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REVIEW

REVIEWS IN Aquaculture

The rise of the opportunists: What are the drivers of the increase in infectious diseases caused by environmental and commensal bacteria?

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Abstract

The aquaculture sector is currently experiencing a global disease crisis. Emerging bacterial diseases—often opportunistic or syndromic—have collapsed production in nations across the world. Losses in the shrimp industry associated with opportunistic *Vibrio* spp. exceed 40% of global capacity. This paper reviews potential drivers of syndromic diseases involving opportunistic bacterial pathogens affecting global aquaculture. We provide key examples from major industries where such conditions have prompted greater antibiotic use and have resulted in significant mortality. We challenge the conventional definitions of opportunistic pathogens and propose a fluid categorisation that acknowledges the continuum of host adaptation and the complexity of microbial ecology. We discuss the implications of environmental and dietary stressors such as climate change, coastal eutrophication and pollution, and the transition to plant-based feeds, which have been linked to impaired epithelial barrier function, gut health disorders and increased disease susceptibility. We critique the 'one-pathogen one-disease' paradigm, suggesting that Rothman's causal pie model is more useful for understanding opportunistic infections as it emphasises the multicausal nature of disease. We provide examples of bacterial and viral interactions in aquatic disease and occurrence of bacterial diseases resulting from host damage from eukaryotic parasites or increasing frequency and severity of interventions to control such parasites. We recognise the need for corroborative evidence to validate the rise of opportunistic bacterial pathogens as a global trend, and we advocate for the application of nuanced disease causation models to reduce the incidence of opportunistic infections and improve the sustainability of the aquaculture industry.

KEYWORDS
aquatic health and welfare, climate change, disease causality, disease ecology, microbial evolution

1 | THE RISE OF THE OPPORTUNISTS

Climate change, anthropogenic stressors and the rapid intensification of the aquaculture sector have resulted in a global disease crisis.[1,2] Shifts in climate patterns and the increased frequency of extreme weather events are altering the incidence, severity and geographic distributions of disease outbreaks,[3,4] with much of the risk of emerging disease concentrated in tropical and subtropical aquaculture regions where industry growth and need is greatest.[5,6]

Most emerging and re-emerging diseases have cryptic or syndromic aetiology, with growing consensus that the shrimp industry is experiencing a 'rise of the syndrome', characterised by the surge in sub-optimal growth disorders (reviewed in the study by Kooloth Valappil et al.[7]). The emergence of 'monodon slow growth syndrome' in *Penaeus monodon* was first noted in Thailand between 2001 and 2002,[8] with severe cases leading to 30% of farmed stock with significantly low average body weights. Similar disease presentations of unusual slow growth and wide size variations have been recorded in India[9] and East Africa.[10] Sub-optimal growth disorders in *P. monodon* have been cited as a reason for changing the farmed species to *Litopenaeus vannamei* in Thailand.[7] Similarly, the emergence and re-emergence of complex bacterial septicaemic syndromes in Norwegian salmonid aquaculture has resulted in increased antibiotic consumption in the period between 2015 and 2022 in an industry where the need for antimicrobials had been largely eliminated through vaccination programmes since the early 1990s.[11,12] Indeed, mortality of farmed salmon during grow-out phase reached an average of 16.1% in 2022, increasing to 16.7% in 2023, with the highest mortality production zone reaching 23.7% in 2022 and 25.5% in 2023.[13,14] Mortality figures in 2023, both in number and percentage, are the highest recorded so far for salmon in the grow-out phase in Norway. These elevated mortalities are associated with the development of disease syndromes including winter ulcer disease and complex gill disease. Winter ulcer disease, caused by *Moritella viscosa* and/or *Tenacibaculum* spp., constitutes the biggest health and welfare challenge related to bacterial diseases in Norwegian aquaculture. Skin wounds are not subject to notification and there are no precise figures, but their diagnosis has increased and there is widespread perception in the industry that the prevalence of winter ulcer disease across the country has worsened significantly in recent years.[15,16] In the tropics and subtropics, many of the bacterial diseases of tilapia (*Oreochromis niloticus*) described in recent reviews could be classed as opportunistic,[17,18] including those caused by motile *Aeromonas*, *Flexibacter*, *Edwardsiella* and *Streptococcus*.

2 | WHAT IS AN OPPORTUNIST?

