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POLICY & PROGRAM ANALYSIS

# Disease in Central Valley Salmon: Status and Lessons from Other Systems

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## ABSTRACT

Chinook Salmon (*Oncorhynchus tshawytscha*) are increasingly vulnerable to anthropogenic activities and climate change, especially at their most southern range in California's Central Valley. There is considerable interest in understanding stressors that contribute to population decline and in identifying management actions that reduce the effects of those stressors. Along the west coast of North America, disease has been linked to declining numbers of salmonids, and identified as a key stressor that results in mortality. In the Central Valley, targeted studies have revealed extremely high prevalence of infectious agents and disease. However, there has been insufficient monitoring to understand the effect that disease may have on salmon populations. To inform future research, monitoring, and management efforts, a two-day workshop on salmon disease was

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held at the University of California, Davis (UC Davis) on March 14–15, 2018. This paper summarizes the science presented at this workshop, including the current state of knowledge of salmonid disease in the Central Valley, and current and emerging tools to better understand its effects on salmon. We highlight case studies from other systems where successful monitoring programs have been implemented. First, in the Klamath River where the integration of several data-collection and modeling approaches led to the development of successful management actions, and second in British Columbia where investment in researching novel technologies led to breakthroughs in the understanding of salmon disease dynamics. Finally, we identify key information and knowledge gaps necessary to guide research and management of disease in Central Valley salmon populations.

## KEY WORDS

pathogen, infectious disease, *Ceratonova shasta* (previously *Ceratomyxa shasta*), Pacific salmon

## INTRODUCTION

Salmon populations along the west coast of North America have been in decline since the early 1900s. Pacific Salmon are culturally iconic and economically important, and there is considerable interest in understanding factors that contribute to their decline as well as in identifying management tools to facilitate population recovery. Salmon have adapted to persist through extreme environmental conditions, predation pressures, variable resource availability, and disease. However, humans have altered freshwater systems, reducing the amount of spawning, rearing, and migratory habitat required for abundant and persistent populations of anadromous fishes.

Infectious agents likely play a role in salmonid population dynamics. Yet, quantifying this role remains challenging because of difficulties observing and sampling diseased fish in the wild (Hedrick 1998). Diseased fish functionally disappear from existing monitoring programs because they suffer disease-associated mortality such as being eaten by predators (Miller et al. 2014). Therefore, by only sampling survivors, researchers are often left with incomplete and inadequate information, making it difficult to implement sound, scientifically accurate management decisions. Despite the challenges, substantial progress has been made toward understanding the effects of infectious agents on Pacific Salmon at both the individual and population levels. For example, novel research techniques (Hallett and Bartholomew 2006; Miller et al. 2014) and the implementation of comprehensive multi-agency monitoring networks (e.g., for *Ceratonova shasta* in the Klamath River) have led to integration of pathogen monitoring into adaptive management strategies. Along the west coast of the United States and Canada, pathogens and associated disease are increasingly identified as a stressor that contributes to mortality, and are hypothesized to be one potential factor in declining salmonid populations (St-Hilaire et al. 2002; Belchik et al. 2004; Fujiwara et al. 2011; Jeffries et al. 2014a; Bass et al. 2019; Teffer et al. forthcoming [2020]).

Improving the condition and survival of both rearing and migrating Chinook Salmon is necessary for their recovery in California's Central Valley (NMFS 2014). To implement effective management actions to increase survival, we need to understand the individual and interactive effects of factors such as temperature, flow, food availability, habitat quality, predator-prey interactions, and disease. Several salmon monitoring programs in the Central Valley already exist to monitor these factors. There have also been recent efforts to improve the efficacy of these programs and their ability to inform relevant management questions (Johnson et al. 2017). To date, however, pathogen and disease monitoring in the Central Valley as important components of fish condition have

been omitted from status and trend monitoring frameworks, resulting in a lack of information for practitioners to incorporate disease into robust management plans (Johnson et al. 2017).

On March 14-15, 2018, UC Davis hosted a Salmon Disease Symposium aimed at understanding the present state of knowledge of Central Valley salmon disease ecology, defining past and current monitoring efforts, and identifying key knowledge gaps. The goal of this review is to summarize the information presented by the attendees of this workshop. Additionally, we draw on research and case studies from other systems to present potential future research opportunities that could provide fisheries and water managers with better information for managing salmon populations. Last, we provide recommendations for designing a monitoring framework for salmon disease in the Central Valley.[1]

## INFECTIOUS AGENTS AND DISEASE OVERVIEW

Infectious agents that cause disease in salmon include viral, bacterial, fungal, protozoan, and myxozoan microparasites (Table 1) as well as macroparasites such as sea lice. They are innately part of the ecosystems in which salmon live and have co-evolved with their salmon hosts. However, rapid environmental changes can upset the balance of host-pathogen interaction. While some pathogens are highly virulent, many more opportunistic pathogens only cause disease when the host becomes compromised for other reasons, such as unfavorable environmental factors. Even under favorable conditions, salmon are constantly exposed to a variety of pathogens. Whether or not infection develops into a disease state in a fish depends on pathogen exposure levels (external agent), the susceptibility of the individual (host), and the environment in which host and agent are brought together. Collectively, this is known as the epidemiological triad (Box 1).

It is important to distinguish the differences among the presence of infectious agents in the environment, whether or not those agents have infected the host, and whether that infection has led to disease. Dozens of infectious agents known to infect Pacific salmonids persist in the environment at all times. For example, many microparasites such as the myxozoans *Ceratonova shasta* and *Parvicapsula minibicornis* are present in freshwater environments year-round, but the density and virulence of spores fluctuates through time and space (Bartholomew et al. 2007; Hallett et al. 2012). Host organisms have developed immune system coping mechanisms to deal with constant exposure. Often, fish host multiple pathogens and parasitic organisms at any given time without exhibiting any noticeable disease or adverse effect. For bacterial or viral infections, an infected fish only becomes diseased if the replication of the pathogen within its body becomes sufficiently aggressive that homeostasis is compromised. Alternatively, homeostasis is compromised by the effects of other environmental stressors, which facilitates the invasion and proliferation of a pathogen in the organism. Additionally, disease can be caused by the host's response to the pathogen (e.g., inflammation in response to *Tetracapsuloides bryosalmonae* causing proliferative kidney disease (PKD) (Hedrick et al. 1993).

Water quality, contaminants, food availability, and other stressors in the environment can facilitate pathogen invasion (Hedrick 1998). Disease occurrence and progression in fish is critically dependent on water temperature

1. To address the critical knowledge gaps of how infectious agents may be affecting Central Valley Chinook Salmon populations, the Delta Stewardship Council and the UC Davis Coastal and Marine Sciences Institute convened a 2-day symposium to address our current state of knowledge about infectious agents that affect salmon, and discussed developing and available tools that can be used to study infectious agents. On Day 1, case studies were presented from other watersheds for which frameworks have been developed to effectively monitor programs or model approaches to understanding pathogen-host dynamics. Participants included representatives from the US Fish and Wildlife Service, California Department of Fish and Wildlife, University of California-Davis, University of California-Santa Cruz, Canadian Department of Fisheries and Oceans, Yurok Tribe, US Bureau of Reclamation, US Geological Survey, Oregon State University, Marine Institute of Ireland, Delta Science Program, The Metropolitan Water District of Southern California and NOAA Fisheries. Day 2 was a focused discussion with these experts on how their insights may be applied to the Central Valley to develop a more comprehensive understanding of how infectious agents affect Central Valley Chinook Salmon. Recordings of the presentations are made available at *https://ats.ucdavis.edu/ats-video/?kpid=0_9d46tt27*. Contributions authored entirely by non-USGS authors do not represent the views or position of the USGS

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**Table 1** Common pathogens of Pacific salmonids and brief descriptions of their effect

| Infectious agent and disease | Life form | Description |
|---|---|---|
| *Ceratonova shasta* Enteronecrosis | Myxozoan parasite (Cnidaria) | *C. shasta* is a myxosporean parasite that infects the digestive tract of salmonids. It has a complex life cycle that includes an invertebrate freshwater host: an annelid that lives on the benthic substrate of low gradient rivers. *C. shasta* actinospores are released into the water column by annelid hosts and go on to infect salmon where they replicate in the tissue of the fish, infecting primarily the intestinal tract but becoming systemic in more severe infections. Infected juveniles or postmortem (post-spawn) adult salmon release myxospores, which are not infectious to other fish until completing their life cycle within an annelid host. Warmer water temperatures increase the rate of replication and chance of infection. Juvenile fish inhabiting water with particularly elevated densities of *C. shasta* actinospores are likely to become overloaded and die. |
| *Parvicapsula minibicornis* Glomerulonephritis | Myxozoan parasite (Cnidaria) | *P. minibicornis* is a myxosporean parasite with the same invertebrate host as *C. shasta*. It infects the kidney and the cause of death is presumed to be renal failure. |
| *Tetracapsuloides bryosalmonae* Proliferative kidney disease (PKD) | Myxozoan parasite (Cnidaria) | *T. bryosalmonae* is a malacosporean parasite with a two-host life cycle that alternates between salmonids and freshwater bryozoans (colonial single-celled animals). It causes swelling of the kidney and spleen, and ultimately death. |
| *Ichthyophthirius multifiliis* White spot disease | Protozoan ectoparasite (Ciliophora) | One of the most common parasites of freshwater fishes, also known as Ich. It is detectable as white spots (trophozoites) on the skin of fish. The ciliate damages gills and skin, causing ulcers and reducing the respiratory efficiency of the fish. Heavy infection can result in death. The infectious stage is a theront. It has a direct life cycle but typically is not transmitted fish to fish (requires some development off fish). |
| *Flavobacterium columnare* Columnaris | Bacterium | *F. columnare* is a gram-negative bacterium that can exist in water for several weeks. Infected fish develop external lesions (skin and gill) during warm water conditions which affect oxygen uptake and osmotic regulation. |
| *Renibacterium salmoninarum* Bacterial kidney disease (BKD) | Bacterium | Diseased salmon are often identifiable by abdominal fluid build-up and swelling. The bacteria cannot survive in the water column for long periods, and transmission between fish can occur both vertically and horizontally. *R. salmonarium* can stay dormant within its salmonid host until the fish undergoes stress such as temperature shock or malnourishment. |
| Infectious hematopoetic necrosis (IHN) | Virus | The IHN virus is a rhabdovirus that affects all life stages of salmonids. It is transmitted both horizontally (waterborne) and vertically (from adults to eggs). It causes abdominal distension and hemorrhaging and may cause high mortality in juvenile salmon. |

