



## Modelling the spread of Salmonid Rickettsial Septicaemia and assessing regional control strategies for saltwater salmon farms in Aysén, Chile

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### ABSTRACT

Salmonid Rickettsial Septicaemia (SRS) is a highly infectious, endemic disease that spreads among saltwater salmonid farms in Chile, making control efforts challenging. Here, we present a model that simulates SRS transmission between saltwater salmonid farms in the Aysén region of Chile, using the state-transition model framework InterSpread Plus (ISP). In ISP, the status (e.g., susceptible or infectious) of farms is individually defined, and the simulation determines the transition of the farms' state over time. Farm characteristics, such as fish species and production size, were incorporated into the model. The model parameters were estimated based on data collected from 432 farms between 2011 and 2020, expert opinions, and literature reviews. The simulation included an average of 150 active farms per week, with a total of 46,380 active farm-weeks. The model had a one-year simulation period and was used to simulate the annual spread of *P. salmonis* between salmonid farms for each year from 2013 to 2019 (i.e., six one-year model simulations, each starting in September of the respective year). Model accuracy was estimated based on 1 minus the cumulative difference between the simulated and observed weekly SRS prevalence at the regional level. The average annual model accuracy for the six one-year models was 95.0% (range: 91.7 – 96.0%). The baseline model was used to explore a total of 19 “what-if” control scenarios addressing one of the three following strategies: (i) depopulation of infected farms, (ii) reducing number of farms in neighbourhoods, and (iii) vaccination. The impact of these scenarios was assessed based on the estimated annual incidence rate of SRS over 6 years (i.e., 2013–2019). The three most effective scenarios for reducing the annual incidence rate of SRS were: (i) immediate depopulation of infected farms, (ii) strategic removal of 30% of highly connected farms per neighbourhood, and (iii) industry-wide implementation of a hypothetical vaccine with at least 75% efficacy for a minimum of 9 months. However, the estimated number of fish harvested and the estimated use of antibiotics for each of these control scenarios, compared to the baseline models, suggested that they may not be cost-effective for the industry. Future research should include cost-effectiveness analyses to identify the most economical measures for the industry. The ISP model in this study introduces a novel application of this software for managing SRS in the Chilean Aysén region and could serve as a decision-support tool for policymakers, epidemiologists and fish health professionals.

**Abbreviations:** ISP, InterSpread Plus; ISAC, ISP-SRS-Aysén-Chile; *P. Salmonis*, *Piscirickettsia salmonis*; Sernapesca, Servicio Nacional de Pesca y Acuicultura; SRS, Salmonid Rickettsial Septicaemia.

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## 1. Introduction

Salmonid Rickettsial Septicaemia disease (SRS), caused by *Piscirickettsia salmonis* (*P. salmonis*), also known as piscirickettsiosis, has been one of the costliest diseases for the Chilean salmonid industry in the last two decades (Mardones et al., 2018; Rees et al., 2014; Rozas and Enriquez, 2014; Sernapesca, 2022). The first major outbreak of SRS occurred in the area of Calbuco, Southern Chile in 1989 and caused the death of over 1.5 million market-sized coho salmon (*Oncorhynchus kisutch*) (Almendras and Fuentealba, 1997; Bravo and Campos, 1989). Since then, SRS has remained a substantial problem for the Chilean salmonid aquaculture industry. The annual economic loss due to this disease was estimated to be at least US\$ 700 million in 2016 (Avenida-Herrera, 2018; Ibieta Hillerns et al., 2011; Mardones et al., 2018). Since 2005, SRS has been the leading infectious-disease-related cause of mortality, and the primary reason for antibiotic use in saltwater salmonid farms in Chile (Sernapesca, 2012; Sernapesca, 2013; Sernapesca, 2014; Sernapesca, 2015; Sernapesca, 2016; Sernapesca, 2017; Sernapesca, 2018; Sernapesca, 2019; Sernapesca, 2020; Sernapesca, 2021; Sernapesca, 2022). The latter has raised concerns regarding antimicrobial resistance, impacting both public health and veterinary medicine.

Despite government-regulated husbandry requirements on biosecurity, vaccination, and other evidence-based management strategies, such as mandatory fallowing (Lozano-Muñoz et al., 2021), SRS is still endemic in the industry (Sernapesca, 2022). The endemicity of SRS is likely due to the connectedness of the industry and the transmission of the bacteria among farms via water (Rees et al., 2014). The efficacy of vaccines has been sub-optimal, as vaccines do not offer complete protection for the entire duration of a production cycle even when all fish are vaccinated on a farm (Happold et al., 2020). As such, the industry has been relying on the use of antibiotic treatment to control mortalities associated with this bacterial disease, which has led to the emergence of antimicrobial resistance (Cabello et al., 2013; Hillman et al., 2020; Lozano-Muñoz et al., 2021). In view of this, both the salmonid aquaculture industry in Chile and the Chilean National Fisheries and Aquaculture Service (Servicio Nacional de Pesca y Acuicultura or Sernapesca) have been looking for alternative ways to control the disease without increasing the use of antibiotics (Sernapesca, 2022; CSARP, 2020). In the context of managing SRS, developing a disease simulation model is important for understanding the spread of SRS outbreaks and identifying knowledge gaps in the epidemiology of this disease in this region (Mardones et al., 2018; Wada et al., 2021). This type of tool is also useful for evaluating control strategies against SRS at the regional level.

InterSpread Plus (ISP) is a spatially explicit state-transition model framework that has been used to simulate the spread of various pathogens in a variety of settings to either improve disease preparedness or to model the spread and control of outbreaks in real-time (Hiesel et al., 2016; Sanson et al., 2016, 2021; Stevenson et al., 2013; Wada et al., 2021). This tool is commercially available and has a user-friendly interface with built-in equations to model the transition of different farm states on farms over time. The user simply has to define a few specific parameters and their distributions for ISP to operate. While ISP was initially developed for terrestrial animal disease simulations (Rosanowski et al., 2016; Stevenson et al., 2013), our research team previously developed a rudimentary ISP model for the spread of *P. salmonis* in the Los Lagos region of Chile (Wada et al., 2021). The model for the Los Lagos region suggested that ISP may be useful in predicting the spread of pathogens in an aquaculture system with interconnected farms and its potential use for evaluating alternative control policies. However, the Aysén region, another predominant region of aquaculture in Chile, has different geographical and environmental characteristics, and the underlying between-farm transmission of SRS outbreaks may be different. Thus, an independent investigation was warranted to test this tool in different aquaculture regions of Chile. As such, this study aimed to achieve two objectives: (i) constructing and validating an SRS simulation model for the Aysén administrative region

of Chile, and (ii) utilizing the model to quantify the impact of various “what if” control strategies against SRS. These strategies included depopulation, reduction of farm densities in the government-defined salmonid farming neighbourhoods, and various regional hypothetical vaccination strategies against SRS.

## 2. Material and methods

The original dataset used in this study was comprised of data from Sernapesca collected between 1st January 2011 and 25th October 2020 under their government-regulated Piscirickettsiosis control surveillance program (PSEVC-Piscirickettsiosis, Res.  $\text{N}^{\circ}$  3174/2012; Sernapesca, 2022), and Technological Institute of Salmon (Intesa; the technical branch of SalmonChile). Both datasets contained weekly production and fish health data on saltwater salmonid farms and were combined using unique farm IDs and geographical coordinates. The combined dataset contained 1053 saltwater salmonid production cycles from 432 farms in the Aysén region of Chile. The farm-level information included the farm site ID, geographical coordinates of the farm, salmonid species on the farm (i.e., coho salmon (*Oncorhynchus kisutch*), Atlantic salmon (*Salmo salar*), and rainbow trout (*Oncorhynchus mykiss*)), weekly total farm mortality count, weekly SRS-specific mortality count, weekly total fish count, and environmental variables such as sea water temperature ( $^{\circ}\text{C}$ ). This dataset was used to provide descriptive summary statistics and to inform model parameter development.

The onset of an SRS outbreak on a farm was defined when there were at least three consecutive weeks with documented SRS-specific mortality. The outbreak was considered resolved when the farm had not reported SRS-specific mortality for three consecutive weeks. This definition aligns with the previously published study by Jakob and colleagues (2014). The production cycle was determined based on the period from when fish were introduced to the farm until the site was fallowed. The number of fish on a farm was categorized into three groups (i.e., small: <850,000, medium: 850,000–1,000,000, or large: >1,000,000) based on the maximum number of fish for each production cycle at peak production. A total of nine different farm classes were created based on the species and production size categories ( $3 \times 3$ ).

Farm geographical coordinates (point data) were obtained as latitude and longitude, and these were transformed to Universal Transverse Mercator (UTM) coordinates using SIRGAS-Chile / UTM zone 18S (EPSG: 9154). The geographic information system ArcGIS Pro v2.8.0 (Esri, 2020) was used to manage spatial data and map farm locations, with reference to the 37 government-defined administrative farming neighbourhoods (also called barrios). All data management, analysis, and generation of graphical presentations of all model outputs were carried out using STATA IC/16 (StataCorp, 2019). Eighty-four farms had missing data regarding species and/or production size. To avoid altering the underlying farm population in the industry, these 84 farms were included in the model as medium-sized Atlantic salmon farms, naïve at the start of the simulation. These farms were assumed to be medium-sized Atlantic farms, as these were the most common type of farm in Chile (data not shown). For the simulation modelling in this study, we only used a study period spanning from 1st January 2012–31st December 2019, as we needed information on complete production cycles. For this period, we had a total of 889 saltwater salmonid production cycles from 284 farms, equivalent to 46,380 farm-weeks of data.