Defining opportunistic bacterial pathogens is not straightforward. A good starting point is the simple ecological definition proposed by Brown et al.[19] viz. opportunistic pathogens are non-obligate and/or non-specialist parasites of a focal host.[19] Here, the term parasites refers to organisms, in this case bacteria, characterised by their fitness-reducing effect on their host.[20] Further subcategorization of the definition of obligate pathogens as proposed by Brown et al. is useful in evolutionary modelling of human clinical disease (Figure 2a) but becomes much more difficult in aquatic ecosystems. With possibly 48,000 extant species of fish, even highly host-adapted bacterial pathogens may cause disease in multiple species, therefore defining a focal host akin to 'human' is constraining. For aquatic disease models, we propose that obligate bacterial parasites are placed on a continuum of increasing host adaptation from broad generalists to single species specialists such as some viruses and helminth parasites (Figure 2b). Similarly, the differentiation of environmental and commensal opportunists proposed by Brown et al.[19] is much more fluid in aquatic systems where animals live immersed in richly diverse microbial ecosystems and drink them continuously. For example, *Tenacibaculum maritimum* is often found in the skin mucosae of non-diseased marine fish, invertebrates and mammals,[21–24] but is also found in sediments and seawater.[23,25] We cannot, therefore, define *T. maritimum* as an environmental or commensal opportunist, but rather as both. Similarly, members of the genera *Photobacterium* and *Vibrio* are the most abundant facultatively anaerobic heterotrophs found in the digestive tract of marine fish and invertebrates,[26,27] yet are also ubiquitous in marine waters and phytoplankton.[28–30] Consequently, a more fluid categorisation of opportunists is proposed to reflect the complexity of aquatic microbial ecology, in which obligate bacterial parasites exist along a continuum of specialisation, whilst facultative bacterial parasites can be interchangeably environmental and commensal opportunists (Figure 2b).

3 | UNEQUAL OPPORTUNITIES

Even in the aquaculture community, there is robust discussion over whether certain pathogens are opportunists or specialists.[31–33] This is unsurprising as within a species of bacterial opportunists there exists a non-static parasite-mutualist continuum where some strains or isolates will have, or develop, greater potential to damage the host than others via horizontal gene transfer (HGT) or phenotypic plasticity driven by host or environmental conditions.[34] Evolution along this continuum may increase or decrease virulence and, at its most extreme, highly host-adapted primary pathogens may arise from commensal opportunists. For example, in an evolutionary trajectory mirroring the evolution of the plague bacterium *Yersinia pestis* from the environmental generalist *Yersinia pseudotuberculosis*, highly virulent *Photobacterium damselae* subspecies *piscicida* evolved from a subclade of the commensal opportunist *P. damselae* subspecies *damselae* through a combination of chromosomal gene loss and acquisition of plasmids.[35] In the case of opportunists, the presence of a plasmid or an additional gene copy may increase the potential for a strain to cause disease but may be insufficient on its own. For example, there are strains of *Vibrio harveyi* and *P. damselae* subsp. *damselae* with greater potential for disease, influenced by phage and plasmids respectively but there are generally other causalities required for overt disease.[36–39] More subtly, phenotypic plasticity of the pathogen

may contribute to outbreaks of disease when environmental conditions such as salinity[40] or temperature[41,42] modulate gene expression in *P. damselae* and *Lactococcus garvieae*, respectively.

4 | RETHINKING DISEASE CAUSATION MODELS

While historic focus on a 'one-pathogen one-disease model' for specific (listed) pathogens has undeniably been critical in alerting the community of emerging issues, this pathogen-centred approach, based on Koch's postulates and germ-theory from the 19th century, has constrained research to specific facets of those pathogens, at the expense of investigating the very context in which they occur (host, microbiomes and environment).[2] Even Koch had to bend the strictest interpretation of his first postulate (pathogens are only found in diseased, but not healthy individuals) when he discovered asymptomatic carriers of *Vibrio cholera*.

A familiar model of disease causation is the disease triad[43] (Figure 2). This model elegantly encapsulates disease causation within a tripartite Venn Diagram intersecting host, pathogen and environment (Figure 3a). While this model can still be used to delineate the aetiology of diseases caused by highly host-adapted pathogens, it falls short in addressing the multifaceted interactions that characterise diseases arising from opportunistic pathogens. Such complex scenarios demand more nuanced frameworks that can dissect and illustrate the causal factors culminating in clinical disease.

Rothman's causal pie model[44] (Figure 3b), provides a fitting framework for diseases caused by opportunistic pathogens. This model accommodates the concept that diseases, particularly those with syndromic aetiologies, may result from diverse causal mechanisms, each involving multiple contributory factors. The model's strength lies in its emphasis on multicausality, whereby a sufficient cause of disease is a constellation of component causes, the causal pie, that leads to an outcome, and a component cause can be a component of more than one causal pie.[44] For example, exposure to someone who has tuberculosis (TB) does not necessarily result in the occurrence of TB. Moreover, the set of determinants that produce TB in one individual may not be the same set of conditions that were responsible for the occurrence of TB in others. In this conceptual model, the pathogen (e.g., *Mycobacterium tuberculosis*) is considered a necessary cause—a component cause that is essential for the manifestation of a disease, yet not solely capable of inducing the disease as a sufficient cause without the concurrent presence of other contributing factors. For instance, syndromes such as AHPND or winter ulcer disease may implicate *Vibrio parahaemolyticus* or *M. viscosa*, respectively, as primary agents. However, the full expression of the disease, which often presents as a continuum within a population, requires additional component causes.[7,15]