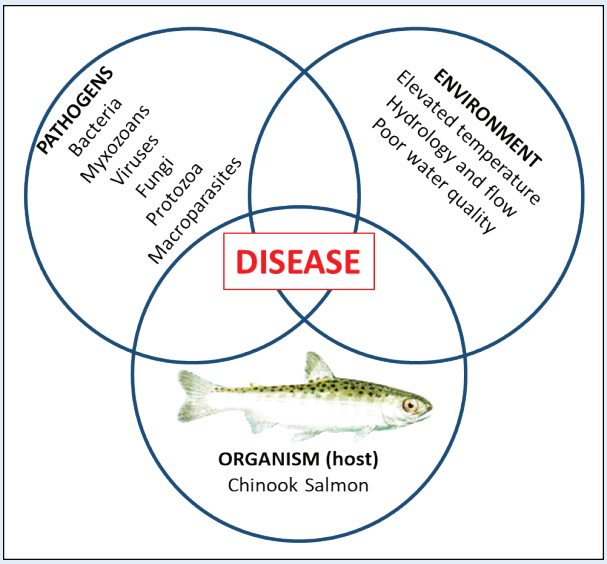
because it affects both the immune functions of the host and contributes to increased pathogen replication (Noe and Dickerson 1995; Marcogliese 2008). Poor water quality in close proximity to effluent discharge from large point sources (such as water treatment facilities) includes a multitude of chemicals that may directly affect fish health (Hasenbein et al. 2014; Sutton et al. 2016; McGovarin et al. 2018). Low dissolved oxygen, elevated temperatures, salinity intrusion during drought years, and contaminants can also have synergistic effects with water quality and infection. Not only are fish more susceptible to infection after poor water quality induces stress," but the opposite also holds true: an infected fish may be more sensitive to effects from poor water quality (Clifford et al. 2005; Eder et al. 2008), because both directly affect their immune system.

Much of what is known about Pacific salmonid diseases comes from rearing fish at high densities in hatchery settings (Naish et al. 2007). Effects of disease are more readily observed in captive populations compared to wild animal

**BOX 1**

## Epidemiological Triad

Occurrence of disease results from the interaction among host, environment, and disease-agent components (e.g., salmon, water quality, and pathogen). Critical host components might be age, sex, genetic background, and nutritional and physiological status affected during or before exposure to a pathogen. Environmental components include alterations in climate, contaminants, food availability, habitat type, etc. Each of the three components can alter the others (e.g., proximity to a contaminant discharge [effluent/runoff] may affect water quality and decrease food availability, thus changing the nutritional status of an individual, or may allow a pathogen to establish in a new area or host). In the context of a rapidly changing environment, and increases in extreme events, all three components will be subject to changes that can alter salmonid success. Understanding the role of pathogens in the Central Valley is crucial to management and conservation of salmonid species.




populations. In a hatchery setting, the sub-lethal effects of temporary disease outbreaks are less ecologically relevant than in the wild because food availability is not limited and there are no predators. Fish health staff can often respond to outbreaks by providing treatment or manipulating water quality, such that disease can be a negligible factor to their survival. Conversely, adult salmon that are tightly confined in pre-spawning areas can be highly susceptible to pathogen transfer between individuals.

The potential disease risks posed by hatchery stocks to free-ranging salmon is a topic of high concern, but there are relatively few examples demonstrating an effect (see Naish et al. 2007). In recent decades, using fish health approaches to control disease in hatcheries has been successful (Munson et al. 2010). Many freshwater salmon hatcheries rely on strict biosecurity—including a secure water supply—to prevent entry of pathogens from free-ranging fish in adjacent waters.

Because salmon are migratory and move through different environments (freshwater, estuarine, marine), they have an extremely energetically demanding life history. Their immune function can be compromised at many critical life stages, making them more susceptible to infectious agents (Miller et al. 2014). While not all pathogens can transcend these environments, some are transmitted by the host between these environments, where they can become more—or less—virulent (Miller et al. 2014). The viral load of piscine orthoreovirus (PRV) detected in juvenile Atlantic salmon (*Salmo salar*) in freshwater was observed to increase in fish transferred to seawater (Løvoll et al. 2012). It is thus possible for a fish to become infected in one environment and for a disease outbreak to occur after it transitions to another environment, creating further difficulties in determining sources of infectious mortalities.

While disease outbreaks occasionally affect cohorts of fish catastrophically, the indirect effects of decreased physiological functions may have additional consequences on salmon populations that are less evident. Individuals that expend energy to suppress infection may do so to the detriment of swimming performance, thus decreasing their ability to avoid predators, forage, and negotiate complex migratory

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**BOX 2**

## Disease Terminology

| Term | Description |
|---|---|
| Clinical | Recognizable and/or standardized signs and symptoms of disease progression. |
| Endemic | An infectious agent or disease that is established in a particular population in a given geographical area. |
| Epidemic | An often sudden increase in the level of disease in a specific population over a given period of time. |
| Exposed | When an individual has encountered an infectious agent. Necessary for infection to take place. However, not necessarily the case that infection occurs. |
| Infection | The entry, establishment, and replication of pathogens inside a host organism, but not necessarily resulting in disease. |
| Infectious | Individuals who are infected and can transmit an infectious agent to other individuals. |
| Infectious agent | Something that infiltrates another living thing. An infectious agent may or may not be a pathogen. |
| Infectious disease | A type of illness caused by a pathogenic agent, including viruses, bacteria, fungi, protozoa, parasites. |
| Latent period | Period of time between occurrence of infection and the onset of infectiousness (when the infected individual becomes infectious). |
| Morbidity | Being in a diseased, or non-normal state. |
| Outbreak | An unexpected increase in the prevalence of a particular disease over a given time-period and geographic range. A general term that may refer either to an epidemic or a pandemic. |
| Pandemic | An increase in the occurrence of a particular disease over a very large region, such as a continent or the entire globe, that is greater than what is expected over a given period of time. |
| Parasite | An organism that lives in or on an organism of another species (its host) and benefits by deriving nutrients at the host's expense. Parasites can be a category of pathogen, but not all parasitic organisms are pathogens. |
| Pathogen | A biological agent that causes disease. |
| Prevalence | The proportion of cases of diseased individuals at a specific time. |
| Virulence | The ability of an infectious agent to produce disease. |

pathways. Several studies have observed salmon challenged with pathogens to have decreased critical swimming speed (Tierney and Farrell 2004; Kocan et al. 2009) and increased risk of predation (Miller et al. 2014). To date, there is a limited understanding of how these indirect effects influence salmon population dynamics because they are difficult to measure in situ since diseased fish that have died and dropped out of the system cannot be sampled. This is further confounded by the complex and dynamic environmental conditions that salmon experience throughout their life cycle.

Salmonid diseases can present a significant challenge to the aquaculture industry, where outbreaks can substantially affect the economic viability of a single fish farm or an industry as a whole. For example, in 2007, a widespread outbreak of infectious salmon anemia (ISA) disrupted the Chilean salmon farming industry, and led to a 700,000-ton decrease in production worth about $2 billion (Asche et al. 2009). These disease-related losses went beyond the decline in production. ISA also reduced output quality, causing Chile to suffer lower prices and lose market share, at least temporarily. New

regulations to control ISA increased production costs for salmon farms. The effects of ISA led to economic losses for both the industry and the national economy. In 2009, 79% of salmon farms shut down, costing 20,000 jobs. Disease management strategies that have developed in aquaculture may inform future efforts to manage disease in wild fish populations.

## QUANTIFYING DISEASE RISK, SPREAD, AND EFFECTS ON A POPULATION LEVEL

Population-level effects from infectious agents are not easily observed, and successful evaluation requires a combination of high-quality data and robust models (Peeler and Taylor 2011). Data obtained from research and monitoring programs can be used in models to test hypotheses about pathogen transmission, disease risk, and effects on a population (e.g., how does water temperature influence disease progression). Although some infectious agents cause disease quickly (acute pathogens), other agents may not cause a disease state until weeks or months after infection. Infection or disease prevalence can also be underestimated as a result of only sampling survivors, because affected fish have been lost to direct or indirect mortality (e.g., predation). This makes monitoring cohorts of fish through large complex systems such as the Central Valley difficult.

### Data Collection

Many different sampling and survey methodologies are available to collect data on infectious agents and determine their effect on salmon. Tools exist to quantify the presence of infectious agents in the system as well as determine their effect on fish health.

River water samples can be used to map the spatial and temporal distribution of infectious agents and potential exposure landscapes of salmon to diseases in a watershed (Hallett and Bartholomew 2006; Richey et al. 2018). Advancements in environmental DNA (eDNA) technology are allowing researchers to rapidly determine the presence and abundance (e.g., cells $L^{-1}$) of multiple agents in a single sample in near-real time (Nguyen et al. 2018). As costs fall and sensitivity increases, it will become easier to pinpoint hot spots of infectious agents and associate them with environmental variables and/or identify sources. For infectious agents with indirect life cycles that involve an additional host, this non-salmonid can be assessed for prevalence of infection. This additional host infection prevalence and density can provide information on infectious hot spots (e.g., annelid host (*Manayunkia occidentalis*; [Atkinson et al. 2020]) for *Ceratonova shasta*; [Alexander et al. 2014]).

To determine whether infectious agents present in the environment result in infected or diseased individuals, it is necessary to sample fish. Non-lethal testing methods to assess infection status are reliable for some but not all fish pathogens, but assessing disease status by non-lethal methods is often more difficult. However, diseases that can be assessed by visual or non-lethal methods allow disease state to be integrated with other populations assessments (e.g., mark-recapture approaches; [Groner et al. 2018]). Typically, more invasive techniques are needed to determine disease state. Histopathology is one of the more traditional methods used to assess the progression of disease within fish (Kent et al. 2013). Researchers examine thinly cut sections of fixed and stained tissue under a microscope for the presence of pathogens, parasites, or tissue damage associated with a particular pathogen or parasite. Histopathology is highly effective in determining the disease state of a fish, but usually requires lethal sampling and that tissues be carefully preserved and transported, which may be difficult in field settings. Moreover, histopathology, traditionally applied on dead and dying cultured fish to determine cause of death, may not be highly sensitive to detection of early stages of disease development that would be more commonly observed in random samples of wild fish (Miller et al. 2014, 2017).

