with the model matrix component are assumed i.i.d. normal, with unknown variance to be estimated. The within-farm autocorrelation terms of lag order 1 and 2 were modelled as linear regression terms, again for ease of implementation. These terms correspond to the mortality on the same farm during the last and before-last weeks before the observation week. Exploratory analysis showed that the within-farm autocorrelation for larger temporal lags (> 2) was not significant.

2.3.5. Model selection

Consistent with the information theoretic approach (Burnham and Anderson, 2002), eight nested statistical models were built to compare the significance of different covariates. The full model included all the covariates described in the above sections. In three other models, some variables were not included, namely the spatiotemporal autocorrelation term, the latitude effect and the farm and company effects. The maximum lag of the spatiotemporal correlation was changed from 10 to 4 and 15 weeks in two other models, respectively. Last, a model based on the Euclidean distances rather than the seaway distances was also built, as well as a model using the mortality incidence count on source farms rather than the incidence rate (Table 1).

Once fitted to the observed data, the eight statistical models were ranked according to their AIC and Akaike weights (Akaike, 1974). Models with an AIC difference greater than ten points from the model with the lowest AIC were considered to be substantially less supported by the data than the highest-ranking model (Burnham and Anderson, 2002; Wagenmakers and Farrell, 2004).

2.4. Distance calculations

The sea-way distance between farms was computed using a least-cost path algorithm implemented in Python by the scikit-image package.[2] A raster map of the region of interest, with a cell resolution of 0.003°, was used. Resistance values of one for seawater pixels and of one million for land pixels were selected to prevent the optimal route from crossing land pixels. The routing algorithm was applied to each pair of farms available in the dataset. Both the sea-way distance and the Euclidean (straight-line) distance were recorded for each pair.

2.5. Interpretation of the results

Partial effects were obtained from the most supported model for a range of time lag, distance and source farm mortality values. We obtained the partial effects for the influence of a single source farm on the target farm, although the models were fitted by considering the influence of the 50 closest source farms. In addition, the concepts of source and target farms are used here for clarity, but it is important to note that the linear functional term considers an undirected spatiotemporal correlation. The partial effects displayed in Fig. 2 indicate the direction and intensity of the correlation between the mortality on source and target farms, at different values of time lag, distance and source farm mortality.

Then, predicted values of SRS mortality on the source farm were obtained considering the influence of SRS mortality on the 50 closest source farms, distributed as per the average neighbourhood configuration in the dataset. Continuous and categorical fixed effect values were set to the dataset mean or reference category, respectively. The within-farm autocorrelation terms were set to 0. This allowed us to compare the changes attributable to the spatiotemporal correlation in time and space, all other factors remaining equal (Fig. 3).

3. Results

Sea farms in the Los Lagos region reported a total of 49,724 farm-week records between January 2nd, 2012 and September 24th, 2018. Species farmed during that period were rainbow trout, Atlantic salmon, coho salmon, King salmon and pink salmon. There were only very few records for the two latter species, and they were removed before analysis. The number of fish present each week on the farm and the average sea temperature were missing from 1.2% and 25% of the records, respectively. These values were approximated using the previous and following weekly records where possible. A total of 48,791 complete farm-week records (1010 production cycles) were retained for this analysis. These records originated from 334 farms (Fig. 1).

The best-fitting statistical model according to the Akaike weight was model 7, which was the model based on mortality incidence rates on source farms during the previous 10 weeks, without the latitude effect (Table 2). There was only a small difference with the full model (model

[2] http://scikit-image.org/docs/0.7.0/api/skimage.graph.mcp.html

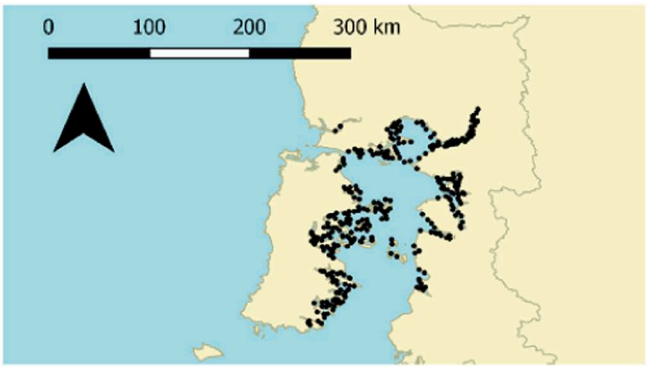

Fig. 1. Location of the 334 farms for which data were available, in the Los Lagos region of Chile.