A disease that can be explained using the causal pie model framework is Pacific Oyster Mortality Syndrome (POMS) caused by ostreid herpesvirus 1 (OsHV-1). In a very elegant study using field-based observations and controlled laboratory infection models, Oyanedel et al.[45] demonstrated that POMS is a polymicrobial disease characterised by a web of interdependencies and synergies between the virus (OsHV-1) and associated *Vibrio* spp. (*V. harveyi and V. rotiferianus*). The authors of this study demonstrate that both the viral and bacterial components of POMS are needed to induce oyster mortality, and the combined effects of these agents triggered faster host death than that observed when the microorganisms were used in isolation. In other words, the causal pie model for POMS includes at least the viral (OsHV-1) and bacterial components (certain *Vibrio* spp.), in addition to host and environmental risk factors. The complexity of the microbial interactions in POMS can be captured in the pathobiome conceptual model proposed by Bass et al.[46] Strategies to mitigate this disease could therefore consider *Vibrio*-specific control strategies, such as vibriophages[47] or quorum-quenching molecules[48] to disarm bacterial communication, or the priming of the oyster's immune system with OsHV-1 antigen (de Kantzow et al.[49]). Deciphering the complex causal relationship of opportunistic infections by assembling the causal pie model will allow us to establish targeted preventive approaches to mitigate their impact on the health and welfare of aquatic animals.

5 | CHALLENGES CONTRIBUTING TO THE RISE OF THE OPPORTUNISTS

A confluence of challenges is contributing to the rise of opportunistic infections affecting global aquaculture. These challenges include environmental, dietary, production intensification and emerging viral disease challenges. One of the common denominators is that most of them have a direct or indirect impact on host immunity, including the first line of defence of aquatic organisms, the mucosal epithelial barriers in the gut, skin and gills.

Influenced by climate change, coastal marine and estuarine environments are experiencing higher average temperatures, greater frequency of extreme temperature events and altered salinities.[50] These changes generate stress in aquatic organisms, reducing immunocompetency and increasing disease susceptibility. Increased water temperatures have a profound impact on skin barrier functions[51] and may induce dysbiosis by increasing the load of opportunistic pathogens in the *Vibrionacea* family.[52] Higher water temperatures also increase *Vibrio* loads in the water, with the taxa being labelled the 'microbial barometer of climate change'.[53] Importantly, there is evidence of a tight interaction between temperature and antimicrobial resistance in aquaculture.[6] Climatic factors, alongside the escalating eutrophication of coastal zones, have also amplified the incidence of harmful algal blooms, with recent catastrophic losses in the salmon industry in Chile.[54] These blooms are also implicated in the rise of complex gill disease disorders,[55] occasionally resulting in devastating outcomes for farmed fish populations.

Environmental pollution is one of the most serious problems affecting human and animal health.[56] In humans, death by non-communicable diseases attributable to pollution has been estimated to reach 20%–25%.[57] There is now compelling evidence that environmental pollutants and xenobiotics disrupt the immune system and

critical epithelial barrier functions in both mammals and fish. Epithelial barriers are an intricately complex interface between the animal and its environment, fulfilling multiple roles in homeostasis, highly selective transport and permeability, as well as defence. Disruption of epithelial barriers leading to leakiness underly most chronic and debilitating illnesses in humans.[58] Surfactants used as emulsifiers in processed foods (and extruded feeds),[59–61] in dishwasher detergents[62] or as wetting agents in agricultural pesticides[63] are responsible for epithelial damage, leaky gut and autoimmune disease in humans. Aquatic animals are particularly exposed to a high variety of pollutants including pesticides, herbicides, medicines, surfactants and other products through wastewater, agricultural practices and run-off that impact our shared water resources (Figure 1).

An important xenobiotic receptor that mediates the effects of environmental pollutants is the aryl hydrocarbon receptor (AhR) (reviewed by the study by Segner et al.[64] and Suzuki et al.[56]). Xenobiotic receptors, including the AhR, sense and respond to environmental pollutants by activating the expression of detoxification enzymes to protect the body, but chronic activation of this receptor leads to inflammation and immunotoxicity. The immunological role of the AhR is particularly relevant in epithelial barriers like the skin or the gut as they are the first sites where the immune system encounters with exogenous AhR ligands. Xenobiotics that act as agonists of the AhR can interfere with immune functions, including disturbance of the intestinal microbiome and gut health. A study in adult zebrafish exposed to model pollutants (atrazine, estradiol and polychlorinated biphenyls) determined that xenobiotics can impair intestinal and hepatic physiological activities, including gut motility, epithelial permeability, inflammation and oxidative stress, inducing the dysregulation of the intestinal microbiota, and this process involved the AhR and, to a lesser extent, the oestrogen receptor.[65]