Molecular and genomic methods have been established to detect the presence and/or abundance of infectious agent DNA within a host fish (Miller et al. 2014, 2016; Teffer et al. 2009, 2017). For instance, quantitative polymerase

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chain reaction PCR (qPCR) is often but not always more sensitive than traditional diagnostic techniques based on culture. Additionally, these molecular diagnostic tests are especially relevant for the detection of unculturable organisms. The detection of an infectious agent within host tissue does not necessarily indicate that the individual is progressing to a diseased state, but rather highlights that the fish is infected. As described above, other techniques such as histopathology are often used in conjunction to assess whether infection is resulting in physiological harm to the fish. These molecular/genomic techniques can also be used to determine the expression of host genes, for example, those associated with immunity, as a means to quantify host response and predict the potential for disease (Connon et al. 2012; Jeffries et al. 2014a, 2014b; Teffer et al. 2018; Hurst et al. 2019). In fact, specific gene expression signatures of infection are being identified using this approach (Miller et al. 2017). Integration of pathogen and host gene profiling may represent a better non-lethal approach—particularly for systemic infections that often occur with viral diseases—and potentially requires only a small amount of gill tissue (Mordecai et al. 2019, 2020).

Deploying sentinel fish allows researchers to experimentally test the "infectiousness" of a particular area (Foott and Imrie 2017; Richey et al. 2018). Typically, juvenile salmon from hatcheries are pre-screened for pathogens and then placed in cages in situ for several days to several weeks; brought back to an aquarium facility where they are reared and monitored for a period of time, potentially under different thermal regimes; and then assessed for either infection or disease. Data on severity of infection—percent morbidity and time to morbidity—are also collected (e.g., Ray et al. 2015). When performed across multiple locations and over time, sentinel fish studies can be a powerful tool to describe the risk of infection throughout a system.

Stress challenge studies can also be carried out to determine how stress affects replication and disease development of naturally occurring pathogens (e.g., Teffer et al. 2018; Bass et al. 2019). These studies have not only revealed thermally sensitive pathogens, but have addressed the role of catch-and-release fisheries on disease development and survival.

To understand disease dynamics in a system, disease studies need to incorporate multiple types of sampling. Where few or no specific resources are available for disease monitoring, simple metrics of fish health can easily be added to already existing sampling programs. On the Columbia River, established juvenile fish-collection facilities collect information on simple metrics that include—but are not limited to—the number of fish with body injury, predation marks, and disease and parasite symptoms (FPC 2017). Recent studies have demonstrated that some of these simple metrics can provide invaluable insight into the factors associated with juvenile salmonid survival and, ultimately, adult returns. Evans et al. (2014) found that steelhead from the Snake River and upper Columbia River without external disease symptoms were 3.7 and 4.5 times more likely, respectively, to survive to adulthood than steelhead with severe external symptoms of disease. Additionally, they found that Snake River steelhead were 1.2 times more likely, and upper Columbia River steelhead were 7.7 times more likely, to survive if they had no signs of fin damage. The same fish were evaluated for expression of gene response to immune functions using qPCR. Visual fish condition estimates were found to match genetically determined bad, poor, and healthy individuals (Connon et al. 2012), confirming that these relatively simple metrics of fish condition and disease monitoring represent an approach untapped in California to evaluate factors associated with juvenile salmonid survival and adult returns.

## Models and Decision Support Tools

Both knowledge-driven (i.e., mechanistic) and data-driven approaches (or combination of both) can be used to develop models to aid in decision-making. For example, compartmental-based models, in which we assume that each individual in the population can be considered "susceptible," "infected," or "recovered" (SIR models) in specific time-periods, can be used to model disease progression based on just a few

parameters such as infection and recovery rates (Ogut et al. 2005). More advanced SIR-extended models can consider environmental factors such as the effect of water temperature, water quality, or flow. However, these models may contain many unrealistic assumptions (e.g., homogeneous population, random mixing, closed population, lifetime immunity, single transmission mode, static incubation period, etc.), leading to complex parameterization, and limiting their capacity to effectively represent reality. Therefore, to better inform decision-making, more complicated models are often required. Bayesian models to reconstruct aquatic pathogen transmission or ecological niche models to predict potential spread are now being developed for certain economically important pathogens such as infectious hematopoietic necrosis virus (IHNV) and viral hemorrhagic septicemia virus (VHSV) (Escobar et al. 2017; Ferguson et al. 2018; Paez et al. 2020). Although more complex models for free-ranging salmon populations are still relatively scarce, in the commercial salmon industry similarly complex models are increasingly being used to simulate disease transmission, and to identify risk factors and high-risk areas where management should be prioritized (Haredasht et al. 2019).

With increases in computational power and the ability to collect ever more demographic, environmental, and spatio-temporal surveillance data, the use of disease forecasting models will increasingly inform decision-making for surveillance and control. For example, platforms such as Disease BioPortal (*http://bioportal.ucdavis.edu*), allow for the rapid visualization and analysis of multiple databases. The possibility to access multiple data types (e.g., disease surveillance, fish demographics, and environmental information) in one place and to use multi-scale analytical capabilities (e.g., space-time-genomic visualization and analysis) allows diverse analyses. These include risk factor analysis, social network analysis, molecular epidemiology, cluster analysis and anomaly detection, risk assessment, and spatio-temporal risk mapping. The integration of novel machine learning algorithms, agent-based simulation models, and other Big Data analytics can be used to help prevent and control infectious diseases in animal populations. They can identify patterns and high-risk areas and inform the implementation of targeted, more cost-effective interventions. The goal of platforms like this is to improve surveillance, risk assessment, and modeling of infectious diseases by optimizing data collection, integration, standardization, and storage. Disease BioPortal also improves data accessibility and usability to improve risk communication, awareness, and involvement (e.g., citizen science, participatory epidemiology, etc.) among decision-makers and the general public.

## INFECTIOUS AGENTS AND DISEASE MONITORING IN CENTRAL VALLEY SALMON

Currently, there is no system-wide monitoring framework for aquatic infectious agents that cause disease in wild salmon in the Central Valley. However, there have been multiple short-term sampling efforts since 1997. Many of these studies identified biologically significant concentrations of infectious agents in the water and high prevalence among wild fish.

Infectious agents associated with diseased Chinook Salmon in the wild have been observed in the Feather, Merced, Sacramento, San Joaquin, and Stanislaus rivers as well as in the Sacramento-San Joaquin River Delta (Table 2). Survey approaches, sampling locations and dates, and species of interest were not consistent, and varied among years. The longest sampling effort was conducted by the US Fish and Wildlife Service's National Wild Fish Health Survey (NWFHS). The NWFHS was developed in 1997 after the discovery that the infectious agent of salmonid Whirling Disease, *Myxobolus cerebralis*, was responsible for decimating wild trout populations in the Intermountain West.

At the time, little was known about infectious agents in fisheries and the US Fish and Wildlife Service (USFWS) recognized that valued fishery stocks were at risk. Knowledge about infectious agents was needed to improve management of hatchery and wild populations, so the USFWS developed standardized methodologies to ensure

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**Table 2** Summary and findings of major salmonid disease-related monitoring efforts performed by the US Fish and Wildlife Service in the Central Valley since 2000

| Salmonid spp.[a] | Region | Significant finding[b] | Pathogens of interest[b] | Methods | Life stages | Study years | Lead agency | Funding agency[d] |
|---|---|---|---|---|---|---|---|---|
| Chinook, spring and fall-run | Feather River | High POI for *C. shasta* in most years | *C. shasta*, *P. minibicornis* | Sentinel fish | Juveniles | 2015–2018 | USFWS | USBR |
| **Relevant citation:** Foott JS, Imrie A. 2016. Prevalence and severity of *Ceratonova shasta* and *Parvicapsula minibicornis* infection of natural Feather River juvenile Chinook Salmon (January–May 2016). Anderson (CA): US Fish and Wildlife Service California–Nevada Fish Health Center. Available from: http://www.fws.gov/canvfhc/reports.asp | | | | | | | | |
| Chinook, winter-run | Upper Sacramento River | *C. shasta* infectivity deemed low during survey period | *C. shasta*, *P. minibicornis* | Sentinel fish, eDNA, wild fish sampling | Juveniles | 2015–2016 | USFWS | CVPIA |
| **Relevant citation:** Foott JS, Stone R, Voss S, Nichols K. 2017. *Ceratonova shasta* and *Parvicapsula minibicornis* (Phylum Cnidaria: Myxosporea ) infectivity for juvenile Chinook salmon (*Oncorhynchus tshawytscha*) in the upper Sacramento River: July–November 2016. Anderson (CA): US Fish and Wildlife Service California–Nevada Fish Health Center. Available from: http://www.fws.gov/canvfhc/reports.asp | | | | | | | | |
| Chinook, fall-run | Stanislaus River | No viral agents or significant parasite or systemic bacterial infections were detected in smolts | *General fish health screen* | Wild fish sampling | Juveniles | 2011 | USFWS | AFRP |
| **Relevant citation:** Foott S, Fogerty R. 2011. FY2011: Juvenile Stanislaus River Chinook salmon pathogen and physiology assessment: January–May 2011. Anderson (CA): US Fish and Wildlife Service California–Nevada Fish Health Center. Technical report. Available from: http://www.fws.gov/canvfhc/reports.asp | | | | | | | | |
| Chinook, fall-run | Stanislaus River | No significant infections detected in smolt survival to San Joaquin R; no notable disease | *T. bryosalmonae* | Wild fish sampling | Juveniles | 2010 | USFWS | AFRP |
| **Relevant citation:** Nichols K. 2010. California-Nevada Fish Health Center FY2010 health, energy reserves and smolt development of juvenile Stanislaus River Chinook Salmon, 2010. Anderson (CA): US Fish & Wildlife Service California-Nevada Fish Health Center. Technical report. Available from: http://www.fws.gov/canvfhc/reports.asp | | | | | | | | |
| Chinook, fall-run | Stanislaus, Tuolumne, Merced, and San Joaquin rivers | *T. bryosalmonae* detected in 80% of Merced, 7% of Stanislaus and 25% of mainstem San Joaquin River smolts. | *T. bryosalmonae* | Wild fish sampling | Juveniles | 2013 | USFWS | NWFHS |
| **Relevant Citation:** Nichols K. 2013. FY2013 San Joaquin, Stanislaus, Tuolumne and Merced River Chinook smolt quality assessment. Anderson (CA): US Fish and Wildlife Service California–Nevada Fish Health Center. Technical report. Available from: http://www.fws.gov/canvfhc/reports.asp | | | | | | | | |
| Chinook, fall-run | San Joaquin River | *T. bryosalmonae* observed in smolts | *T. bryosalmonae* | Wild fish sampling | Juveniles | 2000 | USFWS | CALFED |
| **Relevant Citation:** Nichols K, Foott JS, Burmester R. 2001. Health monitoring of hatchery and natural fall-run Chinook Salmon juveniles in the San Joaquin River and Delta, April June 2000. Anderson (CA): US Fish and Wildlife Service California–Nevada Fish Health Center. | | | | | | | | |
| Chinook, fall-run | Stanislaus, Toulumne, Merced, and San Joaquin rivers | *T. bryosalmonae* observed in smolts | *T. byrosalmonae* | Wild fish sampling | Juveniles | 2001 | USFWS | CALFED |
| **Relevant Citation:** Nichols K, Foott JS. 2002. Health monitoring of hatchery and natural fall-run Chinook Salmon juveniles in the San Joaquin River and tributaries, April–June 2001. Anderson (CA): US Fish and Wildlife Service California–Nevada Fish Health Center. | | | | | | | | |
| Chinook, fall-run | Merced River | *T. bryosalmonae* observed in Chipps Island re-captures | *T. byrosalmonae* | Laboratory studies, surveyed marked fish | Juveniles | 2005 | USFWS | AFRP |
| **Relevant citation:** Foott JS, Stone E, Nichols K. 2007. Proliferative kidney disease (*Tetracapsuloides bryosalmonae*) in Merced River hatchery juvenile Chinook Salmon: mortality and performance impairment in 2005 smolts. California Fish and Game 93(2):57-76. | | | | | | | | |

