

## The application of risk and disease modelling to emerging freshwater diseases in wild aquatic animals

MARK A. THRUSH\*, ALEXANDER G. MURRAY<sup>†</sup>, EDGAR BRUN<sup>‡</sup>, STUART WALLACE<sup>†</sup> AND EDMUND J. PEELER\*

\*Centre for Environment, Fisheries and Aquaculture Science, Weymouth, U.K.

<sup>†</sup>Marine Scotland, Marine Laboratory, Aberdeen, U.K.

<sup>‡</sup>National Veterinary Institute, Oslo, Norway

### SUMMARY

1. Emerging diseases pose significant ecological and economic threats in fresh waters. Both risk assessment and mathematical modelling have potential to improve our understanding of the uncertainties associated with emerging disease events and make informed predictions about their likely impact.
2. We review the different methodologies that may be used to estimate the likely geographic spread and potential impact of new and emerging diseases in fresh waters. We also highlight the limitations of the currently available methods and requirements for future development.
3. In the realm of aquatic animal health, risk assessment has been used mainly to examine the risks of disease spread through international trade import risk analysis (IRA). Import risk analysis of newly emerged diseases underpins the development of appropriate risk mitigation measures to minimise further spread. This is best illustrated by assessments of the spread of *Gyrodactylus salaris* and also illustrates how risk assessment can examine disease interaction between wild and farmed fish.
4. Various approaches have been employed to study disease transmission within freshwater fish populations at a range of spatial scales. There is scope for the application of these techniques to predict the impact of economically and environmentally important emerging freshwater diseases that arise from new pathogens, known diseases spreading to new locations or changes in pathogenicity owing to changing environmental conditions (e.g. because of climate change).
5. Population models are widely used in freshwater fishery management. The integration of disease processes within freshwater aquatic animal population models is required to provide tools to assess the likely impact of newly emerged diseases and allow mitigation measures to be assessed.
6. Compared with their use in other areas of animal health, modelling has been relatively little used for aquatic animal disease studies. The wide range of modelling methods used to study disease in human and terrestrial animals can usefully be applied to inform the development of policies to protect the health of wild stocks from emerging diseases.

*Keywords:* aquatic, disease modelling, emerging disease, epidemiology, risk assessment

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Correspondence: Mark A. Thrush, Centre for Environment, Fisheries and Aquaculture Science, Barrack Road, Weymouth, DT4 8UB, U.K. E-mail: mark.thrush@cefas.co.uk

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## Introduction

Emerging diseases include new diseases and known diseases that appear in a new species or are increasing in virulence, incidence or showing new pathology (Brown, 2000). Globally, emerging diseases cause substantial economic and environmental impact, and their importance in the aquatic environment is recognised by the World Organisation for Animal Health (OIE), whose members are obliged to report emerging disease events. Similarly, the European fish health directive (EC 2006/08) requires Member States to report and control emerging diseases. Pathogens are a natural component of any ecosystem, and diseases may emerge through entirely natural processes (Coutant, 1998). In recent years, it is anthropogenic activities that have served to drive the occurrence of emerging diseases in the terrestrial and marine environments (Harvell *et al.*, 1999; Daszak, Cunningham & Hyatt, 2003). The absence of reviews focused on emerging diseases in fresh waters has resulted in these being less widely recognised; however, it is clear that extensive trade in aquatic animals and animal products and the movement of live fish and gametes to sustain the expansion of freshwater aquaculture have led to the introduction of exotic pathogens (O.I.E., 2001) and increased the scope for the exchange of pathogens between wild and farmed aquatic animal populations (Murray & Peeler, 2005). In the future, climate change has the potential to effect host/pathogen interactions and allow endemic pathogens to exert a greater influence in the aquatic environment (Marcogliese, 2008).

