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Optimizing surveillance for early disease detection: Expert guidance for Ostreid herpesvirus surveillance design and system sensitivity calculation

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Abstract :

To keep pace with rising opportunities for disease emergence and spread, surveillance in aquaculture must enable the early detection of both known and new pathogens. Conventional surveillance systems (designed to provide proof of disease freedom) may not support detection outside of periodic sampling windows, leaving substantial blind spots to pathogens that emerge in other times and places. To address this problem, we organized an expert panel to envision optimal systems for early disease detection, focusing on Ostreid herpesvirus 1 (OsHV-1), a pathogen of panzootic consequence to oyster industries. The panel followed an integrative group process to identify and weight surveillance system traits perceived as critical to the early detection of OsHV-1. Results offer a road map with fourteen factors to consider when building surveillance systems geared to early detection; factor weights can be used by planners and analysts to compare the relative value of different designs or enhancements. The results were also used to build a simple, but replicable, model estimating the system sensitivity (SSe) of observational surveillance and, in turn, the confidence in disease freedom that negative reporting can provide. Findings suggest that optimally designed observational systems can contribute substantially to both early detection and disease freedom confidence. In contrast, active surveillance as a singular system is likely insufficient for early detection. The strongest systems combined active with observational surveillance and engaged joint industry and government involvement: results suggest that effective partnerships can generate highly sensitive systems, whereas ineffective partnerships may seriously erode early detection capability. Given the costs of routine testing, and the value (via averted losses) of early detection, we conclude that observational surveillance is an important and potentially very effective tool for health management and disease prevention on oyster farms, but one that demands careful planning and participation. This evaluation centered on OsHV-1 detection in farmed oyster populations. However, many of the features likely generalize to other pathogens and settings, with the important caveat that the pathogens need to manifest via morbidity or mortality events in the species, life stages and environments under observation.

Highlights

► Experts identified surveillance traits important for OsHV-1 early detection. ► Observation frequency, guidance, incentives, advocates, and risk-based focus were key. ► Strong industry-government partnership appears crucial to effective implementation. ► Methods introduce a simple approach to observational surveillance sensitivity estimation. ► Results hold value for both early detection design and disease freedom assessment.

Keywords : Ostreid herpesvirus, observational surveillance, passive surveillance, early detection, system sensitivity, expert elicitation

Introduction

Variants of the Ostreid herpesvirus 1 (OsHV-1), including the reference strain and microvariants, are best known as causal agents of mortality events of consequence for *Crassostrea gigas* (Pacific oyster) populations in many locations globally since the early 1990s (EFSA AHAW Panel, 2015; Castinel et al., 2015; Arzul et al., 2017; Burge et al., 2018; OIE, 2019). Microvariant genotypes of OsHV-1 were first identified in 2008 associated with large-scale *C. gigas* mortality in France (Segarra et al., 2010), and are distinguished from the reference genotype (Davison et al., 2005) by sequence variation in select regions of the genome (OIE, 2019). OsHV-1 variants have also been associated with events of lesser impact (Burge et al., 2006; Cáceres-Martínez and Vásquez-Yeomans, 2013; Bai et al., 2015). Though typically linked to large-scale losses in *C. gigas*, microvariants have been found in apparently healthy *C. gigas*, both during post-outbreak recovery (e.g., in Australia, Evans et al., 2017) and alongside mortality in other species (e.g., in Asia, Bai et al., 2015). Failure to apply efficient detection systems, as well as movement controls, contributed to dissemination throughout many affected regions (Carnegie, 2012; Carnegie et al., 2016;

Fuhrmann, 2019). As such, early detection and timely response are critical to the goal of curtailing damage otherwise associated with rapid spread. However, the pathogen's short incubation period and rapid transition from extremely low to high prevalence, alongside a tendency for spatiotemporal clustering of infection (Paul-Pont et al., 2013), make OsHV-1 difficult (and costly) to detect prior to a large outbreak using conventional surveillance modalities (Whittington et al., 2019).

Pathogen surveillance in aquaculture is largely built around intermittent submission of samples for laboratory testing (termed "active surveillance" when coordinated externally). While active surveillance can offer very strong evidence of disease absence *at test-time*, it is less well-suited for early detection of incursions that can occur *at any time* or location (Vennerstrom et al., 2017). Often designed to support translocation of stock for production or trade, active surveillance can be patchy in both space and time. Though bolstering active systems (via increased frequency, for example) is one way to improve early detection capacity, it may not be the most efficient. Rather, surveillance built to address both disease freedom and early detection objectives may need to couple periodic testing with observational systems for the most cost-effective designs (Cameron et al., 2020). Risk-based surveillance, targeting animals with the highest risk of exposure, infection, or consequence, may further improve detection capability, for both active and passive systems (Oidtmann et al., 2013).

Frequent observation of animal appearance, behavior, or mortality (here termed "observational surveillance", also known as "passive surveillance" if led by the producer) can signal abnormalities in population health. Mortality investigations, for example, were key to the initial diagnosis of OsHV-1 µvar in France (Lupo et al., 2014). When observers are versed in disease recognition and networked with health professionals and response agencies, unexplained morbidity or mortality can trigger disease investigations, targeted laboratory diagnostics, and subsequent reporting. Similarly, the absence of reports from these same networks can provide baseline assurance of disease absence in the monitored systems if trust and mutual confidence are present between stakeholders (World Bank, 2010). However, the degree of assurance generated will vary by pathogen, population, and system, and its quantification requires an estimate of the sensitivity of observational surveillance.