**Table 2** Summary and findings of major salmonid disease-related monitoring efforts performed by the US Fish and Wildlife Service in the Central Valley since 2000 *(Continued)*

| Salmonid spp.[a] | Region | Significant finding[b] | Pathogens of interest[b] | Methods | Life stages | Study years | Lead agency | Funding agency[d] |
|---|---|---|---|---|---|---|---|---|
| Chinook, fall-run | Merced River | *T. bryosalmonae* observed in wild smolts | *T. byrosalmonae* | Sentinel and wild fish sampling | Juveniles | 2012 | USFWS | |
| **Relevant citation:** Nichols K, Bolick A, Foott JS. 2012. FY2012 Merced River Chinook Salmon health and physiology assessment, March-May 2012. Anderson (CA): US Fish and Wildlife Service California–Nevada Fish Health Center. Technical report. http://www.fws.gov/canvfhc/reports.asp | | | | | | | | |
| Chinook, fall-run | Sacramento and San Joaquin rivers | *C. shasta* in Sacramento River | *C. shasta* | Wild fish sampling | Juveniles | 1997–2016 | USFWS | NWFHS |
| **Relevant citation:** https://www.fws.gov/wildfishsurvey/ | | | | | | | | |
| Chinook all runs | Sacramento River | IHNV, *C. shasta*, bacterial infections | IHN virus, *C. shasta* | Adult brood stock | adults | 1997–2016 | USFWS | NWFHS |
| **Relevant citation:** https://www.fws.gov/wildfishsurvey/ | | | | | | | | |
| Chinook, fall-run | Sacramento River | IHNV transmission from sick hatchery fish to wild fry is unlikely in natural conditions | IHN virus | Laboratory studies, surveyed marked fish | Juveniles | early 2000's | USFWS | |
| **Relevant citation:** Foott JS, Free T, McDowell KD, Arkush KD, Hedrick RP. 2006. Infectious hematopoietic necrosis virus transmission and disease among juvenile Chinook salmon exposed in culture compared to environmentally relevant conditions. San Franc Estuary Watershed Sci 4(1). https://doi.org/10.15447/sfews.2006v4iss1art2 | | | | | | | | |

a. Chinook = Chinook Salmon
b. POI = prevalence of infection, *C. shasta* = *Ceratonova shasta*, *P. minibicornis* = *Parvicapsula minibicornis*, *T. bryosalmonae* = *Tetracapsuloides bryosalmonae*, IHNV = infectious hematopoietic necrosis virus
c. USFWS = US Fish and Wildlife Service
d. USBR (US Bureau of Reclamation), CVPIA (Central Valley Improvement Act), AFRP (Anadromous Fish Restoration Program), USFWS (US Fish and Wildlife Service), CALFED (CALFED Bay-Delta Program), NWFHS (National Wild Fish Health Survey

that data collected in different regions were comparable and useful for management decisions. Unfortunately, funding for the program is limited, and sampling events in the Central Valley have been driven by staff availability, sample permits, and collection opportunities. A few multi-year data sets on the Feather and Sacramento rivers have provided some insight into prevalence and infection levels of fish (Foott 2014; Foott and Imrie 2016, 2017; Foott et al. 2017).

The USFWS sampled wild-origin Chinook Salmon fry caught in rotary screw traps and beach seines to investigate infections of *C. shasta* and *P. minibicornis* in the Feather River during 2013-2018 (Foott and Imrie 2017). Collection of longitudinal water samples revealed a 12-mile section of the river that is highly infective for *C. shasta*, but just 26 river miles downstream of this reach, below the confluence with the Yuba River, there is reduced infectivity. Initial detection in fry occurred in late January through February when water temperature was 10 °C to 12 °C. In the highly infective reach, sampling of Chinook Salmon at river mile 45 showed that the prevalence of *C. shasta* infection was fairly consistent (46% to 68%) during drought years (2015, 2016, and 2018) (Figure 1) but dropped significantly during a high-flow year in 2017 (Foott and Imrie 2016). The prevalence of *C. shasta* was similar or greater 26 miles downstream, but the number of fish in a clinical diseased state was 3 to 6 times lower. This is likely because diseased upstream fish died from direct (disease) or indirect (e.g., predation) mortality before reaching the downstream sampling location.

Concentrations of *C. shasta* and *P. minibicornis* in the Feather River are variable throughout the out-migration season. Since the majority of Feather River juvenile Chinook Salmon out-migrate as fry early in the season (December-February), it is difficult to say how the severe infection levels in

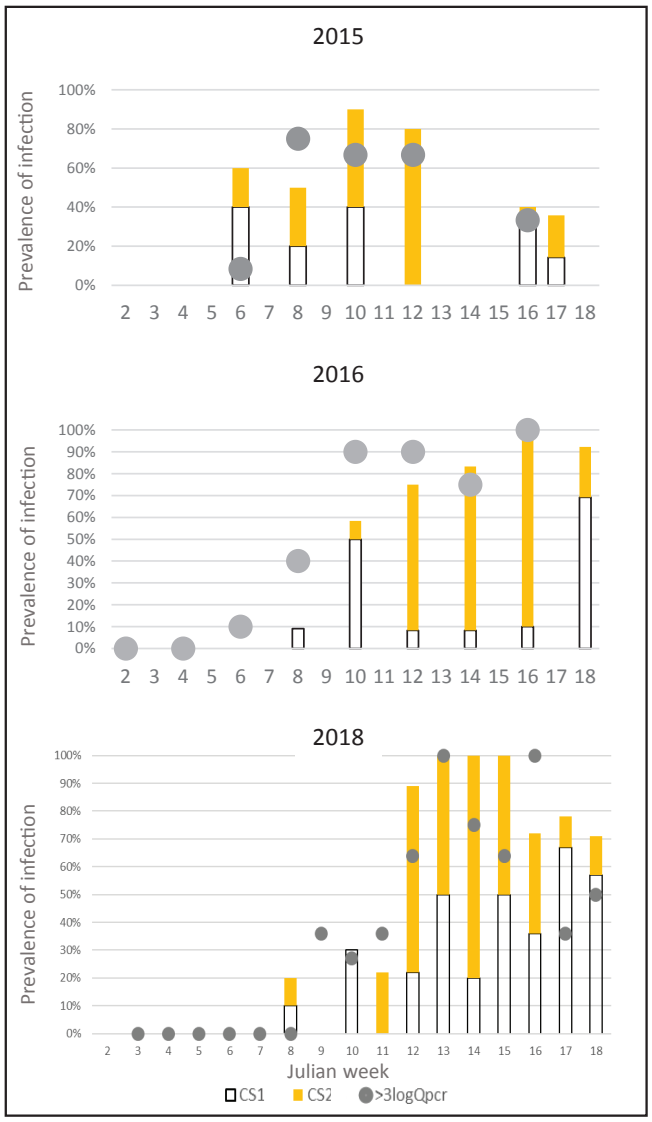


**Figure 1** Prevalence of *Ceratonova shasta* infection in wild juvenile Feather River Chinook Salmon sampled near river mile 45 in Julian weeks 2 through 18 during 2015, 2016, and 2018. Infectious rates in 2017 were substantially lower because of high water flow, but sampling design was different from other years and should not be directly compared (*data not shown*). Julian week corresponds to January (2–4), February (5–8), March (6–13), April (14–17), and May (18). Infection prevalence is categorized as CS1 (infected with little to no histological signs of inflammation, *open columns*) or CS2 (infected with histological signs of inflammation and determined to be in a disease state, *yellow columns*). Percentage of fish tested that had quantitative PCR levels > 3 $\log_{10}$ of copies of parasite DNA are represented with *gray dot*. Parasite DNA levels > 3 $\log_{10}$ are predictive of a disease state.

March and April (Figure 1) may affect population dynamics. Approximately 6% to 13% of the out-migrating juveniles pass through the highly infective zone in March as older, larger fish.