Table 2
Statistical model ranking based on the observed data.

Statistical model identifier	No. of parameters	AIC	ΔAIC	Akaike weight
7	1007	394,303	0	0.97
2	1007	394,310	7	0.03
3	997	394,351	48	0.00
6	997	394,520	217	0.00
4	993	394,572	269	0.00
8	1004	394,673	370	0.00
5	1003	394,820	517	0.00
1	967	396,295	1992	0.00

Table 3
Coefficient estimates from the best statistical model. Edf: estimated degrees of freedom. Estimates for continuous variables are provided for the scaled variables.

Parametric coefficients	Estimate	Standard error	t-value	*p*-value
Intercept	−12.61	0.19	−65.42	< 0.01
Autocorrelation with lag 1	4.15	0.06	73.99	< 0.01
Autocorrelation with lag 2	0.30	0.05	6.21	< 0.01
Time since sea entry	< 0.01	< 0.01	56.10	< 0.01
Sea temperature	0.18	0.03	6.75	< 0.01
Mortality from other infectious causes	0.55	0.07	7.68	< 0.01
Species (reference: Atlantic salmon)	*reference*			
coho salmon	−1.75	0.20	−8.84	< 0.01
Rainbow trout	−0.03	0.23	−0.14	0.89
Smooth terms	**edf**		**F-value**	**p-value**
Linear functional term	42.86		88.01	< 0.01
Long term temporal trend	3.00		145.68	< 0.01
Seasonal trend	1.98		718.74	< 0.01

2). These 2 models performed better than the model based on Euclidean distances (model 6), the model including lags up to 15 weeks (model 4) and the model based on SRS mortality incidence counts on source farms (model 8), with AIC differences larger than 200 points. The models including no spatiotemporal correlation and only 4 weeks of lagged mortalities (models 1 and 5) had the highest AIC values. The spatiotemporal correlation in SRS mortality was statistically significant in all models where it appeared (Table 3).

However, the partial effect of a single source farm on SRS mortality was small in all models (see estimates from best model in Fig. 2, panel A). There were small variations of this effect with distance, time lag and mortality on the source farm, which are described below for the best fitting model (model 7) but were similar for model 2. There was no correlation between the mortality on source and target farms for a wide range of parameters. Within a small time lag (≤3 weeks), there was a negative correlation for very high values of mortality (above 1%) when the distance between the source and target farms was small (up to 10 km). There was also a negative correlation for very high values of mortality for farms located at long distances (≥80 km), with medium time lags between 2 and 8 weeks. For farms located at medium distances (20 to 50 km), there was a positive correlation for very high values of mortality. For longer time lags (≥8 weeks), there was a positive correlation across the range of mortality levels at short and medium distances (up to 25 km). At long time lags, there was also a strong positive correlation for very high values of mortality (above 1%) at very long distances (above 100 km). Although model 4 only ranked 5th in our study, the partial effect plots from this model are presented in Fig. 2, panel B, to illustrate the effect of considering time lags up to 15 weeks. In model 4, the large correlation values mentioned above for long and time lags distances were not observed. Other correlation patterns were similar between models 4 and 7.