Surveillance system sensitivity (SSe), the ability of a system to identify disease or infection in a population, is similar in construct to diagnostic test sensitivity (Se) but focused on populations rather than individual animals. Used in disease freedom calculations, SSe can influence decisions regarding disease control, animal movement, and trade. However, SSe for observational surveillance is notoriously difficult to estimate well, and SSe geared to early (rather than any) disease detection is rarely discussed (Cameron et al., 2020). Several methods are available, e.g., using capture-recapture (Lupo et al., 2012) or mixed qualitative/quantitative (Limon et al., 2014) analyses, to identify traits predicting observational surveillance success. However, data, time or resources required for empirical analyses of observational surveillance systems are often lacking. Therefore, SSe is more commonly derived from estimation of a series of subjective probabilities that are not necessarily data-driven: probabilities that the pathogen will cause clinical signs, the clinical signs will be noticed by a producer, the producer will report the disease, and so on. Expert elicitations, in contrast, offer a replicable mechanism to estimate epidemiologic parameters like SSe when empirical field data are limited (Gustafson et al., 2018). If structured to identify system traits that predict detection capacity, results can be used as guidance for surveillance design. Further, by replicating case-control studies and generating likelihood ratios (LRs, epidemiologic measures of association), the results are portable, informing models that compare the value of different systems or designs.

Expert elicitation accuracy is driven by several processes including whether experts have first-hand knowledge of the topic, whether experts have an opportunity to clarify the wording/meaning of identified factors, and whether elicited parameters are count rather than probability-based (Kynn, 2008; Burgman et al., 2011; McBride et al., 2012). Certain types of group processes, e.g., the integrative group process (IGP) used here, also minimize “group think” (or unjustified peer influence) by eliciting responses from individuals independently prior to group discussion (Gustafson et al., 2003). Finally, group discussion provides a forum for self-calibration as experts with specific knowledge have a chance to share experiences that may, or may not, influence independent revisions by the rest of the group.

Here we describe an expert elicitation to identify and weight factors predicting the capacity of observational surveillance for the early detection of OsHV-1. The expert-identified traits are considered key to early detection and thereby offer guidance to producers and governments aiming to improve surveillance. Results also parameterize a model to compare (1) the sensitivity of different surveillance system designs toward early detection, and (2) the confidence these systems can generate toward disease freedom. For simplicity, we focused this elicitation on the pathogen OsHV-1, regardless of genotype. However, many of the tenets, as well as the estimation process, likely generalize to other pathogens of concern for oyster production systems. Similarly, factors focus on oyster farming sites and their surveillance systems, but the resulting model should also generalize to geographic regions.

Methods

Terms and Assumptions

We use the term "factor" throughout to describe possible predictors (risk factors or protective factors) of a surveillance system's early detection capability, and the term "trait" to classify response or sub-categories of the identified factors. Factor describes a general concept (e.g., color) and trait describes its sub-category (e.g., blue, green, orange, etc.). We use the term "detection" to refer to the full sequence of observing, notifying, diagnosing, and reporting a case to the proper authority. The term "early detection" indicates that timing was sufficient to allow *the opportunity* for implementation of interventions that aim to prevent spread to neighboring farms, wild populations, or production systems. The term "late detection" indicates detection was not early, or never occurred. OsHV-1 is defined broadly, capturing any pathogenic variant. Finally, though mitigations to prevent a pathogen's introduction or its subsequent spread are critical corollaries to successful disease management, the value and design of surveillance to support early detection was the singular focus of this study.

Panel Selection

Panelists were selected for their firsthand field experience in oyster production or management of OsHV-1 or molluscan pathogens. We used a snowball nomination process to include North American, European Union and Australasian experience in oyster health management from both industry and pathology perspectives. In order to ensure active participation, we limited group size and aimed for experts with different experience bases and scope.

Identification

The elicitation followed the format of an IGP, involving three key stages known as "estimate-talk-revise". We added an initial stage to prepare factors for evaluation, here called "identification". In this step, experts were each interviewed independently and informally to discuss the topic of OsHV-1 and early detection. During these conversations, experts were asked about their experience with oyster population health and surveillance for OsHV-1. They were also asked to describe conditions they felt might characterize particularly effective (or particularly poor) early disease detection systems. This process generated a list of potential predictive "factors" (e.g., observation frequency), each with two or three response categories we termed "traits" (e.g., at least weekly, at least monthly, or less frequent than monthly), for experts to independently rank (in terms of importance for predicting early detection capacity) and revise. This revised list was the starting point for the structured "estimate-talk-revise" process.

Estimate-Talk-Revise

In the estimation step, experts were asked to imagine a hypothetical set of 200 OsHV-1 infected farms, 100 of which were detected early and 100 of which were not detected early ("detected late"). From these hypothetical sets of early and late detection farms, experts were asked to estimate, for each general factor, the number of farms exhibiting each of the listed traits. A fictional example was provided to assist the estimation process. Its fictional reach was an intentional effort to avoid "anchoring", a bias that can sometimes occur when experts are given a starting value for the same or similar exercise (O'Hagan, 2019). In this fictional example, werewolves (the example factor), and whether visitations did or did not occur (the example traits), were considered potential predictors of early OsHV-1 detection. Following the IGP format, experts would estimate the number of the 100 early detection, and separately the 100 late detection, farms with the trait "werewolf visitations". Because this factor is dichotomous, the balance for each set was attributed to the counter trait ("no werewolf visitations"). Likelihood ratios, representing the predictive strength (for early detection) of each factor and trait pair, were later constructed from the ratio of the predicted prevalence of a given trait (e.g., werewolf visitations) among farms in the early versus late detection groups. Likelihood ratios were also calculated separately for the counter option(s) (e.g., "no werewolf visitations").