### 2.1. Model construction and set up

A compartment model framework was built using InterSpread Plus version 6.02.44 (EpiSoft NZ; Stevenson et al., 2013). This software has a built-in state transition disease model framework, which only requires users to input a few parameters to operate. For details on the equations behind the state-transition model used in this software, please refer to Stevenson et al. (2013). We used several sources of information to

establish the distribution values for the parameters in ISP which influenced the simulation of SRS on individual farms over time. Our ISP model was constructed to represent the transmission of SRS between saltwater salmonid farms in the Aysén region of Chile, hereby referred to as the “ISP-SRS-Aysén-Chile model”, or the ISAC model. Each week the model framework simulated the transition of farm states (i.e., fallow, vaccinated, susceptible, latent (pre-infectious), infectious and immune) for individual salmonid farms in the Aysén region (Fig. 1). At the start of the simulation, the initial status of all farms was determined from the history of the farm, which includes the start and end date of the production cycle, the species of fish on the site and the size category of the farm. All inactive farms that were undergoing fallow were assigned to a “fallow” state, reflecting the mandatory fallowing period of a minimum of 3 months between subsequent production cycles (Price et al., 2017). A “vaccinated” state was assigned to farms when they began their saltwater production, reflecting the practice of vaccination of fish against SRS prior to saltwater production (Rees et al., 2014). For the parameter distributions on vaccine uptake, efficacy, and duration of immunity, we estimated these from the literature (Happold et al., 2020; Jakob et al., 2014; Rozas-Serri, 2022; Tobar et al., 2011). These distributions were used to estimate the period of protection attributed to the vaccines. A “susceptible” state was then assigned to farms either after the assumed period of vaccine-induced immunity or after the assumed period of natural immunity post-recovery from a simulated SRS outbreak. The latter was assigned using a BetaPert distribution based on data (min, mode, and max) from our original dataset. A susceptible farm could become infected based on the localised transmission mechanisms from nearby infected farms, represented by a probability which was determined using a fitted Weibull survival regression model based on the Euclidean distance from the infected source farm(s) and the time of onset of the source infection (Table 1) as described in Wada et al. (2021). We subsequently modified this probability for each month to adjust for the temperature effect on SRS in Aysén (Supplementary Information A). Once a farm became infected, it was initially given a “latent” state, during which it could not infect other farms. Here, it was assumed the incubation period and the latent period of SRS were the same (i.e., the time from infection to onset of symptoms was equivalent to the time from infection to onset of infectiousness at a weekly time scale). This period for the “latent” state was set up based on a BetaPert distribution, which used data on reported incubation periods for SRS under laboratory conditions (Rozas and Enríquez, 2014; Rozas-Serri et al., 2017). During this period, farms were not able to spread the infection to neighbouring farms. After the latent period, farms transitioned to the “infectious” state, where they could infect other susceptible farms. The duration of the “infectious” state for farms was based on the duration of SRS from our dataset. We generated an empirical distribution for the duration of SRS for each salmonid species from these data and imported

this into ISP. Once the assumed period of infectiousness ended, an infected farm would recover and transition to the “immune” state, where it could not be re-infected for a period of time based on a BetaPert distribution. The data used to generate the distribution was from our original dataset. A description of the sources and types of probability distribution used for the parameters in ISP are outlined in Table 1. A farm returned to the “fallow” state based on its actual harvest time and remained in this state while it was not active until it was restocked. Both the restocking and harvest times for each farm were based on the actual history of the farms in the study area.

The model had a one-year simulation period and was used to simulate the annual spread of SRS between salmonid farms for each year from 2013–2019 (i.e., six separate one-year model simulations). Each of the six one-year simulations commenced on the 23rd of September and spanned a 52-week simulation period (i.e., September 2013 – September 2014, September 2014 – September 2015, September 2015 – September 2016, September 2016 – September 2017, September 2017 – September 2018, and September 2018 – September 2019). For each model iteration, a value for each model parameter was randomly drawn from its specified probability distribution, so each of the six simulations (each comprised of 100 iterations) was uniquely different. Each one-year model had its own initial source of infections and unique distribution of farms. One hundred iterations per model simulation was the minimum number of iterations required for the ISAC model to achieve less than or equal to 0.5 % coefficient of variation based on the mean and standard deviation of the simulated cumulative total incidence of SRS. This was determined by comparing the coefficient of variation of the output among five models with varying iteration numbers (10, 100, 500, 1000, and 3000).

For each model simulation, ISP produced a text file listing the weekly changes in the states of farms for each iteration. This file was summarised using STATA IC/16 (StataCorp, 2019) to estimate the median weekly incidence and prevalence of SRS for each year. The weekly incidence of simulated SRS was estimated as the number of farms newly infected or re-infected with SRS in a given week. The weekly prevalence of farms with simulated SRS cases was calculated based on the total number of farms with the SRS infected status in that week over the total number of active farms during the same week.

## 2.2. Sensitivity analysis for parameters

The two-sided partial rank correlation coefficient (PRCC) evaluation method (Blower et al., 1991; Marino et al., 2008) with Latin hypercube sampling (LHS) technique (McKay et al., 1979) was used to illustrate how changes to key model parameters affected the simulated annual cumulative incidence of SRS cases. The sensitivity analyses were conducted in R 4.0.2 (R Development Core Team, 2022) using the ‘epiR’ R

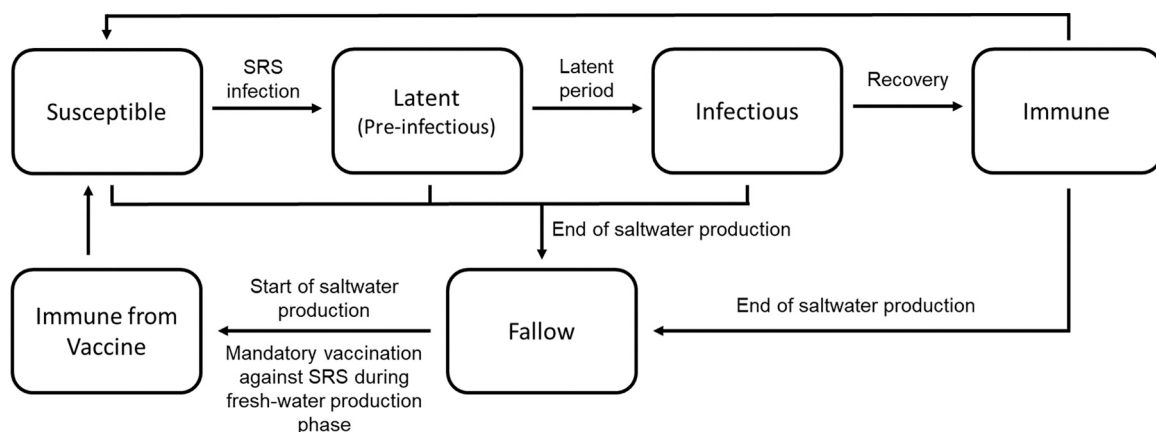


Fig. 1. Illustrative diagram of the state transition of a farm in developing SRS in the ISP-SRS-Aysén-Chile (ISAC) simulation model.

**Table 1**

Model input parameters, descriptions, and sources of information for the determined distribution/value for the spread of piscirickettsiosis between saltwater farms from September 2013 to September 2019 in the Aysén region of Chile.

Parameter	Description	Distribution/Value <sup>A</sup>	Source of information for the determined distribution/value of the parameter <sup>B</sup>
Vaccination Uptake	[One of the three parameters for vaccination] The proportion of farms (%) that undertook vaccination before beginning saltwater production.	BetaPert distribution {0.95,0.99,1}	Based on <a href="#">Happold et al., (2020)</a> and Ibarra R. (Personal communication, May 4 <sup>th</sup> , 2023).
Vaccination Efficacy	[One of the three parameters for vaccination] The percentage effectiveness of the vaccination (%) in preventing the infection of piscirickettsiosis for each individual farm.	BetaPert distribution {0.1,0.4,0.8}	Based on <a href="#">Happold et al., (2020)</a> , <a href="#">Jakob et al., (2014)</a> , <a href="#">Rozas-Serri (2022)</a> and <a href="#">Tobar et al., (2011)</a>
Duration of Immunity	[One of the three parameters for vaccination] The duration of protective immunity induced by vaccination (week) for each individual farm, starting from the beginning of saltwater production, during which it remains immune to infection.	BetaPert distribution {1,3,11}	Based on <a href="#">Happold et al., (2020)</a> , <a href="#">Jakob et al., (2014)</a> , <a href="#">Rozas-Serri (2022)</a> and <a href="#">Tobar et al., (2011)</a>
Probability of Between-Farm Transmission	The probability of transmission of SRS from one farm to another based on: (i) the Euclidean distance between the source infected farm and the recipient susceptible farm and (ii) the time of onset of SRS on the farm which served as the source of infection.	A probability matrix that varied based on distance and time – See <a href="#">Supplementary Information A</a>	Based on our previous work ( <a href="#">Wada et al., 2021</a> )
Temperature Monthly Modifier	A modifying parameter multiplied with the probability of between-farm transmission parameter based on the month of the year.	Fixed value that varied by month – See <a href="#">Supplementary Information A</a>	Based on our industry data
Latent Period	The time period (week) between the occurrence of infection and the onset of infectiousness in an infected farm.	BetaPert distribution {2,4,6}	Based on <a href="#">Rozas and Enríquez (2014)</a> and <a href="#">Rozas-Serri et al., (2017)</a>
Duration of SRS	The time period distribution derived from Kaplan-Meier survival analysis and stratified by species.	Empirical distribution from survival duration of SRS for each species – See <a href="#">Supplementary Information B</a>	Based on our industry data
Immunity Period After Recovery of SRS	The minimum time period (week) after which a newly recovered farm is immune to a new infection.	BetaPert distribution {3,4,5}	Based on our industry data, and from <a href="#">Magnadóttir, 2006</a> and <a href="#">Rozas and Enríquez, (2014)</a>