While the partial effects showed significant spatiotemporal autocorrelation, the influence of a single infected source farm on predicted values of mortality on the target farm was negligible regardless of the time lag and source farm mortality considered (Fig. 3). The mortality on the target farm remained lower than 0.0001% after 3 weeks and increased to 0.0002% after 9 weeks. Predicted values were higher when 10 to 20 of the source farms were infected, remaining under 0.005%. When all neighbour farms were infected for 9 weeks, the mortality on the target farm increased to up to 0.2%. The standard errors for all predicted values were large and the confidence intervals included 0. The effect of the level of mortality on infected source farms was not statistically significant.

In the most supported model, SRS mortality was positively associated with the mortality on the same farm during the previous week and two weeks before the observation (Table 3). Weekly SRS mortality was also positively associated with time since sea entry, sea temperature, mortality from other infectious causes. There were significant long- and short-term temporal trends (Supplementary material, Figures). Mortality in coho salmon was significantly lower than in Atlantic salmon, and there was no difference between Atlantic salmon and rainbow trout.

4. Discussion

This study considered the spatiotemporal correlation of SRS mortality in commercial salmonid farms in southern Chile. The results showed that there was a statistically significant association between the weekly mortality incidence at source farms and the mortality incidence at target farms during the same week and during the previous weeks. The ranking of different model formulae provided additional information on this spatiotemporal correlation in SRS mortality. First, including the spatiotemporal correlation term for time lags of up to 10 weeks substantially improved the model fit compared to the model excluding this term, or including only 4 weeks of lagged mortalities. Extending the correlation term to longer time lags (up to 15 weeks rather than 10) did not provide additional benefits in terms of model fit. The time lag considered between mortality on source and target farms is an important factor to consider when interpreting the model results (see more detailed interpretation below). Under the hypothesis of waterborne pathogen dissemination of *P. salmonis* from a source farm, a substantial time lag is expected before observing an increase in SRS mortality on the target farm. This period can be divided in two: a period of dissemination of bacteria from the source to the target farm and the period before substantial SRS mortality is observed on the target farm. These durations may be affected by many factors, such as the level of shedding of bacteria on the source farm, hydrodynamic parameters, the incubation period of SRS and within-farm disease dynamics.

The exclusion of the latitude effect (model 7) did not substantially modify the fit to the data (small AIC difference with model 2), nor did it modify the spatiotemporal patterns of predicted values (data not shown). Consequently, we considered that the latitude effect was not