Following this example, experts individually scored the actual factors/traits. Group LRs were summarized by median and quartiles (across respondents) and reported back to the expert panel for review and discussion. As panelists were up to 15 hours apart in time zone, opportunities for discussion were held both by video conference and email. During discussion, interpretation of LRs and specific results were reviewed. Factor wording and intent was clarified to ensure common understanding, and perspectives behind factors with wide variation in responses were discussed. Following discussion, experts were given the opportunity to individually revise their responses to adjust for misunderstandings or new information about the factors. No effort was made to force consensus. Rather, LRs calculated from the final round depict both central tendency and variation in group perceptions regarding factors important to early disease detection. Square root transformations of LR median values were calculated for later use in predictive models.

Application

Bayes theorem (Goodman, 2005) guides the use of these LRs to derive site- or region-specific estimates of SSe. When calculating SSe for regional assessments, either the most generalizable (i.e., most common) or the most conservative (i.e., weakest link) of applicable traits should be chosen. This decision should be noted as it may influence interpretation of results.

According to the odds form of Bayes theorem (Equation 1), the posterior odds of early detection are a product of the prior odds of early detection and the LRs representing predictive factors.

$$\text{Posterior Odds} = \text{Prior Odds} \times LR_1 \times LR_2 \times \ldots LR_n \qquad \text{Equation 1}$$

Here, posterior odds reflect system capacity for (early) detection of OsHV-1, akin to SSe (but as an odds, rather than percentage). Likelihood ratios represent the traits (for each of the n factors) that best describe the surveillance system under evaluation. Prior odds are often set at 1 to reflect lack of prior knowledge (Martin et al., 2007). However, prior odds can also be informed by previous studies, or expert opinion, of the general (not system-specific) probability of early detection of OsHV-1. In other words, the *prior* represents the baseline likelihood of early detection (percent of cases detected early), converted to odds

(Equation 2), preceding any knowledge of the surveillance system design. Likewise, converting the *posterior odds* to a probability (Equation 3) provides a site- or region-specific estimate of the likelihood of early detection after accounting for the site's surveillance system design.

$$\text{Odds} = \text{Probability} / (1\text{-Probability}) \quad \text{Equation 2}$$

$$\text{Probability} = \text{Odds} / (1\text{+Odds}) \quad \text{Equation 3}$$

In short, the *posterior probability*, resulting from Equation 1 (where LRs and Odds refer to the capability of early detection) revised by Equation 2, provides an estimate of the surveillance system's SSe.

Following standard methods (Martin et al., 2007), the SSe can next be used to estimate disease freedom probability. These estimates also require a prior probability, this time of disease freedom, which is often considered uninformed. Alternatively, an informed prior can be generated from past or current surveillance data not yet captured in the SSe. Consequently, when the SSe is generated as above, from predictive factors (Gustafson et al., 2010), results from active surveillance (e.g., represented by a beta distribution) are contextualized in a manner that is both replicable and instructive: each LR represents a trait that can be enhanced to improve surveillance capacity.

As an example application, we applied the expert elicitation results to hypothetical Pacific oyster surveillance systems to (1) compare detection capacity (SSe) of different surveillance strategies, and (2) instruct enhancements to improve OsHV-1 early detection. In order to calculate SSe for this example, we needed to specify a prior probability (or odds) of early OsHV-1 detection. Since the prior captures the background rate of early detection (sufficient to initiate strategic containment measures), assuming no knowledge of surveillance system design, it answers the question "Just how common IS early detection"? For this illustration, we chose the low, conservative, value of 5% (odds = 0.0526), acknowledging the numerous instances globally in which an OsHV-1 introduction has led to spread and comparably few that have achieved containment.

Results

Panelist Participation

The twelve invited panelists included 3 industry representatives from the United States, and 9 shellfish health professionals from the U.S. (5), Mexico (1), Australia (1) and France (2). Two of the panelists (one from the U.S. and one from Mexico) invited an additional expert each to provide shared input, bringing the total number of experts involved in discussion and review to fourteen. The twelve core panelists completed the interview and ranking steps, all twelve completed the weighting step, and all but two of the fourteen experts participated in the discussion. Six panelists revised their weights following the discussion, which changed the median scores for three factors: routine active surveillance (more strength), observational monitoring frequency (less strength), and producer relationship with aquatic animal health professionals (more strength). All but two experts also participated as co-authors.

Factor Identification

Initial interviews with experts identified 34 factors potentially predictive of a surveillance system's early detection capability (Supplementary Table S1). Ranks and revisions to that list produced a consolidated set of 14 factors (Table 1). Three of the original 34 factors were removed as they were noted to be prerequisite to any sound surveillance system. These included (1) animal, lot or farm ID allows farm-level tracing, (2) the laboratories are experienced and approved, and (3) the aquatic animal health professional has a sound working relationship with the Competent Authority. Environmental sampling was also removed as methods and standards are still under development (Liu et al, 2020). The remainder were consolidated if possible to reduce redundancy and highlight observational systems.

Table 1: Factors considered predictive of the OsHV-1 early detection capability of a surveillance system or design. Traits provide benchmarks for judging the sufficiency of the factor on a given farm or for a given region. Traits labelled "a" are optimum.