<sup>A</sup> All parameter inputs set as BetaPert distribution followed the format of {minimum, mostly likely, maximum} ([Golenko-Ginzburg, 1988](#)). For each simulation iteration, a value for each parameter with a distribution will be randomly drawn from its specified probability distribution.

<sup>B</sup> Distribution/value for each parameter was either estimated from data or derived based on literature and expert opinion when data was not available.

package ([Stevenson et al., 2023](#)). In short, we programmed it to randomly select values from the entire specified range for each parameter listed in [Table 1](#) for 500 times. In each iteration, the selected parameters were varied simultaneously. The estimated PRCC values for all model parameters across all model iterations were visually assessed by a boxplot. The p-values for PRCC were Bonferroni-corrected based on the number of parameters evaluated ([Dunn, 1961](#); [Neyman and Pearson, 1928](#)).

### 2.3. Model validation

The ISAC model was internally validated by comparing the simulated median and observed weekly prevalence of SRS in the Aysén region of Chile using STATA IC/16 ([StataCorp, 2019](#)). In brief, we generated a metric, model accuracy, calculating the agreement between the simulated weekly prevalence of SRS and the historical data. The weekly agreement was calculated as a percentage using 1 minus the cumulative sum of the differences between the simulated and observed numbers of infected farms per week divided by the cumulative sum of farms in production per week ([Eq.1](#)):

$$\left(1 - \frac{\sum_{k=1}^j |x_k - y_k|}{\sum_{k=1}^j n_k}\right) \times 100 \quad (\text{Eq.1})$$

Where:

- $k$  was the week number,
- $j$  was the total number of weeks for simulation,
- $n_k$  was the total number of farms in production in Week  $k$ ,
- $x_k$  was the number of simulated infected farms in Week  $k$ , and
- $y_k$  was the actual number of infected farms in Week  $k$ .

We assessed the annual model accuracy (median; 2.5th – 97.5th percentiles) for the ISAC model for the Aysén region at both the regional level and the neighbourhood levels by taking a median of the weekly agreement for each year.

### 2.4. Scenario analysis

We conducted scenario analyses to assess the effect of control strategies on the occurrence of SRS in the Aysén region of Chile. In total, 19 different control scenarios were examined ([Table 2](#)). For the scenarios involving depopulation, farms detected with SRS were subject to removal based on four different conditions (Depopulation (D) 1 – 4; [Table 2](#)). The primary difference between these scenarios was the time to implement the depopulation of the fish on sites ([Table 2](#)). Once the depopulation was initiated, the time required to complete the process or removal of fish from a farm (i.e., time associated with the logistics for these procedures) was based on the size of the farm. This variability in time was represented by a BetaPert distribution based on expert opinion (Rolando Ibarra, personal communication, May 4<sup>th</sup>, 2023). For the scenarios involving the reduction of farms in neighbourhoods, different percentages of active farms were either randomly removed (RR) or selectively removed (SR) ([Table 2](#)). Farms for removal were pre-determined for each year regardless of their actual infection status. For scenarios SR1 – 4 ([Table 2](#)), we removed highly-connected farms based on the Euclidean between-farm distance and the number of farms within a 15-km radius (SR1 – 4; [Table 2](#)). Scenarios involving different hypothetical vaccination regimes (Vaccination (V) 1 – 5; [Table 2](#)) explored various vaccination uptake rates, vaccine efficacy, and duration of immunity.

The effect of these scenarios was evaluated by comparing the annual incidence rate of SRS across all six simulation years ([Eq. 2](#)) (i.e., September 2013 – September 2014, September 2014 – September 2015, September 2015 – September 2016, September 2016 – September 2017, September 2017 – September 2018, and September 2018 – September

**Table 2**

Model annotations and description of control scenarios for scenario analysis of three groups of hypothetical control strategies using the ISAC model.

Control Strategies	Description	Model Annotation
Depopulation or "Stamping Out"	Depopulation commenced the following week after the detection of SRS-specific mortality on a farm.	D1
	Depopulation commenced the following week after the farm had reported SRS-specific mortality for at least four consecutive weeks.	D2
	Depopulation commenced the following week after the farm had reported SRS-specific mortality for at least seven consecutive weeks.	D3
	Depopulation commenced the following week after the detection of SRS-specific mortality on a farm, but only if the fish had reached 75 % of their target weight. We approximated the time for fish to reach 75 % of their marker target weight based on the historical data on the duration of production cycle.	D4
Reduction of farm density in each neighbourhood	Random removal of 10 % of all farms in each neighbourhood.	RR1
	Random removal of 20 % of all farms in each neighbourhood.	RR2
	Random removal of 30 % of all farms in each neighbourhood.	RR3
	Random removal of 40 % of all farms in each neighbourhood.	RR4
	Random removal of 50 % of all farms in each neighbourhood.	RR5
	Random removal of 60 % of all farms in each neighbourhood.	RR6
	Selective removal of 10 % of the highly connected farms (as defined by being within a 15 km radius of at least 26 other farms).	SR1
	Selective removal of 20 % of the highly connected farms (as defined by being within a 15 km radius of at least 22 other farms).	SR2
	Selective removal of 30 % of the highly connected farms (as defined by being within a 15 km radius of at least 19 other farms).	SR3
Selective removal of 40 % of the highly connected farms (as defined by being within a 15 km radius of at least 17 other farms).	SR4	
Vaccination	95 % of all farmers adopted a vaccination strategy that offered 95 % efficacy against SRS for the first 13 production weeks (i.e., 3 months). Then, the efficacy of the vaccination gradually decreased by 10 % every week.	V1
	95 % of all farmers adopted a vaccination strategy that offered 95 % efficacy against SRS for the first 26 production weeks (i.e., 6 months). Then, the efficacy of the vaccination gradually decreased by 10 % every week.	V2
	95 % of all farmers adopted a vaccination strategy that offered 95 % efficacy against SRS for the first 39 production weeks (i.e., 9 months). Then, the efficacy of the vaccination gradually decreased by 10 % every week.	V3
	95 % of all farmers adopted a vaccination strategy that offered 95 % efficacy against SRS for the first 52 production weeks (i.e., 12 months). Then, the efficacy of the vaccination gradually decreased by 10 % every week.	V4
	75 % of all farmers adopted a vaccination strategy that offered 95 % efficacy against SRS for the first 39 production weeks (i.e., 9 months). Then, the efficacy of the vaccination gradually decreased by 10 % every week.	V5

2019). We also included the baseline model without any control strategies. A fixed seed within ISP was used in all scenarios, as well as the respective baseline model, to assure a fair (counterfactual) comparison. To ensure a fair comparison between each model pair (baseline vs alternative control scenarios), the model settings were kept identical except for the control strategies being examined. For the depopulation and the vaccination scenarios, we started the simulation with the

(i) in a proposed scenario for each of the 6 years ( $y$ ) with its respective baseline model (repeated for all scenarios) (Eq. 2 and Eq.3):

$$\text{Annual incidence rate}_y = \frac{\text{Total number of new SRS}_y}{\text{Total number of active farm-week}_y} \quad (\text{Eq.2})$$

$$\text{Effectiveness}_{y,i} = \left( \frac{\text{Baseline annual incidence rate}_{y,i} - \text{control scenario annual incidence rate}_{y,i}}{\text{Baseline annual incidence rate}_{y,i}} \right) \times 100 \quad (\text{Eq.3})$$

initially infected farms based on their status in the historical records. In the scenarios where we reduced the number of farms in neighbourhoods at the start of the simulation (i.e., RR1 – 6 and SR1 – 4), it was not possible to maintain the original history file for depicting the infection status of farms in the baseline model because this would have led to a different number of initially infected sites between the baseline model and the control strategy. To address this, if infected farms were selected to be removed in the simulated control strategy "Reduction in farm density", we kept these farms in the baseline model; however, we set their infection state to uninfected at the simulation start irrespective of their true infection status in the historical record. This achieved a comparable infection pressure at the start of the simulations and permitted us to evaluate the effect of farm density on the spread of infection. As each control scenario was tested for each simulation year, a total of 60 baseline models were run for comparison, one for every year-scenario pair (i.e., 6 simulation years  $\times$  10 scenarios: Random Removal (RR) 1 – 6 & Selective Removal (SR) 1 – 4; Table 2).