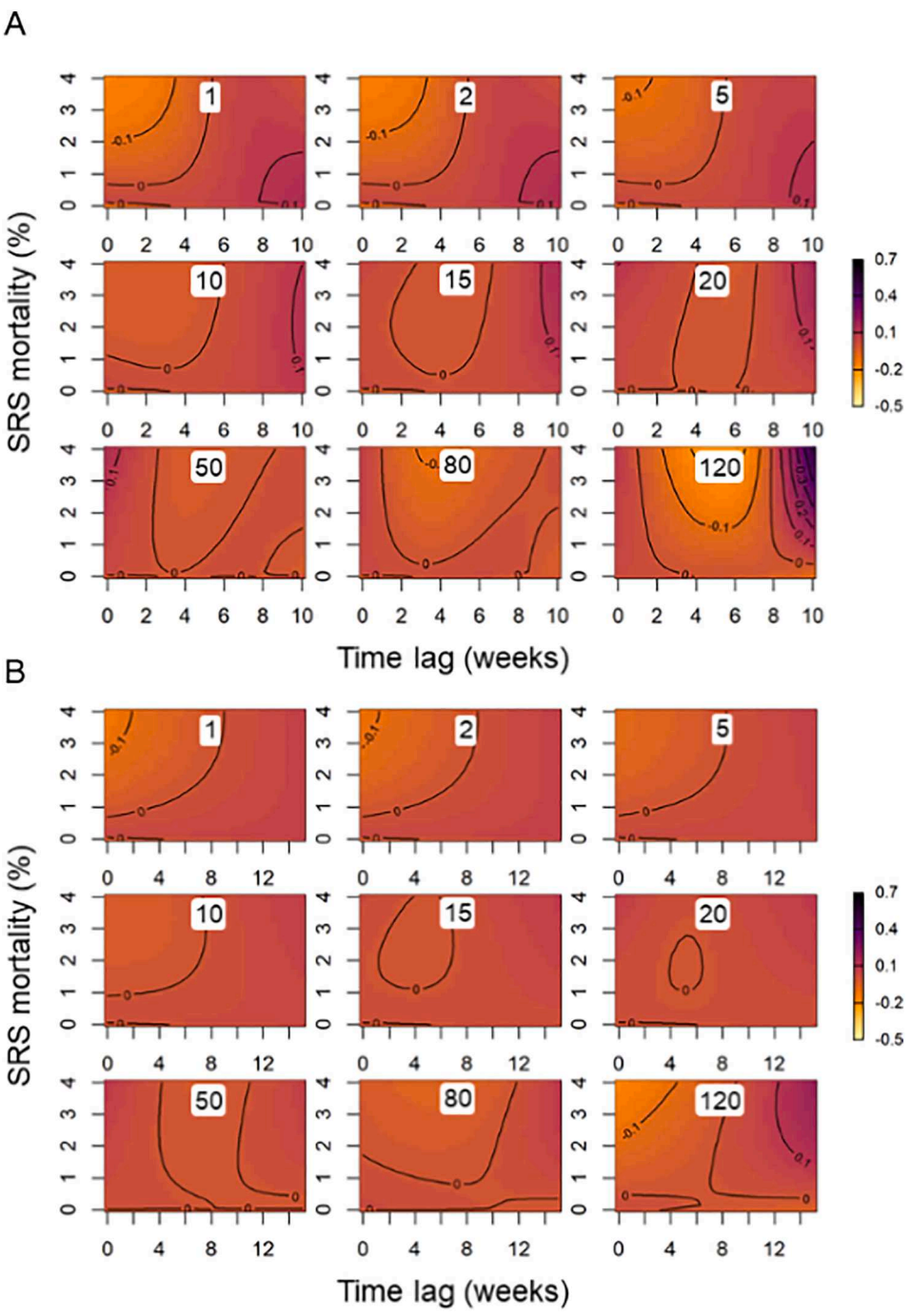

Fig. 2. Partial effect of the SRS mortality of the source farm on the SRS mortality on the target farm, conditional on different distance and time lag values, obtained from model 7 (panel A) and model 4 (panel B). Yellow tones correspond to the lowest values while purple tones correspond to the highest values. The y-axis corresponds to increasing levels of mortality on the source farm. The x-axis corresponds to an increasing time lag between the mortality observations on the source and target farms. The panels correspond to increasing distances between the source and target farms, as indicated by the numbers (in km) in the white boxes. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

unduly capturing the variability due to spatiotemporal autocorrelation in the response in the full model. Previous analyses showed that SRS mortality was influenced by the site latitude in Atlantic salmon (Happold et al., 2020). The present results suggest that the association with latitude may be due to local correlation in mortality between sites. It is also plausible that our results differ because the model was fitted for Los Lagos region only. Within the region, there was a smaller range of variations along the North-South direction.

Interpretation of the partial effects showed local, positive correlation between the mortality on source and target farms within a radius of 20 to 50 km, instantaneously and for time lags of up to 2 weeks. As the incubation period of SRS is assumed to be at least 2 weeks (Rozas and Enriquez, 2014; Smith et al., 2004), such spatial correlation with time lags inferior or equal to the incubation period is unlikely to be explained by water-borne pathogen dissemination between the source and target farms. Alternative mechanisms such as infection by a common (e.g., environmental) reservoir of *P. salmonis* or sharing similar local environmental characteristics that trigger the expression of SRS mortality on already-infected farms may explain the observed correlation in neighbouring farms for small time lags. Local, positive correlation, on sites up to 25 km apart, also occurred for longer time lags, from 7 to 8 weeks onwards. This pattern could be consistent with water-borne pathogen dissemination having occurred between the source and target farms. The longer time lags observed in this case are biologically plausible, as they could reflect a combination of the incubation period of the disease at fish-level and the time for the disease to result in observable levels of fish mortality on a newly infected farm. Published descriptive parameters of the within-farm transmission of SRS were not available at the time of writing. Finally, the positive correlation observed over long distances ($\geq$100 km) may be associated with multiple