Active Surveillance Factors	**Traits**
(1) Routine risk-based sampling	(a) Yes. Laboratory testing is conducted routinely (annually or more frequent) independent of morbidity/mortality events. Testing is OsHV-1 targeted to farmed, wild, or sentinel animals of optimum species, age classes or exposure risks, and is conducted at optimum times/temperatures for virus detection. Sample sizes reflect test sensitivity and desired design prevalence and confidence levels.
	(b) Partial. Laboratory testing is conducted routinely (annually or more frequent) independent of morbidity/mortality events, but it is not OsHV-1 targeted. For example, testing is focused on imports/exports, interstate transfers, research, etc., OR, sample sizes do not reflect test sensitivity, desired detection prevalence or confidence levels.
	(c) Low. Laboratory testing is rarely conducted or is poorly tailored to OsHV-1 detection.
Observational Surveillance Factors	**Traits**
(2) Risk-based Focus	(a) Yes. Observations focus on farm-raised animals of optimum species, age, and environmental conditions.
	(b) Partial. Observations focus not on the target population but on neighboring wild or sentinel animals of optimum species, age, and environmental conditions.
	(c) No. Observations are not risk-based. For example, (1) they focus on imports/exports, interstate transfers, research, or harvest dates, OR (2) optimum species, ages, conditions are not available.
(3) Frequency and Extent	(a) Optimal. Observations are representative of the full population, and are conducted at least weekly, whether by visual examination for abnormal appearance or behavior (e.g., gaping), excess mortality, or auditory (clacking shells when cage is tipped) or data-driven (e.g., feed consumption) means.
	(b) Moderate. As above, but only by partial site or only by biweekly-monthly observations.
	(c) Poor. As above, but only by even less frequent or less direct methods of observation (e.g., olfactory or harvest weight).
(4) Background Mortality	(a) Optimal. Mortality rates are monitored, are generally low (e.g., < 10% through the nursery phase), and tolerance thresholds are set (e.g., in terms of degree, persistence and/or geographic scale) to identify unexpected and unexplained events deserving prompt investigation.
	(b) Moderate. Some, not all, of the above.
	(c) Poor. None of the above.
(5) Monitoring and Sampling Guidance	(a) Optimal. OsHV-1 information is made widely available in the region by a trusted source. This information includes observation strategies, as well as diagnostic sampling guidelines. The latter aim to ensure that sample sizes are sound, that dying animals or fresh mortalities (not decomposed) are collected early in the outbreak, and that diagnostic sampling includes live, seemingly unaffected, animals from affected lots as well as the remainder of the farm (including various age groups).
	(b) Insufficient. Trusted, effective guidance is lacking which may lead to delayed recognition or delayed or inadequate sampling.
(6) Early Detection Incentives	(a) Yes. Early detection benefits are clear and compelling and support both the collective industry and individual producers. These might include indemnity, reduced disease spread, clean animals, improved market confidence, and knowledge to support future production cycles.
	(b) Partial. Early detection benefits are clear for the collective industry (e.g., reduction in site-to-site spread), but not for the impacted producer.
	(c) No. Early detection is expected to lead to an inappropriate response of greater consequence than the disease.
(7) Disease Investigation Sampling Ease/Cost	(a) Facilitated. If an investigation is triggered, someone stops by to collect samples, or kits are provided for easy sample packaging and submission, at minimal cost to producer.

	(b)	Moderate. If an investigation is triggered, someone stops by to collect samples, or kits are provided, but this requires substantial effort or charge.
	(c)	Difficult. Neither of the above.
(8) Disease Investigation Testing Cost	(a)	Low. Disease investigation testing costs are low or shared (e.g., with the laboratory or government agency).
	(b)	High. Disease investigation testing costs are high and borne fully by the producer.
(9) Aquatic Animal Health Professional (AAHP)	(a)	Trusted. Relationship with AAHP (whether veterinarian, extension agent, biologist, pathologist) is well-established (e.g., first name basis) and positive (e.g., AAHP is trusted, input is timely and valued), and includes site visits which set strategies for detection and response and potentially an example for other producers.
	(b)	Not trusted. AAHP relationship is limited, or negative.
(10) Reporting Ease	(a)	Optimal. Reporting requirements are clear, and the process is simplified by on-farm data submission tools.
	(b)	Moderate. Reporting is not simplified by on-farm data submission tools, but the communication chain and requirements are clear and straight-forward.
	(c)	Insufficient. Reporting is difficult, or unclear.
(11) Reporting Feedback	(a)	Optimal. Feedback secondary to reporting is timely, interactive, and informative.
	(b)	Insufficient. Feedback is delayed, absent, or of limited value.
(12) Advocates	(a)	Yes. Industry leaders publicly support early detection and reporting (e.g., via training or outreach), and understand the objectives (e.g., to enable early response, not just retrospective data collection).
	(b)	Partial. Industry leaders encourage compliance, but do not provide public statements or are unclear on the objectives.
	(c)	No. Industry leaders do not support the process.
(13) Leading Producers	(a)	Yes. One or more producers are highly knowledgeable about OsHV-1, set strong examples, and are seen as trusted points of contact for other producers as well as aquatic animal health professionals.
	(b)	No. Examples have not yet been set in the region, or producers are not well networked.
(14) Information Exchange	(a)	Yes. Formal mechanisms (e.g., shared databases, communication chains, advisory councils) ensure timely access to disease information relevant to the region such as local OsHV-1 detections or changes in risk status.
	(b)	Partial. Only informal mechanisms (e.g., community networks) are in place.
	(c)	No. Health status information is rarely exchanged.

Estimate-Talk-Revise

Likelihood ratios representing the importance of different surveillance system traits for early disease detection are shown in Table 2. Group statistics show that although the degree of perceived importance varied between experts, in some cases substantially, the experts found all factors instructive. Frequency of observation stood out as the factor most predictive of strong detection capacity, with a median LR of 15. While most factors were fairly balanced as to the relative value of avoiding the worst trait and ensuring the best, others showed greater impact in one direction. For example, avoiding the consequences of a reporting system that is difficult or unclear far outweighs the additional benefit that comes from technological advances enabling reporting directly from the field. Similarly, the lack of any type of active surveillance (e.g., even movement testing) scored very low, essentially crippling detection efforts. Its median LR is 0.02, which is equivalent in strength to an LR of 50 (its inverse). Whereas, equipping a site with top-rated active surveillance (e.g., routine risk-based sampling) was considered to solve only a portion of the detection puzzle (median LR = 6.42).