The effectiveness of each proposed strategy was evaluated by comparing the median annual incidence rate of SRS over 100 iterations

The overall effectiveness across the six simulation years for the strategies were presented using boxplots.

To better assess the impact of the control scenarios, we estimated the approximate number of fish harvested and the number of antibiotic treatments used for the region that would have occurred under each of the control scenarios. This analysis was conducted only on scenarios that were comparable to the original baseline model (i.e., the depopulation and vaccination strategies) for the simulation year 2013 – 14. The estimates were based on the number of farms simulated with and without SRS. The number of harvested fish for each production cycle was approximated by taking the maximum fish count recorded and subtracting the industry median cumulative total fish mortality for the specific type of farm (i.e., coho salmon, Atlantic salmon, and rainbow trout farms of different sizes). If a farm was simulated to have SRS, the median cumulative farm mortality from farms that reported SRS was used (i.e., the total farm mortality comprised of SRS-specific mortalities and non-SRS related mortalities). Conversely, if SRS was not simulated, we applied the industry median cumulative mortality for farms with no reported SRS (i.e., the total non-SRS related mortalities). For

depopulation scenarios, if a production cycle ended earlier than expected because it was depopulated due to SRS (i.e., depopulation scenarios (D1 – D3)), the number of fish harvested from these sites was considered to be zero. For scenario D4, where depopulation occurred when fish reached approximately 75 % of the target weight, we used the fish count when the depopulation started as our harvest number. To estimate the regional total number of antibiotic treatments associated with SRS under different scenarios, we multiplied the total number of simulated SRS outbreaks on farms by the median number of antibiotic treatments used during SRS outbreaks as described in Hillman et al. (2020). Subsequently, we aggregated all treatments that would have been used in the region during the 2013 – 14 year based on the selected scenarios.

### 3. Result

#### 3.1. Descriptive statistics of the Aysén saltwater salmonid production

Between 1st January 2011 and 25th October 2020, there were a total of 1053 production cycles of salmonid species from 432 farms in the Aysén Region in Chile. Fig. 2 illustrates the spatial distribution of all 432 farm sites among the 37 salmonid farming neighbourhoods in the Aysén Region of Chile. All farms raised a single species throughout one production cycle, with the majority of farms (76.0 %) culturing Atlantic salmon, while 11.5 % cultured coho salmon and 12.5 % cultured rainbow trout. The median length of a production cycle for coho salmon, Atlantic salmon and rainbow trout was 44 weeks (IQR: 39 – 48), 75 weeks (IQR: 69 – 80) and 51 weeks (IQR: 46 – 57), respectively. On average, there were 150 active farms each week within the region (IQR: 133 – 168). The number of fish on farms varied from 111,000 to 1201,760, with 37 % (387/1039) of all recorded production cycles having at least one million fish.

Between 1st January 2012–31 st December 2019, the median weekly prevalence of SRS-infected farms (cases) was 58.6 % (IQR: 48.5 – 66.0 %), with a median of 3 (IQR: 1 – 4) new cases detected every week. There was a total of 1451 recorded SRS cases throughout the study period, with a median duration of SRS at 15 weeks (IQR: 7 – 34 weeks). Overall, the first SRS case on individual farms occurred at a median of 17 weeks (IQR: 11 – 26 weeks) post smolt entry, and the median time between subsequent SRS on a farm was 8 weeks (IQR: 5 – 15 weeks). These data were subsequently used to inform the probability distribution for model parameters (Table 1).

#### 3.2. Sensitivity analysis

The effect of different model input parameters on the primary outcomes analysed using PRCC, are depicted in Fig. 3. The annual cumulative incidence of SRS was moderately impacted (based on a PRCC greater than 0.4) by the following parameters: “duration of SRS for Atlantic salmon farms”, “latent period”, and “vaccine efficacy in Atlantic salmon farms”. The “vaccine efficacy in rainbow trout farms” and the “duration of SRS for rainbow trout farms” had a low influence on this outcome, with PRCCs between 0.2 and 0.4 (Fig. 3).

#### 3.3. Model validation

The median model accuracy for the annual regional-level prevalence of SRS ranged between 91.7 – 96.0 % depending on the year (Table 3). Across all six simulation years, on average, 20 out of 37 neighbourhoods had a model accuracy of at least 80 %. Although the model did not work consistently in all neighbourhoods, there was no apparent pattern in the neighbourhoods across time (i.e., many neighbourhoods were not accurately simulated in some years, but well classified in other years) (Table 4).

Throughout the study period, the ISAC model simulated an average weekly incidence count of 3.1 SRS cases (IQR: 1.9 – 4.2) and an average

weekly prevalence of 45.8 % SRS cases for active farms (IQR: 37.2 – 53.4 %) (Fig. 4). This was similar to what was observed based on the data (weekly average incidence and prevalence were 3 (IQR: 1.0 – 4.0) and 50.79 % (IQR: 43.4 – 63.6 %), respectively).

#### 3.4. Scenario analysis

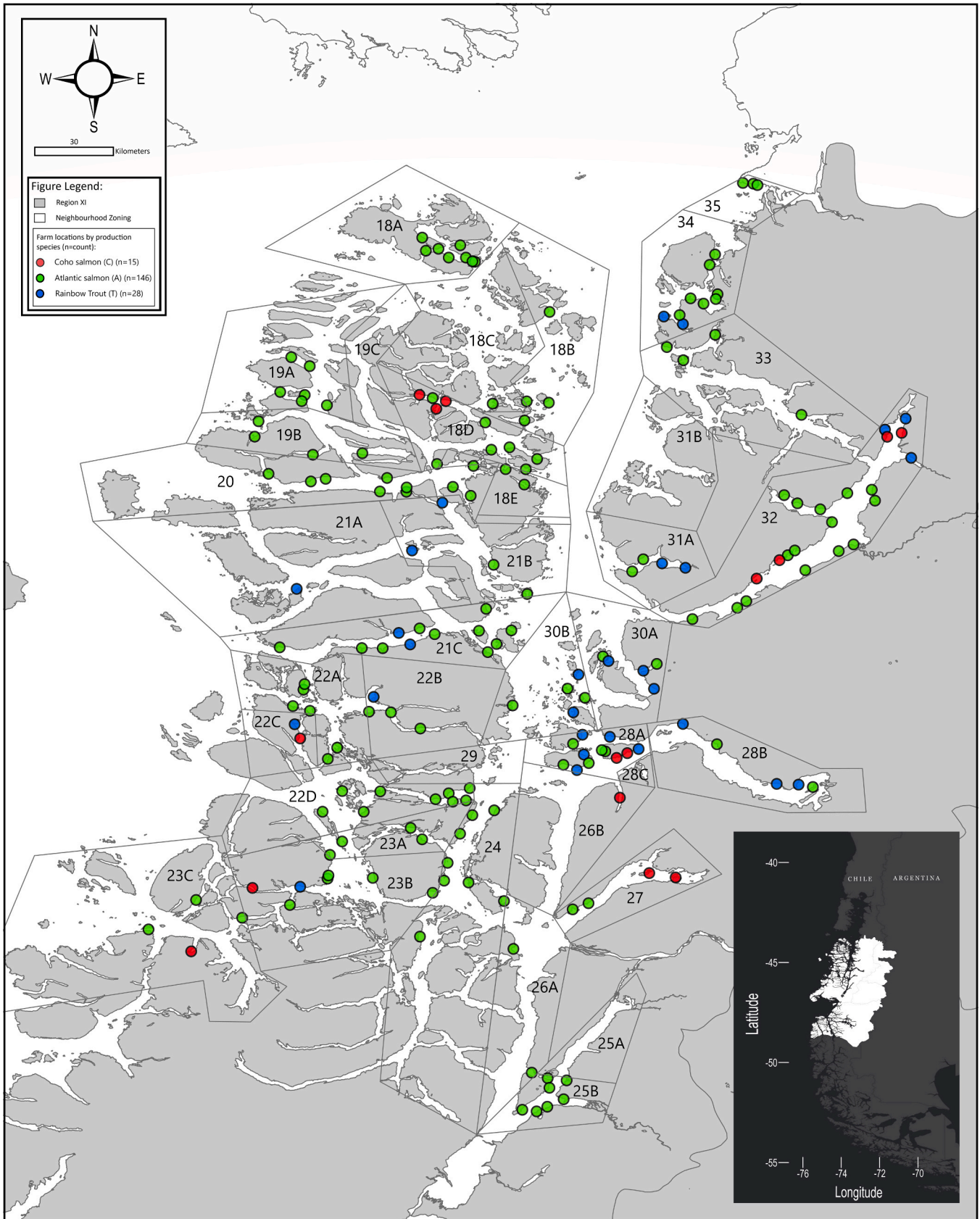
Compared with their respective ISAC baseline models (i.e., the ISAC model without any control strategies but the same starting history file), all the proposed vaccination and depopulation strategies resulted in a reduction in the annual incidence rate of SRS (Fig. 5).