Sampling from the NWFHS also established that a portion of the Sacramento River appears to be infectious for a majority of the year (Foott et al. 2017). In 2013, approximately 27% of the wild fall-run Chinook Salmon fry collected from the Red Bluff Diversion Dam were found to have early stage infections of *C. shasta*. In 2014, wild juvenile fall-run Chinook Salmon from the lower Sacramento River in rotary screw traps at Tisdale and Knights Landing were taken to the lab and held for 21 days. Mortality ranged from 18% to 69% in each captive group; 91% to 100% of those fish exhibited evidence of clinical disease associated with *C. shasta*. In 2015, hatchery-origin fish were used as sentinel fish and placed in cages in the river for 5 days, then held in the lab for 21 days. Histologic examination revealed that most fish had a high level of *C. shasta* infection and were diseased. In the summer and fall of 2016, sentinel fish were deployed and water samples collected between Keswick Dam and Red Bluff Diversion Dam to establish the first longitudinal map of *C. shasta* spore concentrations in the Sacramento River. Concentrations were higher in the downstream reaches, although few were above the > 10 spore $L^{-1}$ threshold previously associated with high mortality (Hallett et al. 2012). In 2016, sentinel fish mortality and rates of infection were lower than the previous 3 years, likely a result of the diluting effect of higher flows and lower water temperature.

Although monitoring of infectious agents and disease severity has been inconsistent in the Sacramento-San Joaquin watershed, results from various NWFHS sampling efforts indicate that there are particular river reaches with high water concentrations of *C. shasta* DNA, at levels shown to cause fish mortality. In high-flow years, the concentrations of parasite DNA at these particular reaches were lower, and the infection rates of juvenile salmon were lower. It is also likely that

lower water temperatures during high-flow years may contribute to lower prevalence of infection.

While monitoring for disease in wild populations has been limited, the California Department of Fish and Wildlife (CDFW) has developed and maintained a robust, long-term disease monitoring program for enhancement and mitigation of salmon and steelhead hatcheries under their management. The CDFW monitoring program begins with the screening of ovarian fluid and tissue samples from the brood fish for Renibacterium salmoninarium, the causative agent of bacterial kidney disease (BKD), and viruses including IHNV. The fertilized eggs are disinfected during the water-hardening process and raised with regular health monitoring until release into the wild. Hatchery staff are continually trained in fish husbandry, biosecurity, and fish pathology so they can quickly identify and respond to issues that affect the health and well-being of their fish stocks. Hatchery staff are trained to identify changes in feeding, behavior, or increased losses that require investigation by department veterinarians for potential health. The CDFW veterinarians diagnose the problem(s) and recommend changes in husbandry or prescribe treatments for pathogens or parasites, if necessary.

## DESIGNING EFFECTIVE MONITORING PROGRAMS

### Leveraging Existing Monitoring Programs

Designing effective fish disease monitoring programs may not always require starting completely from scratch; instead, it may be beneficial to integrate disease evaluation into ongoing monitoring or research programs. In addition to upfront monetary and time savings, existing monitoring programs may be interested in sponsoring related disease work if the new information can be used to address relevant questions of the existing project. For example, adding a disease monitoring framework to existing programs that track key aspects of populations, such as abundance and size (Grote and Desgroseillier 2016; David et al. 2017), or migration timing and survival (McMichael et al. 2011; Harnish et al. 2012) may help these programs to explain variations and trends in past data. In addition, existing monitoring programs that have already implemented efficient methods for safely capturing and handling fish have likely secured the required federal and state agency permits, and it is possible that fish captured under their current program and protocols could be made available for disease monitoring without significant modifications. An additional benefit is that existing monitoring programs will have established protocols for data recording, transfer, quality assurance, and storage. Finally, there is another benefit related to the potential application of models or tools generated from disease monitoring research program data. If coupled to existing data from current monitoring programs, these tools could be coupled with historical data collected before the onset of fish disease work. This may allow hind-casted estimates of fish disease and increase the time-period available for analysis, which in turn could better inform larger-scale biological assessments for resource management planning.

### Metrics That Matter I: For the Population

Although there are tangible benefits to leveraging existing population monitoring programs, it is equally important to make sure that the disease monitoring itself is designed to provide sufficient information about fish demographics to allow population-level effects to be directly assessed. For example, although tracking infection and disease incidence over an out-migration season can provide valuable information about temporal patterns (True et al. 2017a), these data need to be integrated over multiple generations of abundance to estimate population-level infection or disease rates (Som et al. 2016). Further, emerging technologies continue to improve the ability to detect and quantify various disease agents (Hallett et al. 2012; Miller et al. 2014). However, changes in diagnostic test sensitivity or specificity must be considered when analyzing trends in long-term data sets that have been collected over a period when monitoring technologies were also improving. To address these differences and calibrate methods, tests on both historical and new data should initially be

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run in parallel. This approach has been proven successful in the Klamath River watershed during a transition from histology to qPCR as the primary surveillance tool to assess the prevalence of *C. shasta* infection (True et al. 2017b).

To account for potential biases in the data sets, disease surveillance programs must consider the biology of the infective agents and the nature of the fish population under study. Highly acute disease agents that cause rapid mortality may result in an underestimate of infection rates in sampled fish, biasing the true population-level effect of the disease (Heisey et al. 2006). Other disease agents may cause sub-clinical infections that never progress to disease or are cleared by the host. In these cases, the severity of infection within the fish population might inform population-level effects rather than quantifying the prevalence of the pathogen within the environment (True et al. 2015). Finally, some disease agents are strongly driven by environmental variables (e.g., water temperature) and incorporation of these variables may better predict the occurrence and or timing of mortality. It is important that any disease monitoring program develop metrics that matter, not only for the population and infectious agent of interest, but also metrics to inform management.

## Metrics That Matter II: To Inform Management

Disease agent monitoring and research programs are essential to understanding agent-host ecology and estimating effects of the disease agent on fish populations. However, understanding how the disease agent and fish host interact with each other and their environment, and knowing how severely the disease agent may be affecting a fish population, will not likely be the final program objectives. If the effects of a disease agent are severe enough to prompt new monitoring and research programs, the likely goal is remediation via changes to resource management practices. Models and other quantitative tools are increasingly being used to help inform resource management decisions (Parrott et al. 2012). Data collected during monitoring programs help inform models, which in turn identify data gaps that need targeted studies. Building models for effective resource management decision-making requires both an appropriate model structure, and attention to the quality and resolution of the data used to inform the model (Getz et al. 2018). Fish population dynamics models, developed by the motivation to inform future management, have been constructed to include disease agent dynamics (Perry et al. 2018). Additionally, there are models that target specific elements of agent-host ecology (Alexander et al. 2016), which have been applied to simulate how resource management alternatives might affect disease risk (Som et al. 2016). In the above cases, disease agent monitoring and research projects were specifically tailored for inclusion in decision support tools.

The following case studies highlight how the integration of several data collection and modeling approaches led to the development of successful management actions, and where investment in novel technologies led to breakthroughs in understanding salmon disease dynamics.

## Case Study 1: Management of *C. shasta* in the Klamath Watershed

At the UC Davis Salmon Disease Symposium, several researchers presented on the Klamath watershed system as a good example of a comprehensive, established disease monitoring program that is used to inform management. The Klamath system demonstrates why monitoring is needed, how monitoring programs can be developed, and how data may be used to inform management decisions. Many of the approaches used in the Klamath watershed could be directly applicable to the Central Valley region.

In 2002, a large mortality event in the Klamath watershed that involved over 34,000 fish (mostly adults), resulting from infection by *Flavobacterium columnare* (a bacterium, Columnaris) and *Icthyophthirius multifiliis* (a ciliate, Ich) brought awareness to the effects infectious agents can have (Belchik et al. 2004). Since then, *C. shasta* has also been identified as a key factor that limits recovery of salmon in the Klamath River (Foott et al. 2002; Fujiwara

et al. 2011). Although *C. shasta* infects both the adult and juvenile life stages, in the Klamath watershed the disease most affects juveniles. This is in contrast to other watersheds in the Pacific Northwest where adults experience mortality from *C. shasta* infections after re-entering freshwater to spawn (Bartholomew 1998; Hallett and Bartholomew 2006). In 2007, in response to ongoing disease issues, state and federal agencies began working collaboratively with academics, tribal groups, industries, land-owners, and consultants to develop an informative, long-term monitoring program. The goal of this work-group was to improve the understanding of disease dynamics in the Klamath River system, and build predictive epidemiological models and risk assessments to inform management and mitigate disease. This monitoring program can identify spatial and temporal patterns of *C. shasta*, and enables exploration of the relationships among parasite occurrence, host infection, and abiotic factors such as water temperature and flow.

## Monitoring

The monitoring approach was dictated by the life cycle of *C. shasta*, with particular consideration for the specific life stages most likely affected by management actions. *C. shasta* is a waterborne parasite with a two-host life cycle, so a three-pronged monitoring approach was developed that focused on the fish host, the annelid alternate host, and the parasite itself. Index sites were established along the Klamath River mainstem and in several tributaries. Collection of free-ranging, out-migrant juveniles occurs weekly from late March through August. Sentinel fish exposures occur three times during juvenile out-migration (in April, May, and June) and once during adult returns (September). Annelids are sampled quarterly (four times per year), and the water sampling effort occurs weekly at all sites from late March through October and at two sites throughout the year.

### *Fish Sampling*

To collect empirical data on the potential effect of *C. shasta* on out-migrating juvenile salmonids, researchers deploy sentinel fishes at multiple sites and collect free-ranging fish at existing rotary screw traps in different locations. Juveniles are analyzed using both histological and molecular methods (qPCR) to assess their prevalence and severity of infection and determine disease state (Voss et al. 2018). Since heavily diseased fish usually die before being sampled, sentinel fish provide additional data on infection and disease over time and space (with known exposure history). After river exposure, sentinel fishes are held at ambient river temperature in the laboratory to mimic what free-ranging fish may experience, and are eventually subjected to light microscopy and PCR analysis (Stocking et al. 2006).

### *Sampling for Alternate Host*

Similar to many parasites, *C. shasta*, requires an alternate host to complete its life cycle, and it is the alternate host that releases the infectious stage for fish. For *C. shasta*, understanding the distribution of the annelid alternate host and its life history is critical for informing flow management actions to reduce *C. shasta* concentrations. A multi-year study was implemented to evaluate annelid habitat preference in the context of multiple flow regimes (Alexander et al. 2016), which involved two-dimensional hydraulic modeling to predict hydraulic conditions (depth/velocity) across a range of discharge values; optimizing sampling to quantify annelid habitat preferences; and coordinating with the federal reservoir facility to release managed/prescribed flows.