As a reminder for interpretation: LRs greater than 1 reflect a positive association with early detection capability; LRs less than 1 reflect a negative association. The relative strength of negative and positive association traits can be compared by taking the inverse of LRs less than 1. For example, an LR of 0.25 predicts a negative impact (on early detection) of the same strength that an LR of 4 predicts for a positive impact. An LR of 1 suggests no predictive strength.

Table 2: Likelihood ratio (LR) group median, first (Q1) and third (Q3) quartile, and square root (sqrt) values for factors and traits perceived predictive of a surveillance system's capacity for early detection of OsHV-1. Responses indicating non-occurrence in both hypothetical populations (early and late detection subgroups) suggesting the trait does not occur in the expert's experience base, were not included in the total (n) response count.

Factors	Traits	LR, median	LR, Q1	LR, Q3	n	LR median, sqrt
Active Surveillance						
Routine, risk-based sampling	Yes Partial Low	**6.42** 1.00 0.02	1.60 0.67 0.02	8.25 1.08 0.63	12 12 11	**2.53** **1.00** **0.15**
Observational Surveillance						
Risk-based Focus	Yes Partial No	**3.50** 1.00 0.19	1.92 0.69 0.09	6.50 3.58 0.29	12 12 11	**1.87** **1.00** **0.41**
Frequency and Extent	Optimal Moderate Poor	**15.00** 1.50 0.11	4.00 0.92 0.07	60.00 2.33 0.24	11 11 12	**3.87** **1.22** **0.34**
Background Mortality	Optimal Moderate Poor	**6.42** 1.00 0.06	2.17 1.00 0.02	14.00 1.41 0.35	12 12 11	**2.53** **1.00** **0.27**
Monitoring and Sampling Guidance	Optimal Insufficient	**4.00** 0.22	2.47 0.08	10.75 0.35	12 11	**2.00** **0.47**
Early Detection Incentives	Yes Partial No	**4.00** 1.00 0.17	2.90 0.49 0.02	22.25 1.95 0.23	11 12 11	**2.00** **1.00** **0.41**
Disease Investigation Sampling Ease/Cost	Optimal Moderate Insufficient	**6.00** 1.20 0.13	2.88 1.00 0.02	10.00 1.50 0.31	11 11 12	**2.45** **1.10** **0.39**
Disease Investigation Testing Cost	Low High	**3.00** 0.21	2.17 0.11	7.42 0.46	11 12	**1.73** **0.46**
Aquatic Animal Health Professional (AAHP)	Trusted Not trusted	**3.65** 0.18	2.33 0.11	8.63 0.36	12 12	**1.91** **0.43**
Reporting Ease	Optimal Moderate Insufficient	**2.00** 1.67 0.08	1.83 1.25 0.02	5.00 4.85 0.25	11 12 12	**1.41** **1.29** **0.28**
Reporting Feedback	Optimal Insufficient	**2.17** 0.33	1.48 0.26	4.88 0.52	12 11	**1.47** **0.57**
Advocates	Yes Partial No	**6.50** 1.00 0.07	3.68 0.89 0.02	22.00 1.27 0.15	12 12 12	**2.55** **1.00** **0.26**
Leading Producers	Yes No	**3.10** 0.26	2.00 0.13	4.00 0.33	12 12	**1.76** **0.51**
Information Exchange	Yes Partial No	**4.75** 1.00 0.13	2.48 0.66 0.04	7.88 1.04 0.23	12 12 11	**2.18** **1.00** **0.35**

Example Application

The list of expert-identified factors and traits (Table 1) offers benchmarks for the design of observational surveillance systems for Pacific oyster hatcheries, nurseries, or farms. The LRs (Table 2) can help prioritize (and advocate for) inclusion of specific traits. Their square root median LRs (Table 2) can then be used to estimate SSe (Equations 1, 2), and compare assurances derived from different designs for early detection or disease freedom substantiation.

As an example, we calculated SSe for several hypothetical surveillance systems. Results (Table 3) suggest that observational surveillance can be extremely effective (SSe > 0.95) at early detection if formulated and managed appropriately, with the caveat that our ideal systems optimize all design factors including a risk-based focus on susceptible species, environments, and age-classes. We scripted SSe for systems using observational surveillance only (essentially excluding the first factor, or assuming active surveillance was limited to pre-movement testing, i.e., its LR = 1) and then compared results to confidence derived, at the time of testing, from a standard round of active surveillance. Findings suggest that consistently negative results from optimized observational surveillance provide as much confidence of disease absence as a single round of active surveillance (geared to 95% confidence, e.g., 150 animals assuming 2% design prevalence and a perfect test) in that same population. The critical difference is that the assurance provided by point-in-time active surveillance results naturally wanes over time (from the date of sample collection), whereas assurance derived from ongoing observational surveillance persists as long as the system is operational.

We also imagined less than ideal situations. Several of the predictive factors fall under the control of farm managers, e.g., the timing and focus of observations. Others are in the wheelhouse of regulatory bodies or regional industry associations, such as monitoring and sampling guidance, engaged industry leaders, and incentives for reporting. We examined a scenario in which individual farmers adopt all of the early detection strategies in their control but have limited support from government agencies. We also examined the counter scenario in which a government provides all the support under its control but lacks industry involvement. The low calculated SSe for both scenarios illustrates the importance of industry-government partnerships. Implementing government without industry support, or vice versa, risks a dramatic loss in capacity for early detection.