Scenarios which involved depopulation of infected farms showed a general reduction in the annual incidence rate across all six simulation years (Fig. 5). The later the depopulation was implemented from the start of an SRS case, the less effective it was (D1 – D3; Fig. 6). When depopulation was delayed and implemented at the late stage of production (i.e., when fish were at least 75 % of their harvest weight), it appeared to be ineffective in reducing the incidence rate of SRS, consistently across all years (D4; Fig. 5 & 6). Across all six years, scenario D1 had the lowest simulated median incidence rate of 0.95 per 100 farm-weeks (2.5th – 97.5th percentile: 0.52 – 1.59) compared to the baseline ISAC simulated median incidence rate of 2.38 per 100 farm-weeks (2.5th – 97.5th percentile: 1.87 – 2.67). Overall, compared with the baseline model, D1 demonstrated the highest effectiveness in reducing the annual incidence rate of SRS among the four simulated stamping-out scenarios (D1 – D4; Fig. 6).

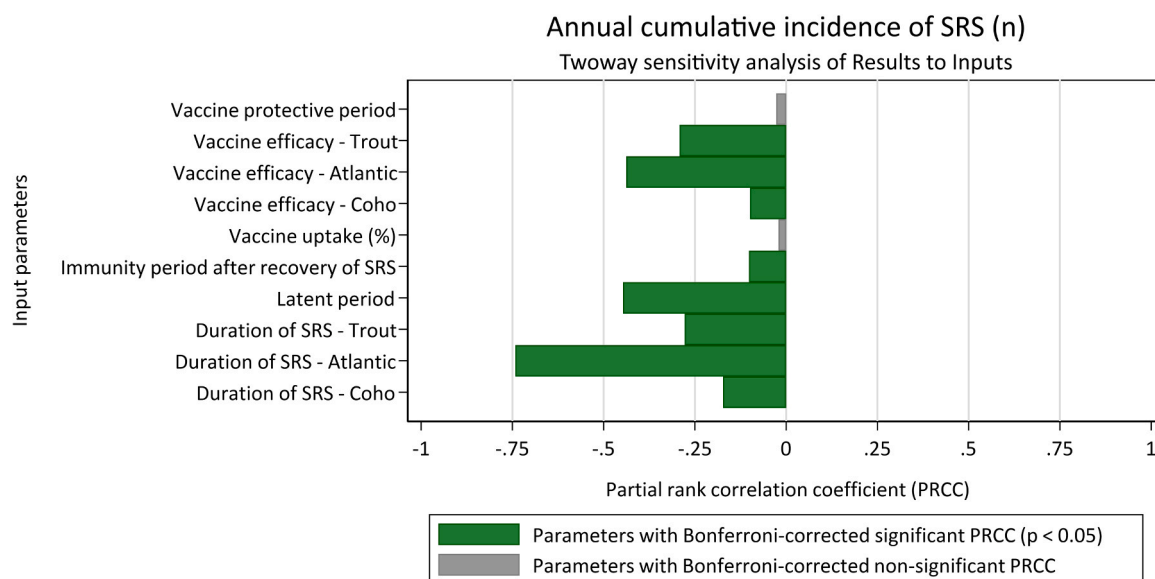
The reduction of greater than 30 % of the neighbourhood farm density appeared to be effective in reducing the annual incidence rate of SRS when compared to the matched baseline models (Fig. 5). Regardless of whether farms were removed randomly or if only the highly-connected farms were removed, the effectiveness of the strategy increased as the percentage of farms removed increased (Fig. 6). When comparing RR1 – 4 with SR1 – 4, where the percentage of farms removed was the same, selectively removing highly-connected farms appeared to be slightly more effective (with an average of 5.49 % higher effectiveness) than randomly removing farms (Fig. 6).

All scenarios implementing vaccination strategies appeared to be effective in reducing the annual incidence rate of SRS across all six simulation years (V1 – V5; Fig. 5). As the duration of vaccine-induced protective immunity increased from 3 months to 9 months, the models simulated a proportional reduction in the annual incidence rate of SRS in the region (V1 – V3; Fig. 6). The duration of protective immunity beyond 9 months did not appear to greatly improve the strategies' effectiveness further (V3 & V4; Fig. 6). It was also noted that a minimum of 75 % vaccine uptake offered similar effectiveness as an uptake rate of 95 % (V3 & V5; Fig. 6). Across all six years, scenario V4 had the lowest simulated median incidence rate of 0.92 per 100 farm-weeks (2.5th – 97.5th percentile: 0.55 – 1.16) compared to the baseline ISAC simulated median incidence rate of 2.38 per 100 farm-weeks (2.5th – 97.5th percentile: 1.87 – 2.67).

The estimated total number of fish harvested in the baseline model (i.e., without control strategies) was 259.6 million (Table 5). For scenarios D1 – 3 where infected farms were depopulated, the median estimated number of fish harvested was between 110.7 – 117.7 million. For scenario D4 (depopulated SRS-infected farm when fish were approximately 75 % of the target harvest weight), the estimated median number of harvested fish was 256.8 million (Table 5). For the scenarios involving vaccinations (V1 – 5), all estimated total fish harvested were slightly higher than the baseline model with a median of 261.8 – 265.1 million (Table 5). For the estimated total number of antibiotic treatments used in different scenarios, the baseline model had the highest total at 864 treatments. The lowest number of antibiotic treatments occurred in the scenario where 95 % of the farms were vaccinated with a vaccine that had 95 % efficacy and a one-year protective period. All vaccination strategies led to a reduction in antibiotic usage relative to the baseline model (Table 5).



**Fig. 2.** Spatial distribution of farms ( $n = 432$ ) between 1st January 2011 and 25th October 2020 in the Aysén region of Chile. A snap-shot of the first week of February 2013 was used as an example for illustration. Farms that were active on the first week of February 2013 are identified by colour by the production salmonid species (Red: Coho salmon (C); Green: Atlantic salmon (A); Blue: Rainbow Trout (T)) and inactive farms are identified as clear circles. Grey zoning illustrates the defined aquaculture farming neighbourhoods.



**Fig. 3.** Sensitivity plots using the two-sided partial rank correlation coefficient (PRCC) to assess the relationships between the values of all model input parameters and the simulated annual cumulative incidence of SRS. Bars with significant PRCCs were colour-coded as dark Green and non-significant PRCCs were colour-coded as grey.

**Table 3**  
The median (2.5th - 97.5th percentile) model accuracy (%) for the ISAC model in the Aysén region of Chile from September 2013 to September 2019.

Simulation year	ISAC	
2013–14	91.7	(86.7–99.6)
2014–15	94.9	(90.3–99.6)
2015–16	96.0	(90.2–99.6)
2016–17	94.7	(88.4–99.8)
2017–18	94.0	(85.1–99.0)
2018–19	93.7	(88.7–99.9)

**4. Discussion**

This study presented a disease spread simulation model that demonstrated the capability to simulate the between-farm transmission of SRS in the Aysén region of Chile over a one-year period. Building upon our previous SRS model for the neighbouring Los Lagos region (Wada et al., 2021), the newly developed ISAC model incorporated several new parameters. This not only showcased the flexibility of ISP to model disease in an aquaculture setting, but also demonstrated its ability to model disease in a topographically more complex region with numerous islands and fjords. With an average annual accuracy of 95 % in simulating the weekly prevalence of SRS on farms in the region, our ISAC model offered a valuable tool for evaluating and optimising SRS control strategies in the salmonid aquaculture industry in Chile. In this study, we explored various “what-if” scenarios and measured the effectiveness of three different types of strategies: depopulating infected farms, reducing neighbourhood farm density, and implementing effective vaccinations against SRS in the region.

The sensitivity analysis of our model identified that all parameters tested, except for “vaccine uptake” and “vaccine protective period”, exerted significant influence on the model. This was due to the limited range we set for the parameter, which reflected the prevalent use of vaccination before salt-water production, and the reported limited protective period in field conditions (Happold et al., 2020; Maisey et al., 2017; Rozas-Serri, 2022; Rozas-Serri et al., 2023). The relatively low vaccine efficacy (BetaPert distribution: minimum = 10 %, maximum = 80 %, most likely = 40 %) in the baseline model further inhibited the impact of the vaccine protective period. When we expanded the range of the distribution, the parameters significantly influenced the model

outcome (data not shown). The lack of significant PRCC values for the “vaccine protective period” indicated a knowledge gap in our understanding of the immunity incurred by the vaccines used in the field, and should be addressed in future research. Overall, the simulated results from ISAC closely aligned with the observed data throughout the study period, demonstrating the temporal trends and the seasonal higher prevalence of SRS during the warmer months at the regional level of Aysén, Chile.