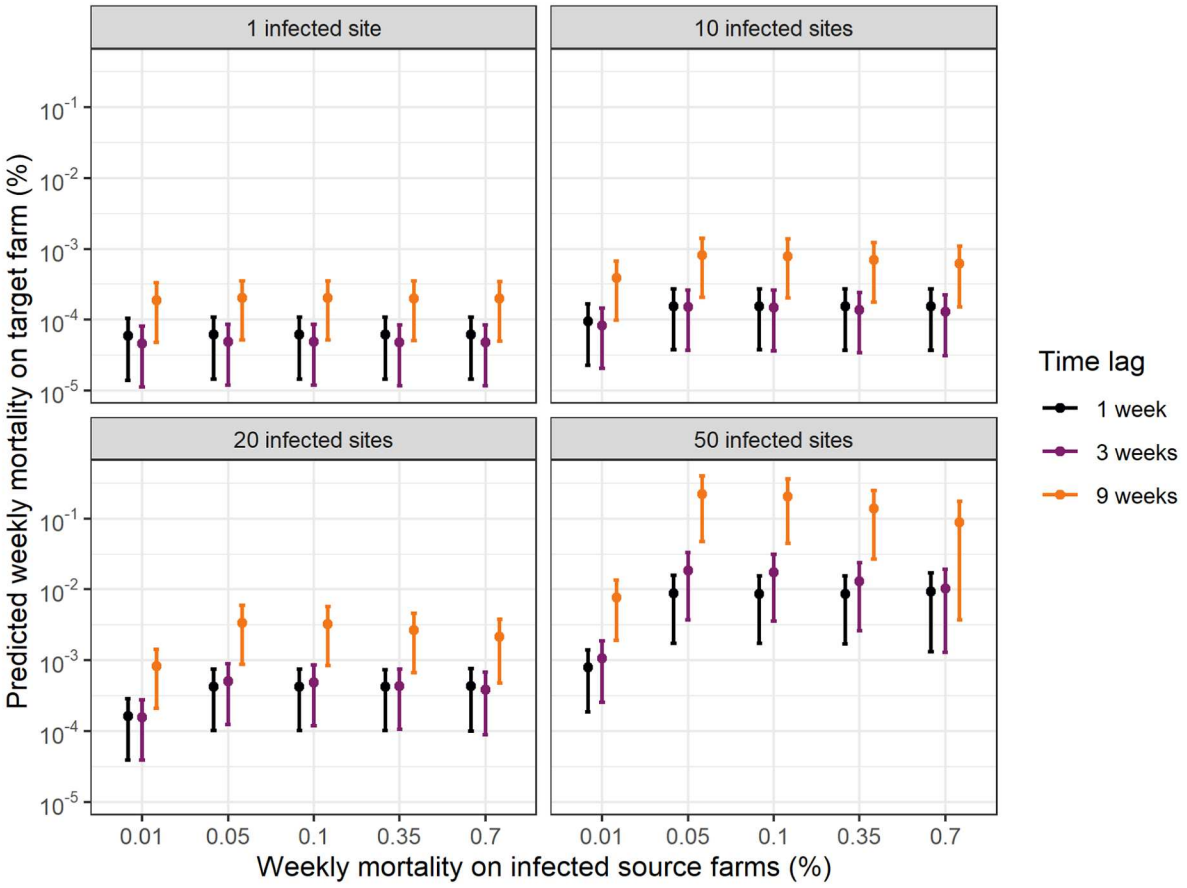

Fig. 3. Predicted values of SRS mortality of the target farm according to the SRS mortality on the neighbour source farms. Distances were set to represent the average neighbourhood configuration in the region. The different line colours represent the cumulative time lag of SRS mortality on the source farms (for example, 3 indicates that we considered the mortality on the target farm after 3 weeks of SRS mortality on the source farms). The panels represent the number of source farms which declare SRS mortality at the level indicated on the x-axis. The error bars represent the standard error of the predicted values. The predicted values were obtained from model 7 and are plotted on a log scale.