Long-term monitoring of annelid populations was initiated by collecting benthic samples at multiple sites throughout the year, providing density estimates through space and time. Following light microscopy counts, the prevalence of infection within annelids was determined using molecular methods (Alexander et al. 2014).

### *Water Sampling for Parasites*

Outside its hosts, *C. shasta* distributes passively through the water column. Water samples can be collected manually or using programmable sampling units. Quantitative molecular analysis can determine parasite density (spore $L^{-1}$) and the genotype (Hallett et al. 2012).

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## Results

These data sets have provided significant insights into the role that *C. shasta* plays in the Klamath River watershed. Monitoring results are shared online in near-real time so that managers can make timely, informed decisions about the timing of release of flows and fish from the hatcheries. Infection rates in free-ranging salmonids, average juvenile salmonid catch-per-day, parasite abundance in water samples, and sentinel fish exposures are updated weekly during the juvenile out-migration season (*https://microbiology.science.oregonstate.edu/content/monitoring-studies; https://www.fws.gov/Arcata/fisheries/projectUpdates/KRTrapCatchSummaries/2019/Klamath%20Trap%20Update%2023apr2019.pdf*).

Samples from free-ranging fish are used to estimate the prevalence of infection (POI; the percentage of fish with *C. shasta* infections). Prevalence of infection can be tracked over time within a year and summarized annually. These data can be overlaid with fish abundance estimates from rotary screw traps. The integration of these weekly estimates is important, because the within-year time-series of each process can vary dramatically. For instance, there are years (e.g., 2014, Figure 2A when weekly POI quickly increased to elevated levels, but only after a majority of juveniles had out-migrated. Other years (e.g., 2009, Figure 2B), peak levels of POI matched peak out-migration of juveniles. And some years (e.g., 2012, Figure 2C) POI and juvenile out-migration completely overlapped, but overall infection levels were very low. If most fish have already moved through the system before POI has increased, the overall effect on the population may be of less concern.

Over the past 10 years, mortality of juvenile Chinook Salmon estimated by sentinel studies as a result of *C. shasta* has varied (Figure 3). True et al. (2017a) established a disease threshold of *C. shasta* in naturally infected fish by defining qPCR levels associated with advanced clinical disease that is highly likely to result in mortality as the infection progresses at temperatures of 15 °C to 18 °C. Over five sampling seasons (2013–2017), even at high prevalence of infection, up to 80% of the fish did not have qPCR levels that would be predictive of severe disease.

The multi-year study to evaluate annelid habitat preference in the context of multiple flow regimes found that under high flow conditions, annelids are scoured from the benthos, and populations

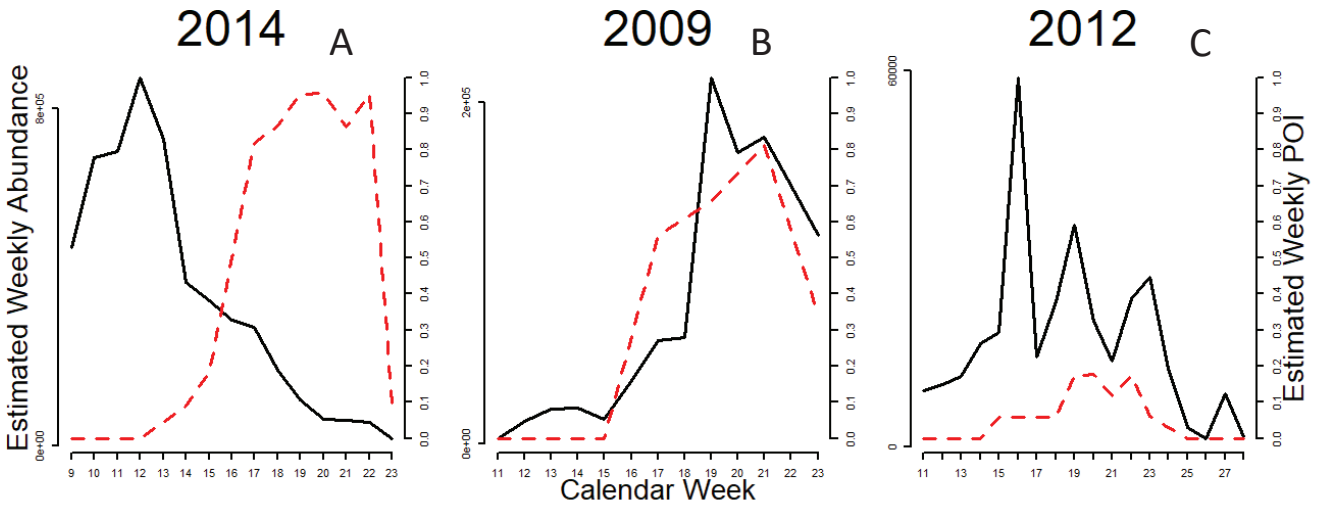


**Figure 2** Weekly stratified abundance estimates of juvenile Chinook Salmon (*solid black lines*) and *Ceratonova shasta* prevalence of infection (POI; *dashed red line*), for 3 years of monitoring on the Klamath River. Typically, the majority of salmon passed before the onset of *C. shasta* (as shown in panel **A**), but in some years there was significant overlap, suggesting increased risk of salmon out-migrants to *C. shasta* than in other years (*see panels* **B** *and* **C**).

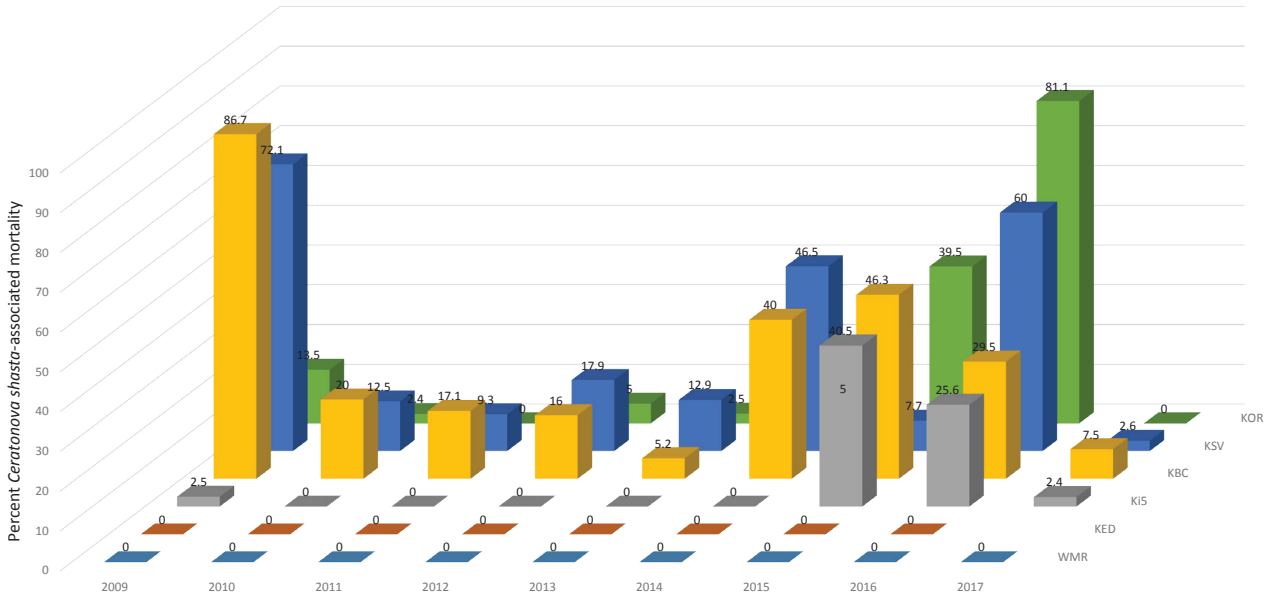


**Figure 3** Comparison of percent mortality from *Ceratonova shasta* of juvenile Iron Gate Hatchery Chinook Salmon at six index sites in the Klamath watershed exposed in June of 2009–2017. The Chinook Salmon (40 in a cage per site) were exposed for 72 hours, then monitored for 60 to 90 days in the laboratory; *zeros* indicate exposure but no loss. The percent change represents fish that were moribund or dead and were removed from the tanks during the post-exposure rearing (any change that occurred during the first 5 days was excluded). Fish were regarded as positive for infections of *C. shasta*, either by microscopic observation for myxospores in intestinal wet mounts or PCR testing of intestinal tissue. Sites are ordered in direction of river flow, upstream (*front*) to downstream (*back*). WMR and KED are in the upper basin, above Iron Gate Dam, a barrier to anadromous salmonid migration. WMR, Williamson River; K, Klamath mainstem; KED, Keno Eddy; Ki5 at I5 Bridge; KBC, near Beaver Creek; KSV, Seiad Valley; KOR, Orleans. Map available at *https://microbiology.science.oregonstate.edu/content/monitoring-studies*

take time to re-establish. Scouring flows might be one method to control the alternate host of *C. shasta* and thus reduce fish being exposed to the infectious stage.

Water sampling efforts have allowed for a higher resolution of where the parasite is located in the system, and the temporal distribution of the parasite. Typically, *C. shasta* levels were found to increase in the spring—overlapping with the peak of rising water temperatures and juvenile salmon out-migration. However, the system varied substantially from one year to the next, with densities in some years remaining below 5 spores $L^{-1}$ and exceeding 100 spores $L^{-1}$ in others (Figure 4). Initial surveys indicated that the tributary rivers that feed the Klamath (Trinity, Salmon, Scott, and Shasta rivers) are not contributing large amounts of spores to the system, which helps direct sampling efforts to continue focusing on the mainstem (Hallett and Bartholomew 2006).