The overall model accuracy at the regional level was relatively high over a one-year period (between 91.7 % and 96.0 %). If simulation was continued beyond one year, however, we could not maintain model accuracy above 90 %. Therefore, we suggest that when utilising this tool to evaluate control strategies, the analysis should be limited to a one-year period. The decline in accuracy over time appeared to be attributed to our model’s occasional inability to precisely classify the disease status of specific farms in neighbourhoods during the exact week when it reported SRS. There was a large variation in the model’s accuracy across the 37 marine farming neighbourhoods, with up to 4 neighbourhoods having less than 50 % accuracy each year (Table 4). Notably, neighbourhoods 28 C, 31 A, and 31B had lower average accuracy across the six years compared to other neighbourhoods, which may be due to fewer active farms in these neighbourhoods (average 1 – 3) compared to the rest of the region (average 2 – 15). These errors in disease classification at the farm level would have accumulated and amplified over time, thus explaining the decline of the model’s accuracy beyond the first simulation year. As such, future research could also explore whether updating model parameters annually using year-specific data improves the model’s accuracy.

The varying accuracy within neighbourhoods over time may indicate changes in the number of fish on farm by year, which was not captured by our model. Additionally, variations in the simulated outbreak’s spatial-temporal dynamics at the neighbourhood level could contribute to the varying accuracy of the model, as geographical landscape features and water currents can influence the spread of infection within and between neighbourhoods depending on the direction of entry. One of the limitations of ISP was the lack of seaway distance method to describe the distance between farms. In aquaculture systems, where infectious pathogens spread via water, using seaway distance based on the shortest possible waterborne connection is preferable to Euclidian distance, as it better reflects the actual distance between study units (Aldrin et al.,

**Table 4**

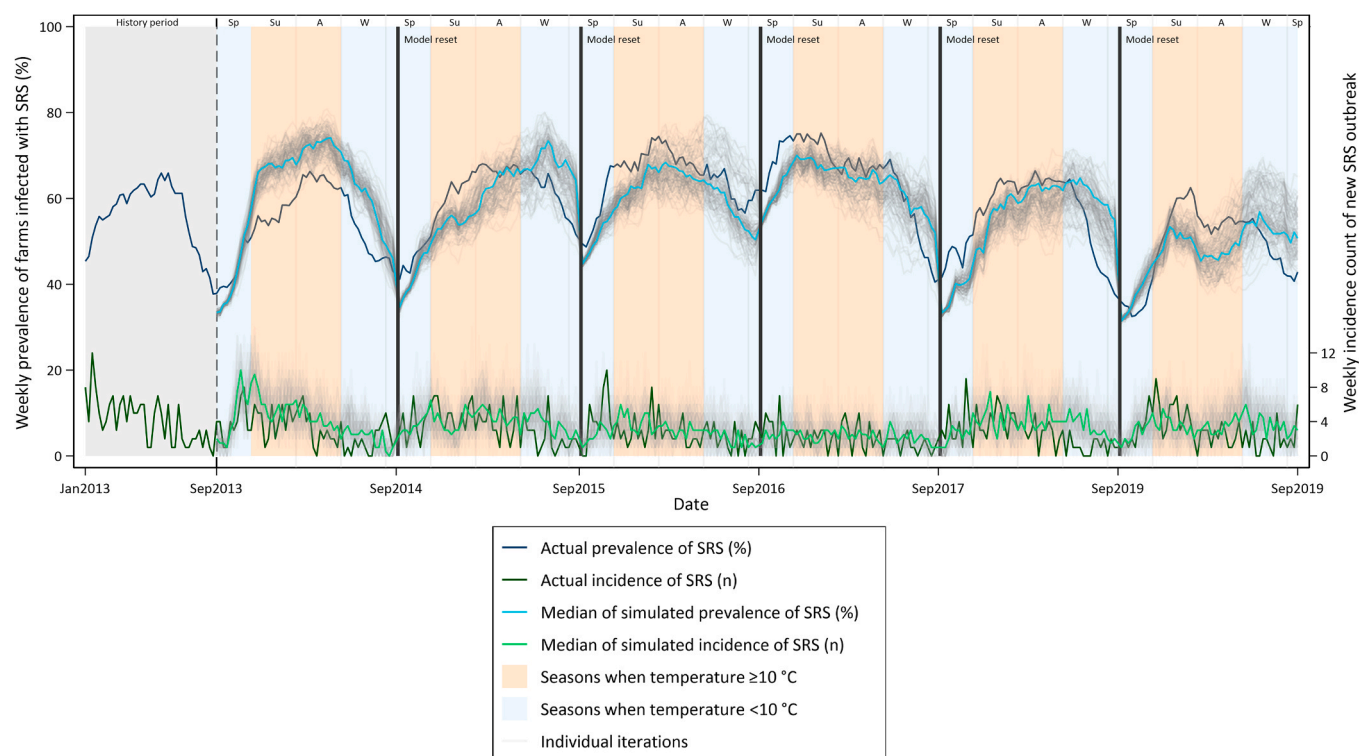
Summary of the annual model accuracy (%) of the ISAC models on the prevalence of simulated SRS at the neighbourhood level. Neighbourhoods that had no record of any production cycle on a particular year were indicated as "NA".

Neighbourhood	2013–14	2014–15	2015–16	2016–17	2017–18	2018–19
18A	92.6	84.3	69.2	87.9	100.0	33.8
18B	72.9	78.0	83.1	75.1	91.7	70.6
18C	75.9	58.0	84.4	72.7	82.2	85.3
18D	52.2	70.8	76.4	90.1	67.8	88.9
18E	100.0	36.8	100.0	NA	46.2	61.5
19A	86.5	85.8	90.8	90.8	92.5	74.5
19B	72.4	52.7	79.9	87.8	80.0	97.2
20	58.2	92.1	87.9	95.8	74.1	87.1
21A	72.8	82.0	82.7	98.6	60.1	89.2
21B	83.2	88.9	89.1	84.5	86.7	79.3
21C	81.7	78.3	92.6	87.6	90.8	84.9
21D	94.6	87.8	84.9	89.7	88.5	84.4
22A	86.3	86.1	92.0	77.3	86.0	93.6
22B	48.7	83.7	74.2	62.7	85.1	86.9
22C	64.5	78.9	98.3	NA	64.1	61.0
22D	90.0	76.6	92.2	90.2	89.7	92.1
23A	72.7	84.4	74.6	100.0	59.0	87.3
23B	84.1	83.1	100.0	100.0	64.1	58.8
23C	86.9	89.7	80.6	96.6	55.1	89.0
24	73.7	90.9	84.8	83.6	65.8	73.9
25A	78.8	93.5	77.6	81.6	90.9	50.3
25B	98.8	66.6	82.3	78.8	77.1	90.0
26A	26.4	100.0	65.2	40.4	79.1	96.3
26B	72.7	78.5	88.6	59.8	65.1	85.1
27	100.0	43.8	64.6	70.7	93.5	68.4
28A	87.7	80.4	57.6	82.8	68.0	67.9
28B	86.9	88.4	84.4	91.8	78.9	76.3
28C	NA	61.8	79.3	52.6	65.9	59.5
29	NA	41.6	63.7	99.8	70.9	77.0
30A	84.1	91.1	72.5	68.6	72.6	86.6
30B	61.2	87.5	88.2	74.7	79.6	100.0
31A	100.0	25.7	87.0	25.3	100.0	31.8
31B	39.5	74.3	56.0	86.7	55.1	63.6
32	89.3	86.2	94.9	63.7	81.7	87.4
33	88.0	86.9	45.5	89.9	79.5	90.8
34	62.5	87.4	93.0	84.1	79.5	72.2
35	100.0	100.0	94.0	NA	NA	NA
Median over all 37 neighbourhoods	83.2	83.7	84.4	84.3	79.3	84.7

2015; Amirpour Haredasht et al., 2019). The ISP model, which connects farms solely based on Euclidean distances, did not accurately capture the complex geography of the Aysén region, characterized by numerous islands and fjords. As a result, the model treated a number of farms (26.9%) as connected when they were actually separated by land masses (Lam, 2023). Comparing the discrepancy between using Euclidian and seaway distance, we underestimated the between-farm seaway distances by a median of 1.02 km (IQR: 0.36 – 3.04 km). The misclassification of the distance between farms may potentially be more problematic for the Aysén region than for Los Lagos, as the latter has large bays and fewer fjords (Strub et al., 2019; Wada et al., 2021). Incorporating seaway distance into ISP would necessitate software modifications, and could be considered in the future to enhance its suitability and specificity for the aquaculture industry. In addition, ISP currently provides a method to incorporate the directional probability of transmission via airborne spread, which could potentially be adjusted to account for hydrodynamic water current information – an aspect not considered in this study due to lack of data. Future studies could explore whether incorporating water current information may improve the model's accuracy, as Bravo and colleagues (2020) found that the prevalence of SRS was positively associated with the frequency and severity of piscirickettsiosis infection in infected farms in upstream water.