disease foci, distributed over the entire study area. These foci of SRS mortality may appear correlated, while actually occurring in parallel without any epidemiological link between them. In addition to between-farm correlation, model results showed temporal, within-farm autocorrelation in mortality, with positive coefficients for 1-week and 2-week lags. These terms represented the within-farm dynamics of the disease, including transmission both between fish and between pens.

In this paper, we used a spline-based model. Others have studied spatiotemporal correlation of animal diseases using kernel-based methods (e.g. Boender et al., 2007; Gubbins et al., 2018; Ypma et al., 2013). Both methods are based on arbitrary values for the 'smoothing' parameter (i.e., bandwidth or degrees of freedom). The spline-based method was chosen in this work as it better allowed for the inclusion of multiple risk factors within the GAM framework, such as seasonality with a cyclic spline. No readily usable framework for kernel-based multivariate GAM estimation was found at the time of this study. In addition, the spline-based GAM framework allowed for the use of continuous mortality data rather than dichotomizing the data according to arbitrary rules. The choice of kernel type is a critical step in kernel-based methods, and may have a significant impact on the outcome, as shown in Gubbins et al. (2018). Other methods used to study spatial correlation of infectious animal disease outbreaks include the space-time K function (Vergne et al., 2017). It is worth noting that any such method may only be used to assess whether spatiotemporal correlation has a substantial effect on the distribution of the cases, and that these studies do not assess whether farm-to-farm transmission is the main cause of such correlation.

A potential caveat of the spline-based method is harmonic behaviour. Higher values observed at the upper extremity of the range of time lags may be due to a model artefact rather than representing biological processes. Such oscillations may have occurred for large time lags in model 7 and did not appear in the model using longer time lags (model 4). Harmonic behaviour may also explain the negative correlations observed for some of the parameter combinations, which are unlikely to be biologically plausible. Oscillations in the spline functions may be a consequence of the harmonic behaviour of the smoothing process, as demonstrated by previous authors (Bowman and Azzalini, 1997; Wüst et al., 2017). In addition, it is worth noting that the uncertainty associated with the smooth effect was large, which leads to the necessity of interpreting the shape of the surfaces carefully.

An important limitation of this study is the use of on-farm mortality classification data as the only form of SRS diagnosis. We were unable to determine the sensitivity and specificity of the classification process of fish mortalities. These indicators may depend on the qualifications and experience of farm personnel as well as previous SRS laboratory diagnoses for the fish group. Classification inaccuracies may have affected our results, by misestimating the level of SRS mortality on the source or target farms. The data used in this study could be improved by including results from farm-level or area-level laboratory diagnosis of SRS.

Our model results suggest a small dose-response effect where increasing SRS mortality on the source farms (up to 0.05%) resulted in increasing mortality predicted values on target farms. However, this response was not statistically significant and only appeared when a very

large proportion of the neighbouring farms were affected. The infection pressure from a few farms in the neighbourhood, even with very high SRS mortality and at short distances did not increase the mortality on the target farm. Overall, the mortality on source farms did not explain a substantial proportion of the variance in the SRS mortality on the farms included in our dataset. Hence, this study does not provide evidence that the spatiotemporal correlation observed in SRS mortality could be due to water-borne pathogen dissemination between farms. Although the pathogen may abundantly disperse in the sea environment of infected farms, our models do not support a substantial effect of this dissemination in causing mortality in neighbour farms. Overall, the models provide evidence in favour of alternative explanations of the mechanisms behind spatiotemporal correlations. Confounding effects due to unaccounted-for factors that influence SRS mortality on neighbouring farms simultaneously or with a certain time lag include various biotic and abiotic factors. The results presented here highlight the complex epidemiology of *P. salmonis* infection in salmonid farms.