All scenarios originally assumed active surveillance was limited to pre-movement testing (LR = 1.0). Adding strong active surveillance (sqrt median LR = 2.53) to either of the imperfect partnership scenarios essentially doubles their assurance, but still does not achieve target confidence (e.g., SSe = 0.219 and 0.570 for revised Scenarios C and D, respectively). In contrast, removing all forms (even pre-movement testing) of active surveillance (sqrt median LR = 0.15) drops assurance below 95% in all but the most optimized scenario (e.g., SSe = 0.990 and 0.893 for revised Scenarios A and B, respectively). This suggests that some form of active surveillance, while insufficient as a sole provider of early detection assurance, is an important complement to passive systems.

Table 3: Example use of median LRs (square root values) to model surveillance strength (or System Sensitivity, SSe) for the early detection of OsHV-1. This example presumes that the emerging OsHV-1 genotype would cause morbidity or mortality in the affected systems. System A depicts an optimal observational design for a nursery, wherein all predictive factors are top-rated. An optimal design for a hatchery would score similarly, except for background mortality (which may be stochastic). System B depicts an optimal design for a marine grow-out farm, wherein all factors are top-rated except observational frequency and focus (more difficult to coordinate off-shore). System C depicts a nursery with strong producer participation but limited government support. System D depicts a nursery with strong government support but limited producer buy-in. System E represents routine, risk-based sampling (active surveillance) for comparison. The displayed values are the median square root LRs (from Table 2) for the traits that best describe each system.

Predictive Factors	**A: Optimal Nursery**	**B: Optimal Grow-out**	**C: Producer Only, Nursery**	**D: Government Only, Nursery**	**E: Active Surveillance**
Active Surveillance					
Routine risk-based sampling	1.00	1.00	1.00	1.00	2.53
Observational Surveillance					
Focus	1.87	1.00	1.87	1.87	-
Frequency and Extent	3.87	1.22	3.87	1.22	-
Background Mortality	2.53	1.00	2.53	1.00	-
Monitoring and Sampling Guidance	2.00	2.00	0.47	2.00	-
Incentives	2.00	2.00	1.00	2.00	-
Sampling Ease/Cost	2.45	2.45	0.39	2.45	-
Testing Cost	1.73	1.73	0.46	1.73	-
Aquatic Animal Health Professional	1.91	1.91	1.91	0.43	-
Reporting Ease	1.41	1.41	0.28	1.41	-
Reporting Feedback	1.47	1.47	0.57	1.47	-
Advocates	2.55	2.55	2.55	0.26	-
Leading Producers	1.76	1.76	1.76	0.51	-
Information Exchange	2.18	2.18	1.00	2.18	-
Calculations					
LR sqrt product	12023.321	801.145	2.112	9.965	2.530
post odds (assuming prior = 0.05)	632.427	42.140	0.111	0.524	0.133
SSe	0.998	0.977	0.100	0.344	0.117

Discussion

As aquaculture evolves to meet global food security challenges, the resulting intensification and diversification of production systems may heighten the emergence and international spread of aquatic pathogens (Burge et al., 2014; Feist et al., 2019; King et al., 2019). Aquaculture must balance the pathogen risks inherent to natural settings with the costs and complexities of altered rearing environments that support their bioexclusion (Lafferty et al., 2015). Similarly, surveillance should adapt to address the early detection of not just known but also emerging pathogens. Bivalve mollusc aquaculture industries, providing ecosystem services while marketing an efficient, sustainable, and healthy source of protein, are likely to contribute greatly to future food security. With direct ties to their environments, such industries are particularly vulnerable to climate (Stewart-Sinclair et al. 2020) and pathogen (Pernet et al., 2016) shifts and extremes. We organized an expert panel to direct early disease detection for this globally important and growing aquaculture segment (FAO, 2018), focusing on the example pathogen OsHV-1 for its recent and wide-ranging emergence and consequence (Arzul et al., 2017; Burge et al., 2018; Fuhrman et al., 2019).

Early detection maximizes options available to mitigate spread and production impacts of disease pathogens. Surveillance for early detection, however, is geared very differently than that for disease freedom, though the latter drives most conventional surveillance designs. Typically, disease freedom status is achieved by testing sufficient numbers of animals with sufficiently accurate diagnostic tests, and rests more heavily on the extent of testing than its timing. However, surveillance optimized for disease freedom assurance may be poorly suited for rapid detection should a breach in biosecurity arise, as intermittent surveys are not likely well-timed to rare introductions. Diagnostic testing modalities, even if highly sensitive in laboratory settings, may fail (at early detection) in the field where disease introductions can occur at any point between samplings (Cameron et al., 2020). Consequently, while active surveillance can set the stage for health assessment, early detection surveillance (often based on observation) is a necessary and distinct complement. Unfortunately, observational surveillance typically receives minimal guidance, perhaps because it is assumed that watching for clinical disease requires little more than commitment. However, amidst a rise in globally emerging and high consequence pathogen occurrence, it is important to optimize this critical, and potentially resource-efficient, surveillance component.

Expert elicitation offers a method to identify and weight predictive factors, in this case to optimize surveillance design, when opportunities for their field study are limited. However, human judgment is also subject to biases resulting from heuristics (judgment shortcuts) characterizing human efforts to quickly process and successfully respond to the complex and unending variety of information that life continually presents. Structured group processes have been developed expressly to minimize these biases (O'Hagan, 2019). IGP's independent estimation step, for example, minimizes anchoring, the tendency to adjust estimates toward a starting value, by eliciting values from experts independently and in advance of discussion. IGP also allows the opportunity for internal calibration through its discussion step wherein experts can further clarify terms or share evidence with which they may hone (again independently) their initial estimates. Additionally, we selected experts with first-hand experience in oyster population health to reduce availability bias in which the probability of dire events is magnified by the 'availability' our memories assign to emotional consequences. First-hand experience allows experts to counter this tendency with recall of counts of known events for comparison.