The current model could be improved by incorporating various types of data that were either unavailable for this study or represent a current knowledge gap. For example, field data regarding the latent and incubation period of infected salmonids across different species and environmental conditions were not available for this study. Future research on infected salmonids under different field conditions would allow for a

more accurate description of the disease dynamics within farms in the model. Additionally, the study may have been subject to bias due to missing information on salmonid species and the potential under-reporting of disease on farms. There were 84 out of 889 production cycles in which we had to assign the species and size of the farm to our history file for our simulations, as we did not have complete information on these sites. Another limitation of ISAC was our inability to change the susceptibility of fish to SRS with differing husbandry practices that could influence the onset and magnitude of SRS. While movements of fish between farms in Chile are restricted for disease control (Subsecretaría de Pesca., 2002; Subsecretaría de Pesca., 2010), movements of fish from farms to processing plants still occur (Subsecretaría de Pesca., 2002; Subsecretaría de Pesca., 2010). InterSpread Plus currently has a built-in feature to incorporate movement information between units, which is data we currently lack. Future studies could explore whether incorporating detailed movement data, as demonstrated in terrestrial animal settings (Bernini et al., 2019), could enhance model fit in aquatic simulations and provide insights into the occurrence of SRS in areas that did not appear to be connected to existing cases within a 15-km radius. Antimicrobial treatments is another management strategy that could potentially reduce the transmission of SRS between farms as it would reduce the duration and magnitude of outbreaks (Rees et al., 2014). Incorporating this information into the ISP framework would be possible; however, the data were not available. Despite not including treatment information in our model, we were able to simulate the incidence and prevalence of SRS at a regional level relatively well. This is likely because, for this study period, treatments were suggested to have suboptimal efficacy in reducing mortality (Flores-Kossack et al.,



**Fig. 4.** Simulated median weekly prevalence and incidence of SRS from the ISAC model against the observed weekly prevalence and incidence data for the Aysén region of Chile between September 2013 and September 2019. The grey area (on the left-hand side of the figure) indicates the history period. The seasons are indicated at the top of the figure (Sp - Spring, Su - Summer, A - Autumn and W - Winter). The dark blue line indicates the actual regional prevalence of SRS. The light blue line indicates the median simulated regional prevalence of SRS over all iterations. The dark Green line indicates the actual incidence of SRS. The light Green line indicates the median simulated incidence of SRS over all iterations. The grey lines indicate individual trajectories for both the simulated prevalence and incidence of SRS in all 100 iterations.

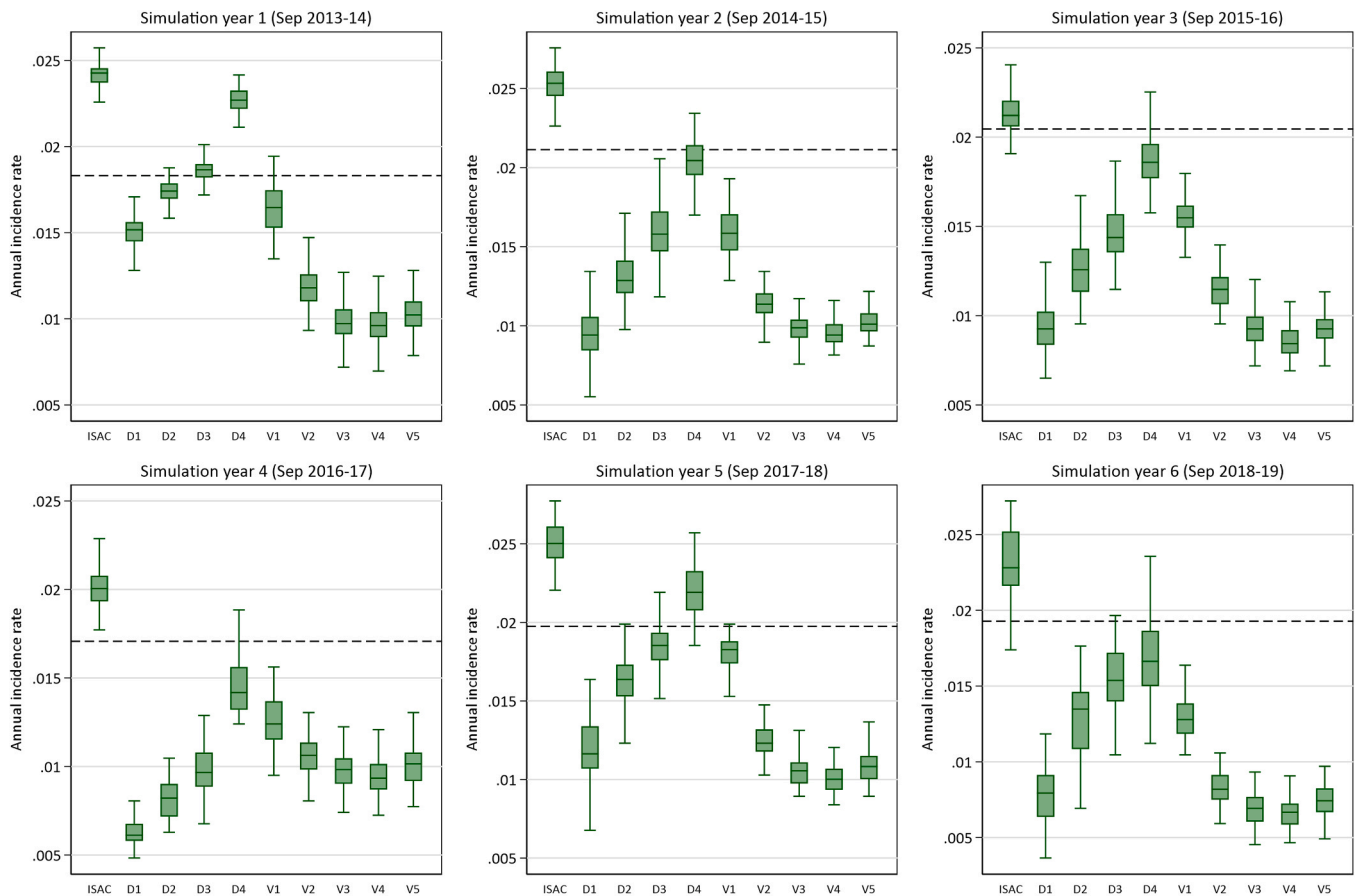
2020; Happold et al., 2020; Price et al., 2017). The information mentioned above would influence the probability of SRS transmission between farms, and including it in future studies would provide a more comprehensive understanding of the spread of SRS in the region. Lastly, as this model has been internally validated, future studies that incorporate external validation using new data would further enhance its validity.

Despite these limitations, the accuracy of ISAC was considered adequate for examining hypothetical area-level management strategies for the Aysén region of Chile over a one-year period. First, we explored the effectiveness of depopulation, a control strategy that is currently not mandatory, but recommended under certain situations in Chile (PSEVC-Piscirickettsiosis, Res. (E) N°3174/2013; Sernapesca, 2013). In general, the success and cost-effectiveness of depopulation depend on prompt implementation to limit the spread of pathogens (Aldrin et al., 2021; Geering et al., 2001; Marschik et al., 2021; Sanson et al., 2022). However, this strategy may present challenges for the salmonid industry due to the long incubation period of SRS, the long distance for waterborne transmission of *P. salmonis* (Long et al., 2021), the potential for wild fish reservoirs (Birkbeck et al., 2004; Contreras-Lynch et al., 2015), and the prolonged time required to harvest a large salmonid farm (6–8 weeks; Rolando Ibarra, personal communication, May 4th, 2023). The cost-effectiveness of depopulation for the industry remains unclear, particularly if the fish cannot be harvested for resale value (i.e., scenarios D1–3). To address this cost concern, scenario D4 was proposed, where fish removal occurred only when fish reached near market size, thereby reducing farmers' expenses. However, this strategy did not appear to be as effective as D1–3 in preventing cases of SRS. Our simulations indicated that early depopulation was the only approach that substantially impacted SRS at the industry-level. Nevertheless, the cost-effectiveness of this approach is questionable, given the average

cumulative losses associated with SRS ranged between 0.07% and 2.87%, depending on the species (Lam, 2023), and the economic losses incurred from depopulation are likely greater. Although the estimated total fish harvested under scenario D4 would be comparable to the baseline model (where no intervention was implemented) (Table 5), it should be noted that approximately 37% of the farms would be harvesting fish at only 75% of the target market weight, thus likely resulting in lower overall returns. Given these considerations, the industry should conduct a more comprehensive analysis of the economics surrounding depopulation as a control strategy.

We also investigated the effect of the neighbourhood farm density on the occurrence of SRS in Aysén, as the distance between farms has been suggested as a risk factor for SRS (Rees et al., 2014). Strategically removing farms that were highly connected appeared to be slightly more effective at reducing SRS occurrence than randomly removing farms. When at least 40% of farms were randomly removed or at least 30% of the highly interconnected farms were removed, there was an approximately 20% decrease in the regional annual incidence rate (Fig. 6). However, implementing such a strategy may not be economically feasible for the industry, as it would result in a considerable reduction in industry production. An alternative approach that could potentially be more cost-effective is reducing the number of fish on each farm. Unfortunately, due to the inability of ISP to model the change of population size within farms, we could not estimate the influence of farm size on SRS transmission.