Previous modelling work showed that larger sea farms were at higher risk of transmitting disease to their neighbours, due to the higher intensity of pathogen shedding (Salama, 2011). Our full model based on SRS mortality *rates* on source farms (model 2) provided a significantly better fit to the data than the alternative model using mortality *counts* instead (model 8), with a large AIC difference. This result is surprising, as it was expected that the number of fish dying from SRS (representing a combination of the level of mortality on the source farm and the farm size) would provide a better estimation of the farm-level infectivity and pathogen shedding. Other variables which could be of interest are the stocking density, the number and size of cages and the production stage on the source farms. However, the effect of these variables could not be studied here, as the models did not converge when including more than three variables in the linear functional terms (time lag, distance and source farm mortality). The importance of SRS mortality rates is consistent with Chilean regulatory thresholds for intervention, which are based on weekly mortality rates rather than counts. However, there was no evidence in our study of a threshold effect above which farms poses a substantially larger health risk to their neighbours.

It is important to note that models based on seaway distances performed better than the model based on Euclidean distances. A spatial study of pancreas disease using a hydrodynamic model in Norway showed that the infection pressure for this disease was best modelled by a variable based on water contact and the fish biomass on infectious sites (Viljugrein et al., 2009). An infection pressure variable based on seaway distances and including the number of fish at infectious sites was an acceptable alternative. Stronger evidence for or against between-farm transmission of *P. salmonis* may be obtained by building and assessing the predictive power of mathematical models of pathogen spread. A large range of methods are available, depending on the spatiotemporal scale of interest for instance (Parry et al., 2013). Existing models of pathogen spread in aquaculture demonstrated the importance of including hydrodynamic features of the study area (Salama and Murray, 2011, 2013; Viljugrein et al., 2009). Little published work on hydrodynamic features is currently available to support such modelling work in our study area. Local parameters for currents and tidal amplitude were reported in a few studies in the Los Lagos and Aysén regions (Atkinson et al., 2002; Aiken, 2008; Shaffer et al., 1999; Figueroa and Moffat, 2000; Sobarzo et al., 2018). Although the Peru-Chile current system affects the general area (Karstensen and Ulloa, 2019), sea farms in the Los Lagos region are located in protected channels, fjords and bays rather than in open water. These farms are less likely to be affected by large-scale oceanic conditions than by local water flows. Such water flows follow complex patterns created by tidal movements, residual currents, freshwater inputs, oceanographic features and local topography (Sobarzo et al., 2018). The development of a mathematical model of SRS spread including hydrodynamic parameters would be expected to provide a substantial contribution to explaining spatiotemporal patterns of SRS mortality in Chile (Steven et al., 2019). Such work could build on previous hydrodynamic modelling for other diseases, such as the work on infectious salmon anaemia presented by Olivares et al. (2015), which was based on the Regional Oceanic Modelling System (Shchepetkin and McWilliams, 2005).

In addition, whole-genome sequencing has proven useful in identifying disease transmission patterns in various situations where traditional contact tracing was not conclusive (Crispell et al., 2017; Kao et al., 2014; Walker et al., 2014; Gardy et al., 2011). Molecular techniques could contribute to clarifying SRS transmission routes in Chilean salmon farms, by characterising the *P. salmonis* isolates identified on different farms and assessing the genetic distance between them. Further research on these topics would contribute to close some important knowledge gaps related to SRS (Mardones et al., 2018) and support the development of more evidence-based policy. In the meantime, the evidence currently available is not strong enough to base all regulatory disease management efforts on the hypothesis of waterborne between-farm transmission. A broader approach to risk management is recommended, with different mitigation measures addressing the potential spread mechanisms.

Declaration of Competing Interest

None.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.aquaculture.2020.735751.

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