Meticulous epidemiological investigations of a cryptic mortality syndrome affecting lobsters were recently attributed to environmental xenobiotics.[66] The study prompted the revision of Sniezko's disease triad to a tetrad model that places anthropogenic inputs into their own category, separate from the environment.[66] This is very useful as it not only raises awareness of the effects of aquatic pollution on animal health but also identifies possibilities for mitigation. There is increasing evidence of pollutants being contributory causes to aquatic animal disease, including fish, oysters, crustaceans, algae and corals through both acute and subacute effects at concentrations that can be well below recommended safety limits.[67–70] Exposure of farm fish to agricultural pesticides may also occur through feed ingredients with the move to increased inclusion of vegetable proteins. Indeed mixtures of contaminants in fish feeds have been shown to impact Atlantic salmon.[71] A revision of permissible pesticide and surfactant residue levels in water and feed ingredients is urgently needed as more data on subacute and contributory cause become available.

Dietary challenges are also contributing to the rise of the opportunist and to reduced disease resilience in aquaculture species. In response to sustainability concerns and the cost of marine-derived feed ingredients, the last decade has seen the aquaculture sector pivot towards plant-based feeds, diminishing the inclusion of fishmeal (FM) and fish oil (FO) in the diets of carnivorous species of high economic value.[72] In Norway, the use of FM and FO in Atlantic salmon diets has decreased from 90% (65% FM, 24% FO) to less than 30% (14% FM, 10% FO) in the last few decades.[73] This transition has been linked with the emergence of gut health disorders, notably increased inflammatory conditions and intestinal permeability, termed 'leaky gut syndrome'. Anti-nutritional factors, such as saponins in legume meals, induce gut inflammation, tight junction disruption and oxidative damage, leading to increased gut permeability.[74–76] Soybean-induced enteritis has been in fact adopted as a model to study inflammatory responses in the gastrointestinal tract of carnivorous fish.[75] In fish fed low levels of essential omega-3 fatty acids, EPA and DHA, present in FM and FO, inflammation and impacts on gut histomorphology are further exacerbated under chronic stress conditions.[77] In contrast, increasing dietary levels of EPA and DHA improve growth, welfare, robustness and fillet quality of Atlantic salmon, and even improve feed utilisation during stressful events such as delousing.[78] Authors of this study suggest that current inclusions levels of EPA and DHA in the diet of Atlantic salmon should be revised to improve disease resilience.

Dietary challenges render hosts more susceptible to opportunistic pathogens.[79,80] However, what is even more concerning is that inflammatory conditions in the gut can favour the emergence of virulent bacterial strains from commensal symbionts. Experiments with clones of commensal *Escherichia coli* in the intestines of young and ageing mice provided direct evidence that inflammatory conditions in the gut favour evolution of more pathogenic strains.[81] In complex, open microbial communities such as those found in the gut, these inflammatory conditions may, therefore, contribute to the rise of opportunistic infections and the emergence of virulent strains from commensal symbionts by favouring HGT, which is a major driver of the evolution of symbiotic relationships.[82,83]

The rapid intensification of the aquaculture industry has been the source of anthropogenic change on a massive scale. Aquatic animals have been displaced from their natural environment and cultured in high densities providing ideal conditions for the emergence and spread of disease.[84–86] Most, if not all, diseases of farmed fish originate in wild populations. However, aquaculture settings create ideal conditions (e.g., high host densities) for pathogen amplification and the spillback to wild fish populations. For sea lice (*Lepeophtheirus salmonis*) in the northern hemisphere, particularly Norway, this creates a vicious circle of increasing disease risk. Strict regulations are in place to protect wild fish by forcing farmers to keep sea lice levels low, increasing treatment frequency. This, in turn, causes stress and increases host susceptibility to infectious diseases, which generally originate in wild fish populations in the first place. These infectious diseases are then amplified and spill-back to wild fish, and this has contributed to a continuous emergence of viral diseases in aquaculture.[87,88] To make matters worse, sea lice have also become resistant to most available chemical antiparasitic treatments,[89] increasing the use of alternative methods involving mechanical and thermal delousing technologies, leading to poor mucosal health (skin and gills) favouring the emergence of opportunistic pathogens.[89–91]