Lastly, we evaluated the impact of vaccination strategies on the occurrence of SRS. First, in our baseline model we reduced the minimum immunity period for fish at the beginning of their production cycle, which resulted in a more rapid spread of SRS compared to the historical data (data not shown). This suggested that current vaccines offered some initial protection against SRS. This observation aligns with existing

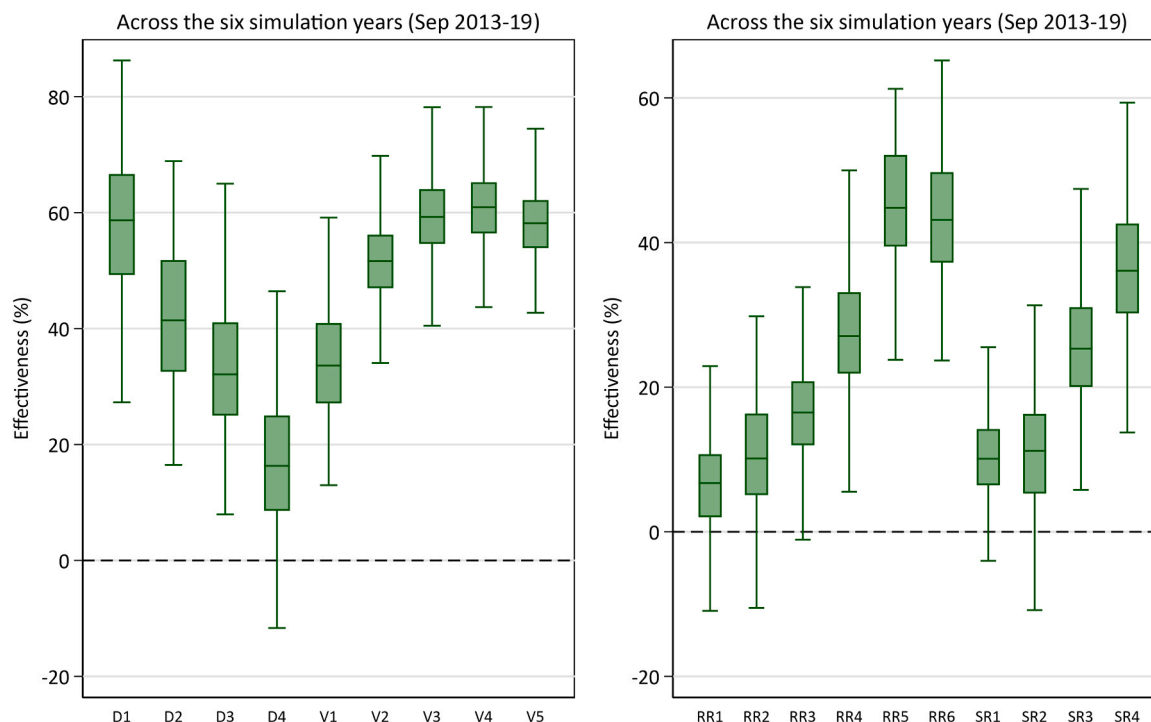


**Fig. 5.** Boxplots of the annual incidence rate of SRS per farm-weeks from the simulations of the scenarios (Depopulation strategies: D1 – 4 & Vaccination scenarios: V1 – 5) (Table 2) and the baseline ISAC model shown individually for each of the six simulation years. The dotted line represents the historical median annual incidence rate estimated in each of the six simulation years (September 2013 – September 2019).

literature on the time-to-first outbreak in vaccinated fish, which suggests that the effectiveness of current vaccines is indeed suboptimal (Happold et al., 2020; Maisey et al., 2017; Rozas-Serri, 2022; Rozas-Serri et al., 2023). When we evaluated different vaccination scenarios (V1 – 5) with hypothetically higher efficacy and longer protective periods, it reduced the annual incidence rate of SRS. This, in turn, would decrease the mortality associated with this disease, increase the number of fish harvested, and decrease the reliance on the use of antibiotics (Table 5), potentially mitigating the associated cost for the Chilean salmonid aquaculture industry. Our results suggested that, for the industry to achieve a significant reduction in the incidence rate of SRS, at least 75 % of the farms need to be vaccinated with a product that provides 95 % efficiency over a 9-month period (Fig. 6). Developing a commercial vaccine for salmon aquaculture that offers 95 % protective efficacy may be difficult (Bastardo et al., 2012; Maisey et al., 2017). Interestingly, the estimated number of fish harvested in the region when effective vaccines were used in our simulation was surprisingly similar to the baseline model (i.e., only slightly higher). We attributed this to the fact that the percentage of fish dying from SRS was quite low (median: 1.15 % (IQR: 0.34 – 2.83 %)). As such, scenarios which prevent the disease would only reduce mortality by this small amount and thus may not be perceived as cost-effective. However, an aspect of preventing SRS outbreaks on farms that should also be considered when deciding on control strategies is the use of antibiotics. We estimated that for each prevented SRS outbreak, farmers would avoid using, on average, four drug treatments based on Hillman et al. (2020). This could represent a significant reduction in production costs, as well as a decreased risk of developing antimicrobial resistance in this aquatic ecosystem. Piscirickettsiosis has

been the primary reason for antibiotic use in salt-water salmonid farming since 2005 (Lam, 2023), costing the industry at least US\$700 million every year (Avendaño-Herrera, 2018; Ibieta Hillerns et al., 2011; Mardones et al., 2018; Rozas and Enríquez, 2014; Sernapesca, 2012 - 2022). A rigorous analysis of economic, environmental, and social impacts is necessary to determine the sustainability of these approaches in Chile.

Overall, our model offers a valuable tool for comparing various industry-scale control strategies, which would otherwise be challenging to evaluate at the industry level. Since these strategies were hypothetical, it was not possible to validate the simulated effectiveness of the control strategies with real data. Additionally, we did not perform statistical tests to compare the effectiveness of these scenarios due to the influence of the number of iterations on statistical power (i.e., replications) in simulation models (White et al., 2014). While the what-if scenarios explored in this study were relatively straightforward and would require further refinement based on different economic considerations, the overall objective of evaluating these hypothetical scenarios was to present the salmonid industry and policymakers with alternative strategies for managing SRS and to reduce the substantial annual use of antimicrobials. Despite the industry's clear commitment and recent successes in reducing antimicrobial usage, the endemicity of this disease and the absence of effective vaccines in the field means that there will be a continued reliance on antimicrobials for disease control until this issue is addressed. Our investigation into a hypothetical highly effective vaccine in the field serves as further impetus for ongoing research. However, until more effective vaccines are developed, we might need to consider alternative strategies, such as mandated culling or limiting the



**Fig. 6.** The effectiveness (%) in all 19 simulated scenarios (Depopulation strategies: D1–4, Random removal: RR1–6, Strategical removal: SR1–4, and Vaccination scenarios: V1–5) (Table 2) across the six simulation years. Effectiveness was estimated based on the percentage reduction in the simulated annual incidence rate for each scenario, comparing it to the observed annual incidence rate in the respective baseline model.

**Table 5**

Summary of the total number of simulated SRS, the simulated incidence rate of SRS per 100 farm-week, the estimated total harvest salmonid count (per million), and the estimated total number of treatments used for the baseline model and the simulated scenarios of depopulation strategies (D1 – 4) and vaccination (V1 – 5) in 2013 – 14.

Model	Total number of simulated SRS (2013–14)	Simulated incidence rate of SRS per 100 farm-week (2013–14)	Estimated total harvest of salmonid (million) (2013–14)	Estimated total number of treatment used (2013–14)
Baseline	216	2.43	259.6	864
D1	135	1.52	110.7	540
D2	155	1.74	111.6	620
D3	166	1.87	117.7	664
D4	202	2.27	256.8	808
V1	147	1.65	261.8	586
V2	105	1.18	264.1	420
V3	87	0.97	265.0	346
V4	86	0.96	265.1	342
V5	91	1.02	265.0	364

number of salmonids within a farming neighbourhood. Future studies could also leverage the existing capabilities of ISP to explore alternative strategies, such as investigating the varying efficacy of antimicrobials in the model or implementing cage-level interventions. Overall, this study demonstrated the potential use of ISP as a decision support tool for stakeholders in the field of aquaculture, while the presented results may serve as a starting point for policymakers to prioritise strategies or resources to control SRS in the Aysén region of Chile.

**5. Conclusion**

In conclusion, the model ISAC presented in this study demonstrated the ability to simulate the prevalence of SRS in the region relatively well over a short period of time (up to one year), with an estimated regional

model accuracy between 91.7 – 96.0 % for the weekly simulated prevalence of SRS. The sensitivity analysis highlighted the importance of several key parameters on the spread of SRS, such as the onset of infectiousness and outbreak duration in Atlantic salmon farms. Three groups of “what-if” scenarios were proposed and explored, and the three most effective scenarios for reducing the incidence rate of SRS in the Aysén region of Chile were: (i) immediate depopulation of infected farms, (ii) strategically reducing farm density by 30 % in each neighbourhood, and (iii) implementing a vaccination strategy with at least 95 % efficacy for nine months in at least 75 % of the farms. The next step is to develop an economic model for these scenarios to determine their cost-effectiveness at the industry level, considering the many direct and indirect costs associated with harvesting, treatment, husbandry, and management. Overall, this study demonstrates the potential use of ISP as a decision-support tool for epidemiologists and policymakers in the field of aquaculture. While we acknowledge the model’s limitations, we urge industry stakeholders to further refine and implement the model in practice. The ISP tool and our ISAC model have the potential to help the industry develop a more effective and sustainable approach to managing SRS and ensure the long-term health and sustainability of the industry.

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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.

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### Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.prevetmed.2025.106595](https://doi.org/10.1016/j.prevetmed.2025.106595).

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