This expert elicitation identified factors deemed essential to surveillance design and estimated their strength as predictors of early detection capacity for OsHV-1 incursions. The factors depict elements important to observational surveillance, including frequency and targeting of observations, disease investigation sampling guidance, degree of background mortality, ease of reporting, advocacy by industry leaders, cost of testing, and incentives for early detection, among others. A resulting model estimates the sensitivity of observational surveillance and, subsequently, the confidence in disease freedom derived from negative reporting. While scripted for OsHV-1, the identified factors may generalize to early detection of other diseases of similar presentation and progression threatening oyster and other mollusc culture industries. However, applicability depends on the pathogenesis of the disease. OsHV-1 has a short incubation period and transmission occurs episodically (Paul-Pont et al., 2013) which can lead to rapid changes in prevalence and spatiotemporal clustering of disease. Diseases of oysters with different epidemiologic characteristics, e.g., diseases progressing slowly or affecting animals less acutely, will require separate assessment.

Observation frequency eclipsed the other factors in its strength as an indicator of early detection capacity. While obvious in its direct link to timing, this result also highlights the limitations inherent in conventional (test-based) surveillance systems that simply cannot afford the necessary repetition. Elicitation results project a large drop in capacity between systems observing animals weekly and those structured around annual or even seasonal observations. Certain farming conventions may not have this degree of visual attention, e.g., if animals are held offshore, continually submerged or simply handled on a limited basis. For these settings, especially where risks of OsHV-1 introduction – and benefits of early detection – are high, the elicitation results raise the importance of investigating alternative monitoring arrangements. These might include the use of remote technologies, monitoring of sentinel or neighboring populations, environmental sensors, or other novel approaches to health assessment (Rana et al., 2020).

Several factors varied substantially among experts in degree of perceived predictive strength. We expect this variability can be attributed in part to factor wording, also in part to the wide differences in oyster rearing practices under consideration. For example, experts varied in the degree to which they considered incentives key to surveillance function. Discussion revealed that the wording describing the traits grouped indemnity (clearly important to producers) with several other less impactful outcomes. If indemnity had been rated separately, discussions suggest it would have ranked higher and resolved some of the divergence in existing scores. The observation that divergence in interpretation of factor wording led to divergence in elicitation response highlights the importance of clear communication strategies when applying regulatory and management recommendations in the field.

While we aimed for conditional independence between factors (O'Hagan, 2019), some overlaps may remain. For example, industry advocacy for early detection was a strong predictor of early detection capacity, suggesting the importance of internal leadership which is often touted as a critical factor in organizational change (Gustafson et al., 2003). However, industry leaders may also influence producer buy-in of incentives (possibly a dependent factor). Redundancies between factors can exaggerate outcomes of predictive models, essentially over-crediting redundant components. In our model overlaps between industry advocacy and producer buy-in could be solved by re-wording and combining them into a single joint factor. Alternatively, approaches to estimate the correct weights to assign to joint probability distributions in expert elicitation have also been described (O'Hagan, 2019). However, as these particular factors represent different actionable items (advocating versus designing incentives), we left them separate for instructional purposes. Regardless, social and cultural norms and behaviors can influence surveillance efficacy (Brugere et al., 2017), and should be key considerations in surveillance design.

Any occurrence of disease is unfortunate and, especially in an open marine environment, often of lasting consequence (Lafferty et al., 2015; Burge et al., 2018). Further, the emergence of a shellfish pathogen may have little to do with industry activities, e.g., originating instead via biofouling or ballast water on oceanic vessels, rafting of marine organisms on storm debris, an unregulated growing market for exotic oysters, or consumer mishandling of raw seafood or wastes (Whittington et al., 2018). Nevertheless, early detection can deter subsequent spread onto commercial farms, or between farms or regions. Early warning is even more important for industries with centralized stages of production, and potential for rapid dissemination through animal distribution, as is the case for mollusc seed and larvae. In fact, seed transfers are thought to have magnified OsHV-1 spread in many affected countries, with a noted exception of Australia where response in the form of movement restrictions was particularly rapid

(Fuhrmann et al., 2019). Early detection also affords individual producers the opportunity to adapt their production practices to mitigate losses, e.g., whether via limiting movements, overplanting, seeding with resistant or older stock, reducing biofouling, limiting cage densities or handling, altering rearing practices to minimize exposure, or establishing early markets, among other strategies (Guillotreau et al., 2017; Ugalde et al., 2018; Rogers et al., 2019). Finally, although marine water currents are pervasive, environmental conditions impact the distance and time a pathogen is able to travel outside a host (Hick et al., 2016; Aalto et al., 2020; Lupo et al., 2020). Accordingly, reductions in pathogen load through early removal of affected lots may help contain waterborne spread of pathogens, even in marine settings (Gustafson et al., 2007).

The elicitation results can be used in several ways. First, the factors (Table 1) provide a checklist of items critical to the design of surveillance geared for early OsHV-1 detection, wherein the associated descriptions of optimal versus moderate or poor traits offer benchmarks for strategic planning. Second, since traits vary by system, the probability of early detection will also vary by system. As LRs and SSe both reflect early detection capacity (univariable versus multivariable respectively), the relative value of proposed surveillance designs or enhancements can be judged by these metrics. Third, SSe, a core parameter in disease freedom calculations, here represents the confidence derived from negative reporting. Thus, these measures can be used retrospectively to support disease freedom claims. It is also worth emphasis that this particular SSe is scripted for early - rather than any – detection. Consequently, resulting disease freedom estimates are likely conservative, i.e., biased in the direction of under-estimating confidence in disease absence.