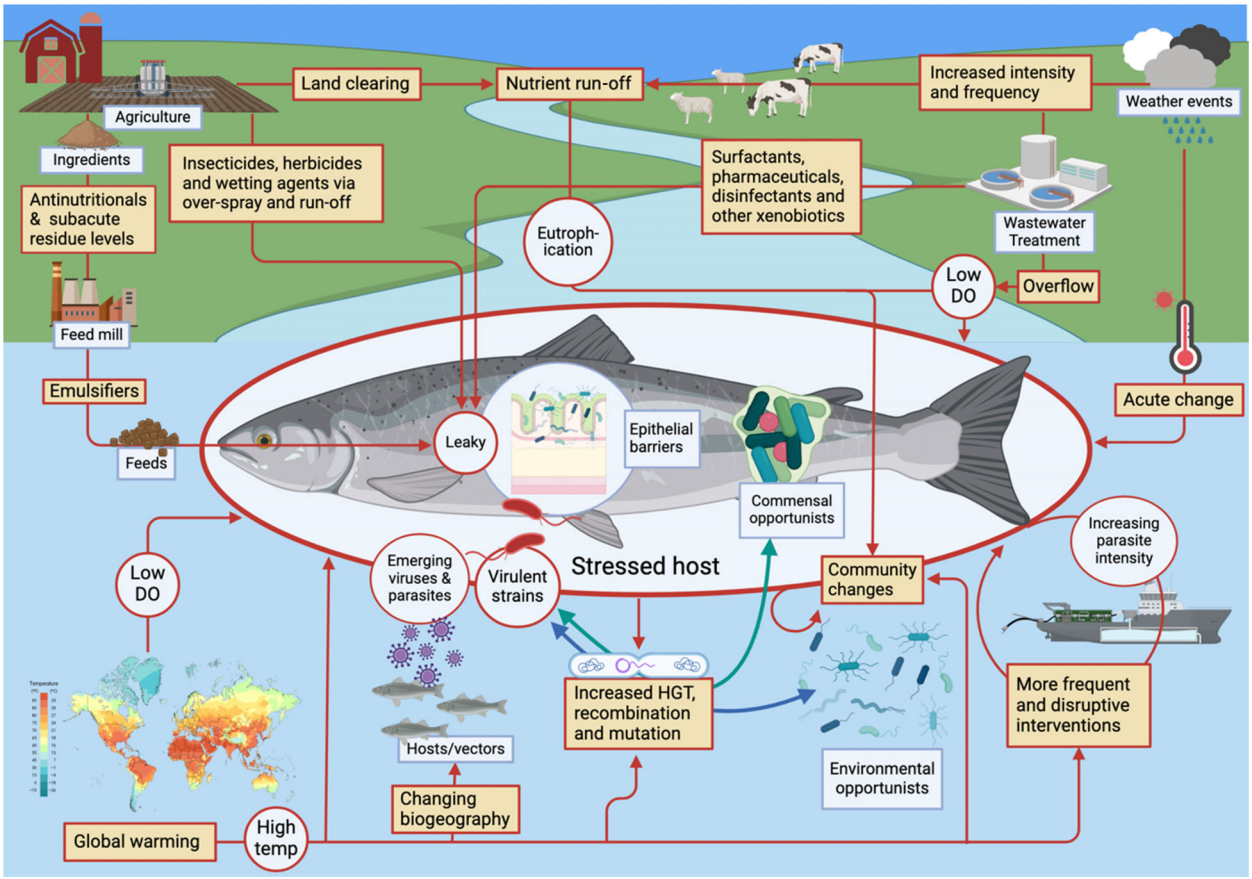

FIGURE 1 Factors contributing to the rise of the opportunists. Factors include environmental challenges (global warming, increased frequency and intensity of extreme weather events, environmental pollution and xenobiotics, and nutrient run-off), dietary challenges (antinutritional factors, residues and emulsifiers in aqua feeds), production intensification challenges (increased frequency of disruptive interventions such as parasite treatments, changing biogeography), and emerging viruses and parasites. Here, we use the term parasites to include, for example, sea lice, amoeba, flukes and myxozoans. Damage to epithelial barrier functions (leaky barriers) mediated by environmental stressors and feed may favour infections with commensal and environmental opportunists. Virulent strains may also emerge from opportunists through horizontal gene transfer (HGT), recombination and mutation. In the figure, orange boxes with red borders represent effectors; red border circles indicate effects (e.g., changes in dissolved oxygen, DO); red arrows indicate links; double headed arrows indicate a continuum with movement in both directions and light blue boxes are labels for elements in the figure.