Water sampling has also enabled identification of multiple parasite genotypes that affect individual salmonid species differently (Atkinson and Bartholomew 2010a, 2010b). This knowledge informs management about the risk posed to different salmon species. For instance, *C. shasta* Type I is associated with increased mortality in Chinook Salmon while Coho Salmon (*Oncorhynchus kisutch*) are more susceptible to Type II (Hallett et al. 2012). The proportion of *C. shasta* genotypes differs throughout the year and among the sites (Atkinson and Bartholomew 2010b; Hallett et al. 2012). Generally, Type I is more abundant in the Klamath watershed, which is consistent with it being a predominantly

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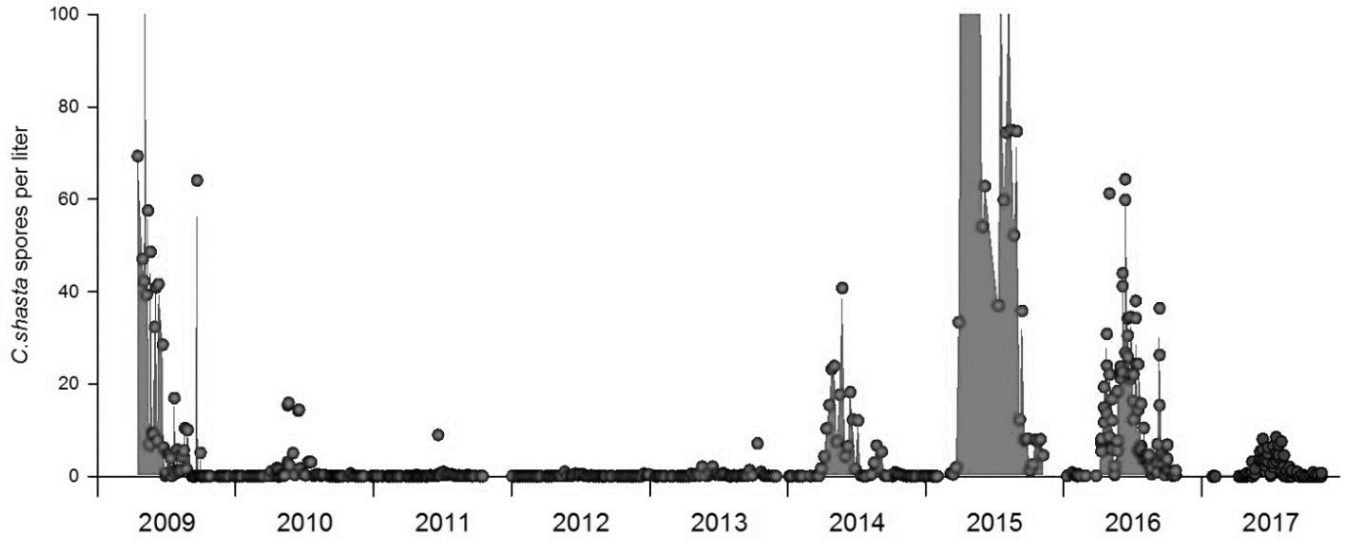


**Figure 4** Density of *Ceratonova shasta* in water samples collected at the Beaver Creek index site (KBC) in the Klamath watershed from 2009–2017. Each *point* is the average of 3 x 1L from a 24-hr composite water sample. The maximum level in 2015 exceeded 1,000 spores $L^{-1}$. Note the high densities of *C. shasta* observed in 2009 and 2014–2016.

Chinook Salmon-dominated system. Results from parallel water sampling and fish exposures revealed that Coho Salmon are sensitive to lower densities of Type II *C. shasta* spores than Chinook Salmon are to Type I spores (Hallett et al. 2012).

## Management Actions

Data from this multi-step monitoring program focused on the complete *C. shasta* life cycle are being used to inform several different types of management actions. Data on prevalence of infection were used in the 2013 Biological Opinion (NMFS 2013) for the federal Klamath Irrigation Project by developing an incidental take statement for Coho Salmon based on prevalence of infection in Chinook Salmon (Chinook Salmon data were used a proxy species because of the limited information available on Coho Salmon).

In 2017 and 2018, water samples and out-migrants were required to be processed as soon as possible and made available to agencies and stake-holders for discussion and possible action. Management actions could include flow releases from reservoirs, or modifying the release timing of juvenile Chinook Salmon from the hatcheries. Potential emergency flow triggers were actinospore density (spores $L^{-1}$) and POI in free-ranging salmonids. Increasing flow from reservoirs could have a range of effects on the parasite that depend on the timing, magnitude, and duration of the event. Increased flows could dilute or move the parasite, disturb the annelid habitat, affect transmission efficiency or move juvenile salmonids downstream or adults upstream past the infection zone. In the 2019 Biological Opinion (NMFS 2019), three types of flow of different dimensions are defined to achieve these outcomes: (1) a surface flushing flow; (2) a deep flushing flow; (3) enhanced flow in the springtime. During salmonid out-migration, a consortium of Klamath Basin technical experts convene weekly via conference call to review data updates (hydrologic, meteorological, and disease) and discuss adaptive management options.

Data on myxospore, actinospore, annelids, and fish were used to develop an epidemiological model that incorporates both the juvenile and adult salmon life stages to identify which life stage of juvenile Chinook Salmon is most sensitive to *C. shasta*. (Ray et al. 2015). Models

are also being developed to predict the infection prevalence of fish, predict the timing of annelid population expansions, and understand how climate change may affect *C. shasta* dynamics.

Multi-agency collaboration has been one of the most important aspects of the development and success of this monitoring program. A consistent source of funding has been essential to plan and execute regular collection and processing of samples. Occasions when funding was absent and lapses in data collection occurred have resulted in critical data gaps.

## Case Study 2—Using Novel Approaches to Study Infectious Agents in British Columbia

Salmon productivity in British Columbia has been declining for >30 years. In the Fraser River, Sockeye Salmon (*Oncorhynchus nerka*) had one of the lowest returns on record in 2009, with <2 million returning fish, a considerable discrepancy from the escapement of 10 million fish predicted by management models. Concern over declining Sockeye Salmon productivity, combined with the increasingly poor predictive power of escapement models used to manage the fisheries, resulted in a federal judicial inquiry (known as the Cohen Commission) into the declines of Sockeye Salmon in the Fraser River. The goal of the Cohen Commission inquiry was to investigate factors contributing to (1) multi-decade declines in survival of Sockeye Salmon, (2) the poor returns in 2009, and (3) high inaccuracy in escapement model predictions used to manage fisheries. Infectious disease as a contributing factor to declining Sockeye Salmon productivity was identified as one of the 13 key hypotheses explored. Through expert testimony, there was general scientific consensus that conditions in the early marine environment was a key determinant of year-class strength, and that infectious disease could contribute to the multiple stressors that affect salmon during this critical stage. However, in the final Recommendations (Cohen 2012), the court ruled that there was insufficient information on the pathogens that affected salmon in the ocean to evaluate the level of contribution of infectious disease to declining productivity, and the specific pathogens that may be involved. Moreover, the court ruled that it was important to determine the risk of infectious agent transmission from marine net pens as a contributing factor in disease occurrence in free-ranging migratory salmon. After the Cohen Commission investigation there was an increase in support and resources to investigate the role of disease in free-ranging salmon, improve disease risk assessment, and build a better understanding of the interplay between cultured and free-ranging fish.

In 2014, in response to the Cohen Commission recommendations, Fisheries and Oceans Canada, the Pacific Salmon Foundation, and Genome British Columbia collaborated in the development of the Strategic Salmon Health Initiative (SSHI), a large multi-disciplinary project that uses science and innovation to identify the role of infectious disease in declines of Sockeye, Chinook, and Coho Salmon. This was the first program of its kind to explore a broad base of potential pathogens (viruses, bacteria, fungal, and protozoan parasites) known or expected to cause disease in salmon worldwide, and the interplay between wild and cultured salmon (both aquaculture and enhancement hatcheries). Over 3 years, the SSHI screened 28,000 fish from wild, hatchery, and aquaculture settings for more than 60 potential pathogens (e.g., Nekouei et al. 2018; Tucker et al. 2018; Laurin et al. 2019) and discovered several novel viruses (Mordecai et al. 2019, 2020). Among this program's accomplishments were characterizing previously unrecognized diseases on salmon farms (Di Cicco et al. 2017, 2018), developing a novel host biomarker panel that predicts the presence of a viral disease state in salmon (Miller et al. 2017), and developing new in situ hybridization techniques to identify where infectious agents are occurring within diseased tissue (Di Cicco et al. 2018).

The foundation of the program was based on the development of a novel high-throughput molecular technology to quantitatively monitor dozens of infectious agents at once (described in Miller et al. 2016). To gain an understanding of what infectious agents were present, the program initially screened for 47 infectious agents

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known or suspected to cause disease in salmon worldwide, with additional agents added as they were discovered. Monitoring was not restricted to infectious agents known in British Columbia because during the testimony in the Cohen Commission, it became clear that many agents associated with emerging disease in other parts of the world had never been assessed in North America. Application of the pathogen monitoring platform revealed detection of 38 of the original 47 infectious agents screened in British Columbia salmon. After replacing assays to agents not detected in the first 10,000 fish surveyed, the program has now documented over 50 infectious agents in British Columbia salmon. Half of these agents were first detected in juvenile salmon in freshwater, of which the majority were natural components of salmon ecosystems (i.e., they had little to do with aquaculture-to-wild transmission).

To study the effects of pathogens on wild migratory fish in freshwater and marine environments, researchers in the SSHI employed other ecological approaches. They paired pathogen-screening gill biopsy samples with telemetry tracking studies, performed holding studies to assess effects of high water temperatures and stress from catch-and-release fisheries on disease progression, and evaluated predation-related consequences of disease. A wide range of new knowledge has come from these studies, including:

1. Wild fish with a high burden of pathogens, or detection of specific pathogens, are more likely to die (Furey et al., forthcoming); Jeffries et al. 2014a; Miller et al. 2014; Teffer et al. 2017);

2. Yearling Chinook Salmon carry higher prevalence and loads of agents than sub-yearling fish, of interest because in British Columbia the yearling Chinook Salmon populations are in the most dramatic decline (Tucker et al. 2018);

3. Sockeye Salmon smolts from a year of record low productivity carried higher prevalence and infective burden of pathogens than those from an average year (Nekouei et al. 2018). Models are currently under development that use up to 10 years of infective agent data to identify agents correlated with cohort strength in Sockeye, Chinook, and Coho Salmon;

4. Infectious profiles in smolts increase their risk from predation, with the presence of specific agents and overall burden of agents a predictor of risk of being consumed by predators (Miller et al. 2014; Furey et al., forthcoming);

5. Adult salmon compromised by stress and/or disease migrate faster than fish that appear to be healthier. These fish "push" to migrate faster and arrive on the spawning grounds earlier, but die prematurely in much higher numbers (Miller et al. 2011; Drenner et al. 2017);

6. The environment in which salmon are sampled has a stronger effect on infectious profiles than stock, hatchery-wild, or life-history type (Tucker et al. 2018; Thakur et al. 2019);

7. Many pathogens replicate faster in higher water temperatures, resulting in stronger disease dynamics (Teffer et al. 2018);

8. Side-by-side tracking and holding studies reveal that the same pathogens that affect juveniles are associated with premature mortality in adult salmon (Teffer et al. 2018; Bass et al. 2019).