Finally, results applied to hypothetical scenarios demonstrate the broad range in detection capacity that different surveillance designs might provide. It is interesting to note that intermittent (annual or twice annual) active surveillance showed limited capacity for early detection. In contrast, observational systems comprising most, or all, of the advantageous attributes scored very high in capacity for early detection, with projected system sensitivities exceeding 95%. Consequently, the supposition that active surveillance systems geared to disease freedom demonstration will also support early detection may be false. Rather, they appear opportunistic at best for early detection of a new disease occurrence. In stark contrast, our examples suggest that well-designed observational systems can strongly support both early detection and disease freedom claims, as long as the monitoring is focused on pathogens, species and contexts in which disease is expected to manifest clinically (or via mortality). In fact, per this model, consistently negative results from an ideal passive surveillance system (which optimizes all design factors) provide as much confidence of disease absence as a recent round of active surveillance geared to 95% confidence in that same population. The difference is that active surveillance results lose confidence through time, whereas ongoing, trusted systems for observational surveillance do not. A caveat is that season and other factors influence the transition from a subclinical infection only detectable by active surveillance (Whittington et al., 2019). However, these nuances also influence the value of active surveys as subclinical infections may also subsist at low prevalence, and thus fall under the detection threshold of systematic testing.

Importantly, the estimated capacity for early detection depends not just on the predictive factors, but also on the prior expectation that early detection occurs in general (Equation 1). Consequently, the choice of a prior can highly influence model outcomes. Experts' thoughts about the best prior for this exercise ranged from essentially zero to 0.1, from which we selected 0.05. We might have improved precision and accuracy by establishing a unique prior for each country or production type (e.g., highest for nurseries where animal behavior and production measures are simpler to monitor, lowest for grow-out settings where animals are continually submerged or inaccessible). But, to facilitate discussion, and since our purpose was to compare hypothetical designs, we used a single value for these examples.

The same examples predict a stark contrast in early detection capacity between systems with solid industry and government support, versus those lacking one or the other. Observational surveillance systems supported optimally by both government and industry were predicted to have an exceptionally strong capacity for early detection. In contrast, systems lacking external support were projected to perform poorly even if individual farmers exceled at every measure in their control. Similarly, systems with sound governmental aquatic animal health infrastructures were projected to perform dismally at early detection without the buy-in of individual farmers. Interestingly, approximately half of the identified factors are under government and the other half under industry control, yet their combined effects were not linear. For example, the model suggests that absence of a strong partnership reduces capacity for early detection by much more than half. This is explained by the extremes to which the worst, compared to best case, traits sometimes fell. As the SSe model is multiplicative, a single trait with a very low LR can negate the aggregate value of several beneficial traits. For example, if industry leaders do not publicly support surveillance (sqrt LR = 0.07), this low value cancels the combined benefits of government-funded testing (sqrt LR = 3), technologies to simplify reporting (sqrt LR = 2), and efforts made to improve feedback (sqrt LR = 2.17), as their product (0.07, 3, 2, and 2.17) is less than 1. The traits with the lowest LRs (most detrimental to early detection) in this analysis were the lack of *any* routine testing, the lack of strong industry advocates, high background mortality in the monitored populations, and reporting processes that are difficult or unclear.

There are several caveats to this study. Subjective probabilities sometimes exaggerate extremes, with experience source (direct versus learned) thought to impact extreme value occurrence and degree (Hertwig et al., 2004). Further, the number of factors included in a model can magnify this effect. Consequently, comparisons of active to passive systems (here comprising different numbers of factors) may be more error prone than comparisons between passive systems (with the same number of factors). We followed a structured elicitation process to improve estimation accuracy and applied a square root transformation to mitigate the overconfidence (O'Hagan, 2019) and exaggeration of extreme values that sometimes accompanies subjective probability estimation (Kynn, 2008). Additionally, our focus on early detection biases subsequent disease freedom estimates in a conservative direction (under-estimating confidence). However, the LR magnitudes and modelled quantities are preliminary. When and if field data become available, these results should be tested and revised to reflect empirical findings.

Nevertheless, these results offer expert guidance in the design of observational surveillance for the early detection of OsHV-1 incursions. They also illustrate a new approach to estimating the capacity for early disease detection (SSe) and, retrospectively, the disease freedom confidence associated with different surveillance designs. We conclude that observational surveillance can be a very strong tool in the early detection of OsHV-1 emergence. However, its strength depends on the inclusion of key design elements that, among others, (1) direct attention to highest-risk sub-groups, (2) guide effective investigation of abnormalities, (3) advocate and incentivize reporting, and (4) foster strong partnerships between industry and government or other supporting agencies. This evaluation centered on OsHV-1 detection in oyster populations; although, many of the features likely generalize to other pathogens and cultivated species, with the important caveat that the pathogens need manifest clinically (or via mortality events) in the species, life stages and environments under observation. Further, the utility of surveillance depends on adequate preparedness to subsequently implement effective mitigation strategies, which were outside the scope of the current study. However, given the expense of testing, and the potential averted loss value of early detection, well-designed observational surveillance appears a high-value tool for health management and disease prevention.

Conflict of interest none OsHV expert elicitation

There are no conflicts of interest to declare for this article (“Optimizing surveillance for early disease detection: Expert guidance for Ostreid herpesvirus surveillance design and system sensitivity calculation”) focused on optimizing surveillance for the early detection of an oyster pathogen.

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