Novel viral challenges are also contributing to secondary opportunistic bacterial infections and disease syndromes.[87] For example, scale drop disease syndrome is a novel disease affecting farmed barramundi (*Lates calcarifer*) in Southeast Asia. The disease is believed to be caused by a novel *Megalocytivirus*, but histopathological observations in both naturally and experimentally infected fish suggested the involvement of toxins produced by opportunistic *V. harveyi*.[92] Similarly, Tilapia lake virus (TiLV), a novel orthomyxo-like RNA virus, has recently been reported to cause infection in cultured and wild tilapia globally, and co-infection between TiLV and other bacterial pathogens, including opportunistic agents such as *Streptococcus agalactiae*[93] and *Aeromonas veronii*,[94] contributes to higher mortality. Using controlled infection models, Lukman et al.[93] demonstrated that significantly higher cumulative mortalities were recorded for co-infected tilapia (73% for *S. agalactiae*-TiLV) compared to single infection (40% for TiLV and 20% for *S. agalactiae*). To date, no therapeutics or commercial vaccines exist for TiLV disease control.[95] Therefore, similar to the POMS example above, and using the causal pie model framework, a more comprehensive understanding of co-infections will open new avenues to promote fish health. These may include traditional husbandry practices targeting component causes of the *causal pie* such as reducing bacterial loads by ensuring optimal water quality[96] or using low levels of oxidising agents for temporary water quality improvement.[97] By further capturing epidemiological data and mechanisms for infectivity and virulence during co-infections, treatment regimens may be customised for enhanced efficacy. Correctly identifying the role of pathogens in a co-infection will allow for the appropriate and judicious selection of antibiotics or chemical treatments. A customised approach could also involve the development of autogenous vaccines for local serotypes of variable pathogens[98] targeting bacterial agents contributing to the mortality induced by viral agents, such as TiLV, reducing its burden.

The intensive farm environment has also been shown to promote the evolution of virulence of opportunistic pathogens.[99] For example,

(a) **Ecological classification of human pathogens with examples from Brown *et al.* (2012)**

	Obligate parasite	Facultative parasite
Specialist on humans	*Mycobacterium tuberculosis*, HIV	**Commensal opportunists**: *Staphylococcus aureus, Enterococcus faecalis, Streptococcus pneumoniae*
Non-specialist on humans	**Parasite opportunists** (zoonoses): *Borrelia burgdorferi*, *Salmonella* spp. Rabies	**Environmental opportunists**: *Pseudomonas aeruginosa, Burkholderia cepacia, Vibrio vulnificus*

(b) **Ecological classification of aquatic bacterial pathogens with examples**

	Obligate parasite	Facultative parasite
More host-specialised	*Aeromonas salmonicida* subsp *salmonicia* (Salmonids) *Photobacterium damselae* subspecies *piscicida* (some marine fish) Betanodavirus (most marine fish) *Vibrio parahaemolyticus* (fish, molluscs, crustaceans)	**Commensal opportunists**: *Vibrio harveyi, Photobacterium damselae* subspecies *damselae, Moritella viscosa* **Environmental opportunists**: *Aeromonas hydrophila* group; *Tenacibaculum maritimum*
More generalist		

FIGURE 2 Ecological classifications of human and aquatic pathogens. The model proposed by Brown et al.[19] (a) is unsuitable for the aquatic environment where there is greater interchange between host and environment, represented in (b). The term parasite in the headings refers to the broad definition of a parasite based on the nature of the interaction with host and is carried through from Brown et al.[19]

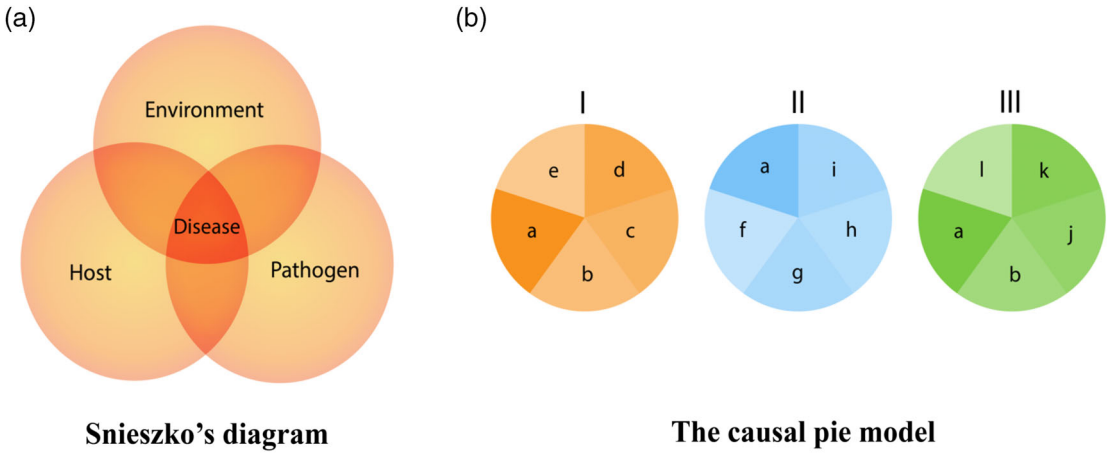

FIGURE 3 Models of disease causation. (a) Sniesko's diagram was first published in a manuscript reviewing the effects of environmental stress on outbreaks of infectious diseases of fish,[43] highlighting the multicausality of diseases in aquatic systems. This model, however, falls short in addressing the multifaceted interactions that characterise diseases arising from opportunistic pathogens, which is better captured by the causal pie framework. (b) In this model, component causes a—l add up to sufficient causes I–III, but every sufficient cause consists of different component causes. Component cause a, which appears in every causal pie producing the same outcome is called a necessary cause of disease.