In evaluations of pathogen distribution between aquaculture and free-ranging fish, SSHI researchers found that free-ranging salmon carry a high diversity of fungal and protozoan parasites, many of which are from the freshwater environment. There is evidence that some of these parasites can cause disease and reduce the survival of wild fish (Jeffries et al. 2014a; Tucker et al. 2018; Wang 2018; Thakur et al. 2019). Conversely, salmon in marine net pens

carry a higher diversity of bacterial pathogens in saltwater (Laurin et al. 2019), most of which are known to cause disease on farms. Current efforts are focused on investigating whether these bacterial agents can be transmitted to free-ranging fish in the vicinity of farms. Finally, research has shown that aquaculture and free-ranging fish carry a diversity of viruses, most of which were not previously known.

The SSHI has been successful in large part because of constant communication among scientists, regulators, and the public. The science agencies in the initiative have regular briefings with managers and regulators, including the Fisheries Minister's and Prime Minister's offices; are actively working with salmon enhancement programs and consulting with industry; and have strong public, non-governmental agency, and First Nation Support for evidence-based science. To effectively communicate findings, lead agencies give regular presentations at scientific conferences and to fisheries and aquaculture advisory boards and media groups.

## RECOMMENDATIONS FOR BUILDING AN INFECTIOUS AGENT MONITORING PROGRAM IN THE CENTRAL VALLEY

Infectious diseases have been routinely documented in Central Valley salmon in nature. Yet, a monitoring and modeling framework is lacking to quantify the extent to which disease may play a significant and unrecognized role in salmon population dynamics. State and federal agencies in California have invested significant resources to improve salmon survival and maintain sustainable populations. These resources are put toward efforts to restore habitat, manage flows and temperature, reduce predation, and monitor juvenile fish emigration at key locations. Despite these efforts and the commitment of resources, salmonid populations remain at a fraction of historical population sizes (NMFS 2016a, 2016b). As agencies implement new methods to identify monitoring metrics intended to improve salmonid survival, such as Structured Decision Making and Life-Cycle Models (Zeug et al. 2012; Hendrix et al. 2014), existing monitoring programs could be improved by including a comprehensive fish-condition and disease-monitoring component to help identify factors that limit salmonid population recovery in the Central Valley (Johnson et al. 2017). This is critical because there may be years where habitat conditions favor pathogen prevalence, salmon susceptibility to infection, and increased prevalence of infection. Conditions such as warm water temperatures with reduced flows may represent such years. Establishing a robust disease monitoring, research, and modeling framework in the Central Valley will be particularly important to ensure actions intended to recover salmon are indeed mitigating for the direct and causal stressors.

Participants of the UC Davis Salmon Disease Symposium workshop agreed that multi-faceted monitoring approaches provide the most useful information. Data collection focused on both the distribution of pathogens (e.g., water sampling) to detect exposure landscapes in concert with monitoring and sentinel fish condition to understand salmon-disease dynamics would provide more value than a single type of data source alone. Novel molecular techniques utilizing eDNA, qPCR, and high-throughput sequencing will improve data resolution when paired with traditional methods such as counting mature spores or observing signs of clinical disease.

In addition, there are a number of opportunities to use data that have already been collected from established monitoring programs. The integration and evaluation of these data sets can provide a foundation for formulating hypotheses, and guide the design and implementation of a well leveraged disease monitoring framework. For example, time-series of salmon survival across the out-migration route from acoustic telemetry studies could be coupled with pathogen prevalence data and used to model prevalence of infection.

Although health monitoring of fish at any of the current Central Valley sampling sites is not consistent, a robust system-wide juvenile salmon monitoring framework is already in place in the Central Valley. There are many opportunities

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to leverage these already existing monitoring efforts by incorporating additional data or sample collection (e.g. non-lethal gill tissue sampling) at rotary screw traps or beach seine sites along the salmon out-migration corridor. This kind of sequential sampling—of prevalence of disease in salmon across space and over time in monitoring locations where salmon abundance is estimated—is one powerful approach used to quantify mortality in salmon populations from disease (Figures 1 and 2). Many of these fish monitoring stations have existed for decades. Designing a disease monitoring framework, with agreed-upon protocols implemented within already existing fish or environmental sampling efforts, may provide the additional benefit of being able to hindcast models to help understand what happened in the past. Streamlining data collection into already existing programs will also reduce the need for obtaining permits, travel, and staffing.

Based on the case studies from other salmon systems highlighted in this paper and the workshop, we recommend initiating a multi-year watershed-wide monitoring effort to establish a reliable baseline for the distribution of infectious agents and disease prevalence in the Sacramento River watershed (Figure 5). Ideally, this monitoring framework would use the following sampling approaches: (1) periodic water sampling at key longitudinal locations to assess the presence and abundance of infectious agents at different times or under varying conditions; (2) sampling of wild juvenile fish from already existing rotary screw traps to provide real-time information on prevalence of infection—using both simple non-lethal visual metrics as well as tissue sampling for histopathology and genetic analysis; and 3) deploying groups of caged sentinel fish at key longitudinal locations in different regions of the watershed through time to quantify the relationship between waterborne pathogen levels and disease. This three-tiered data-collection approach would provide the necessary data to parameterize and develop infectious-disease transmission models linked to key environmental co-variates. These baseline data and decision-support models may identify critical water conditions or infective locations, and inform avenues of future research to develop management tools to mitigate vulnerabilities from infectious disease.

To date, what we do know about salmon disease in the Central Valley has come from different research groups and agencies temporarily funding small-scale studies. To build robust models that describe disease dynamics at the population scale with a focus on management actions that can reduce the effect of disease, a holistic monitoring and research approach with sustained funding is required. There must be sufficient resources to synthesize data in addition to data collection, sample processing, and data reporting into an accessible database. Finally, creating a formal forum for salmon disease researchers to regularly meet, share data, and provide guidance on the implementation of a watershed-scale infectious disease monitoring plan would be of tremendous benefit to advancing and communicating the current state of knowledge within and outside of the scientific community.

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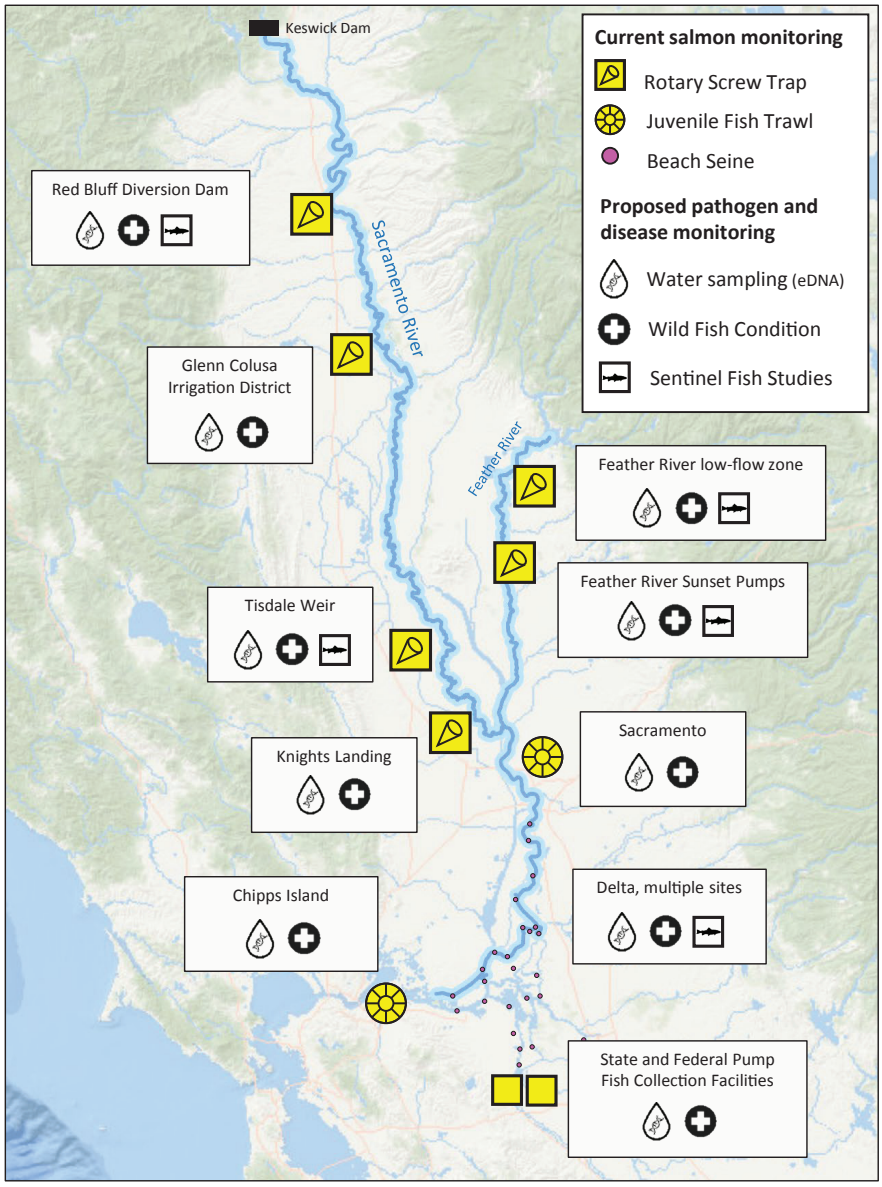


**Figure 5** Map of the Sacramento River watershed with current juvenile salmon monitoring locations led by both federal and state agencies in yellow and pink. Opportunities to incorporate pathogen and disease sampling into already existing monitoring programs are highlighted in key locations.

and related resources in an environmentally and economically sound manner in the interest of the American public. Funding was provided through Interagency Agreement # R15PG00065 to Oregon State University. The views in this publication are the authors' and do not necessarily represent the views of Reclamation.

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