isolates of the globally distributed opportunistic pathogen *Flavobacterium columnare* have shown increased virulence between the intake and outlet of aquaculture farms in Finland.[100] Intensive farming environments, with high host density, are evolutionary hotspots for virulence evolution in pathogen populations as they enhance transmission and frequency of infections.[100,101] Another key example is the evolution of a hypervirulent strain of the opportunistic pathogen *Aeromonas hydrophyla* which has emerged as the etiologic agent of epidemic outbreaks of motile Aeromonas septicemia in high-density aquaculture of carp in China and catfish in the United States.[102] While hosts are alive, pathogens with high virulence tend to have higher transmission rates than strains with low virulence. However, high virulence strains tend to truncate infectious periods by killing their hosts, and thus, pathogen fitness may be evolutionarily optimal at intermediate levels of virulence.[101] Disease modelling predicts that host density alters optimal virulence because the fitness gain of increased infectivity increases with the number of available hosts, but the fitness costs of truncating infection does not. Consequently, increases in host densities can lead to evolutionary increases in virulence even in the absence of a trade-off between infectivity and virulence, as high host densities allow for the maintenance of pathogens that would otherwise kill hosts too quickly to persist.[101]

6 | MANAGEMENT OPTIONS AND POTENTIAL SOLUTIONS

Addressing the rise of opportunistic pathogens in aquaculture needs a holistic strategy encompassing immediate and long-term solutions. Current available interventions include vaccines, such as whole-pathogen-inactivated vaccines, that confer immunity against host-adapted pathogens. Vaccination strategies are effective against bacterial pathogens, but we cannot vaccinate against all bacterial pathogens involved in disease processes, particularly opportunistic ones. By combining advanced genomic sequencing technologies with strategic epidemiological surveillance, we may be able to target our efforts towards developing vaccines against the most virulent host-adapted pathogens. Licenced commercial vaccines, however, may take several years to develop and register. Therefore, a solution for emerging pathogens can include the use of autogenous vaccines (or auto-vaccines), which are custom vaccines produced from pathogens directly isolated from affected farms on which the vaccines are subsequently deployed under a restricted permit (reviewed in the study by Barnes et al.[98]). In terrestrial agriculture, including poultry, pig and cattle farming, autogenous vaccines are already an effective control strategy against bacterial pathogens. Apart from the shorter development track for autogenous vaccines, they are more efficient against the local serotypes of variable pathogens and faster to produce and re-formulate compared to licenced commercial vaccines. Vaccines are not a standalone solution; they need to be part of a comprehensive health and biosecurity strategy. This strategy should encompass balanced nutrition, environmental management practices that promote health and minimise exposure to harmful xenobiotics, and measures to prevent the introduction of pathogens and potential opportunistic organisms.

On the horizon, a suite of innovative solutions is emerging. In the realm of therapeutics, quorum quenching probiotics and phage therapy offer precision tools targeting specific bacterial pathogens without disturbing the beneficial microbiota, albeit the complex evolutionary melting pot of the aquatic biome is still poorly understood. Adding more genetic material into this could send opportunists either way along the evolutionary parasite-mutualist continuum, and this conundrum has not been fully considered. Gene-editing technology clustered regularly interspaced short palindromic repeats (CRISPR) opens avenues for creating disease-resistant fish strains,[103] although challenges remain in shrimp.[104] The CRISPR/Cas9 system can also be used for genome editing of bacterial species to accelerate the development of improved vaccination strategies. Live attenuated bacterial vaccines are known to have higher and longer protective efficacy compared with killed bacterial vaccines, yet the process of attenuation can be laborious and time-consuming.[105] CRISPR/Cas9 systems could, therefore, be used to generate attenuated auxotrophic mutants of pathogenic bacterial strains by efficiently editing their genomes in a process that is much simpler and faster than conventional allelic exchange methods.

Furthermore, the integration of artificial intelligence (AI) for precision farming allows for real-time monitoring and predictive modelling, improving the timeliness and efficacy of interventions. The application of AI to feeding technology has the potential to be a game-changer for health and sustainability in the aquaculture industry. At present, fish are basically fed either artificially or automatically by quantitatively supplying feed at definite time intervals, which can easily result in under-feeding or over-feeding. This reduces water quality and favours poor health outcomes, but also increases feed waste and the environmental impact of the industry. More advanced aquaculture systems have underwater cameras with human operators that can tailor feeding regimes to the feed response observed in real-time. This, however, can also result in issues with under-trained staff or reduced visibility in underwater cameras. The deployment of precision feeding technologies using AI to simultaneously integrate the information from underwater cameras and other sensors deployed on farm, such as acoustic technology to monitor the position of fish in the water column in response to feed, (reviewed in the study by Li et al.[106]) could not only reduce feed waste but also provide early warning systems for disease outbreaks. In countries where cutting-edge technologies remain unaffordable, telehealth or remote veterinary services delivered via telecommunications, which expanded significantly in human medicine following the COVID-19 pandemic, could be extended to aquatic veterinary medicine. This approach could be particularly beneficial for remote areas or developing aquaculture industries in low- to middle-income countries.

Compelling as the current data may be, corroborative evidence from diverse sectors is essential to validate the rise of opportunistic pathogens and to ascertain its status as a global trend. The rise of the opportunists observed in aquatic environments could also be associated with increased detection. As surveillance intensifies and diagnostic methods improve, are we simply detecting diseases more frequently, thus skewing our perception of their true increase? In the interim, it is imperative to scrutinise the underlying factors contributing to this rise. Application of causal pie models to outbreak investigation will help to identify often ignored underlying contributory factors to aquatic animal morbidity. Reflecting on these challenges is not merely an academic exercise; by doing so, we can devise interventions and improve environmental regulation to reduce the incidence of opportunist infections and safeguard an industry integral to global food security and the economic well-being of communities worldwide.

7 | GLOSSARY

7.1 | Disease

Etymology: French *Desaise*; Middle English *Disease*. Not at ease, inconvenienced. Definition of disease is neither easy nor is any definition static. Scully[107] concisely describes the changing nature of disease definition and some of the socioeconomic and scientific drivers of this continuing flux, and some of its consequences. The World Health Organisation (WHO) does not define disease per se, but does carry an updated list of disease classification, the International Disease Classification (currently ICD-11). WHO does define health as 'a

state of complete physical, mental and social wellbeing and not merely the absence of disease or infirmity'. In the livestock space, the World Organisation for Animal Health (formerly OIE) does not define disease in its Animal Health Codes (aquatic and terrestrial). For our purposes then, invoking the causal pie model, opportunistic bacterial infectious disease is a deviation from normal health for the age of animal where infection by one or more bacterial strains is a necessary cause of the deviation.

7.2 | Infection

Etymology. Latin *Infectia*, dipped in dye, stained or tainted. A good definition is provided by Méthot and Alizon[108] in which the infection or host–parasite interaction comprises 'an interactive and dynamical biological system whose outcome is indeterminate and depends largely on the ecological context'. This captures very eloquently the diversity in the nature, fluidity and outcome of the interaction between two organisms.

7.3 | Parasite

Etymology. Prefix: Greek *para*, alongside, Suffix Greek *sitos* grain or food. One who feeds alongside. An organism that derives resources from its host decreasing the host's fitness. From ancient Greek referring to one who dines without bringing food, the modern term parasite captures an organism that exploits a host. In essence, anything from a virus to a fig may be parasitic in its relationship with another organism and therefore a parasite. In the veterinary and medical cases and literature, parasites are often constrained to protozoa, helminths and other invertebrate eukaryotes. In the present manuscript, we generally adhere to the full breadth of the definition centred on the nature of the relationship between the organisms (e.g., bacteria) and their hosts, but we refer more specifically to Eukaryotic parasites where this is what we mean (e.g., sea lice, flukes and gill amoeba).

7.4 | Pathogen

Etymology. Prefix Greek *Pathos*, suffering/sorrow. Suffix Greek, *Genesis*, birth, origin. An organism that causes pathology or virulence in the infected host. There is complexity here, which we cover in the manuscript. One interesting point of discussion that is not covered is the concept of certain mobile genetic elements as the true pathogens behind many well-known diseases. In the study reviewed by Keen,[109] there are many supportive examples of the inclusion of mobile genetic elements (MGE) as 'pathogenic' where host bacteria are generally benign unless infected and expressing particular phage or transposon-related MGE. Perhaps in the marine environment, *V. cholera* is the best-known example where infection by the Cholera Toxin Phage (CTXφ) bacteriophage is necessary for the expression of the cholera toxin and therefore the development of disease.

7.5 | Virulence

Etymology. Latin *Virulentia* poison; *Virulentus* full of poison. The etymology of virulence suggests that it is a quantitative state of the (infected) host. Returning to the review by Méthot and Alizon,[108] virulence is described as one of the possible outcomes of a host–parasite interaction. Their definition founded in evolutionary ecology states that virulence is a quantitative trait that measures the decrease in host fitness due to an infection[108] and is therefore consistent with the etymology in that virulence is a quantitative status related to the fitness of the host. In the microbiological literature, virulence is commonly used to describe the capability of an infecting organism to damage (reduce the fitness of) the host during an interaction and is, therefore, a trait associated with the pathogen. Use of the term in either context would appear to be acceptable without any loss of clarity.

AUTHOR CONTRIBUTIONS

Francisca Samsing: Conceptualization; investigation; writing – original draft; formal analysis; writing – review and editing; visualization. **Andrew C. Barnes:** Conceptualization; investigation; writing – original draft; visualization; writing – review and editing; formal analysis.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

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