The impact of emerging diseases on wild aquatic animals may be devastating. For example in Europe, an introduced oomycete (*Aphanomyces astaci*) has led to the virtual extinction of native crayfish over much of its range (Alderman, 1996); the spread of *Batrachochytrium dendrobatidis*, the causative agent of amphibian chytridiomycosis, has been associated with numerous amphibian mortality events and some species extinctions around the world (Berger *et al.*, 1998; Walker *et al.*, 2008), and most recently, the emergence of a new strain of viral haemorrhagic septicaemia virus has caused widespread multispecies mortalities in freshwater wild fish in the Great Lakes region of the United States and Canada (Lumsden *et al.*, 2007).

Modelling attempts to simplify complex biological processes to an idealised, comprehensible series of

events and relationships (Nokes & Anderson, 1988). This deliberately reductionist approach aims to identify the most important processes and components of complex systems. The purpose of this paper is to demonstrate how modelling techniques may be applied in the aquatic environment to improve our understanding of the uncertainties associated with emerging disease events and make informed predictions about their likely impact. We describe methods developed and applied in other areas of animal health and how they may be adapted to the study of disease emergence in freshwater ecosystems; in particular, we review methods to quantify the risk of introduction and establishment of exotic pathogens and estimate their consequence. We also discuss the application of the results to underpin effective risk mitigation activities and contingency planning for emerging diseases.

## Risk analysis

Risk analysis methodology was originally developed by the nuclear and space industries to identify the likelihood of undesirable events (hazards). It was subsequently adopted by the chemical industry and more recently has been applied to biological systems. In the domain of animal health, risk analysis has been applied mainly to food safety (microbiological risk assessment) (Codex Alimentarius Commission, 1997) and to assess disease introduction through international trade in animals and animal products, i.e. import risk analysis (IRA) (Peeler *et al.*, 2007). The key advantage to using risk analysis is that it provides a comprehensive and disciplined framework for decision-making that produces transparent and defensible results. Guidelines for IRA provided by the OIE (O.I.E., 2009), for example, stipulate that data used and assumptions made in an analysis are comprehensively documented to ensure rigour and transparency. There are two components to a hazard which contribute to its risk: its likelihood and the consequences resulting from the hazard occurring. Some risks have a very low likelihood of occurring, but severe consequence would result (for example, an incident at a nuclear power station).

### *Risk analysis models*

Because of the broad application of risk analysis in different fields, a variety of terms and definitions have

arisen. However, most of the approaches recognise four components: hazard identification, risk assessment, risk management and risk communication (where risk assessment specifically addresses the estimation of likelihood and consequence of the hazard occurring). Three risk analysis frameworks are in common use: the U.S. National Academy of Sciences and National Research Council (NAS-NRC) model (Anon, 1983), the International Plant Protection Convention (IPPC) model (FAO, 2007) and the Covello-Merkhofer (CM) (Covello & Merkhofer, 1993) model. The NAS-NRC system was developed to set maximum limits of chemical substances in the environment (or in food) and has been adopted by the Food and Agriculture Organisation (FAO) and the World Health Organisation (WHO) (Anon, 1983). The IPPC system (also referred to as pest risk analysis) identifies pests (including alien species) and/or pathways of quarantine concern, identifies endangered areas and, if appropriate, identifies risk management options. The CM model is designed to assess the magnitude of a risk for specified consequences for a given situation and is used to decide whether a risk is acceptable as it stands, or whether mitigation is required to reduce the risk to an acceptable level. It is more versatile than either the NAS-NRC or IPPC models and may be applied qualitatively or quantitatively to various risk questions making it the system of choice for many risk assessors in animal health. The CM model provides the framework for the OIE IRA guidelines. A complete risk analysis following this model has the following five stages: (i) hazard identification, (ii) release assessment (description of pathways necessary for introduction), (iii) exposure assessment (description of pathways necessary for the exposure of aquatic species in the importing territory to the introduced exotic pathogen), (iv) consequence assessment (identification of the consequences of pathogen introduction and establishment) and (v) risk management (policies to reduce likelihood of introduction and mitigate the consequences) (O.I.E., 2009). In this framework, components ii, iii and iv provide a risk assessment.

#### *Qualitative and quantitative approaches*

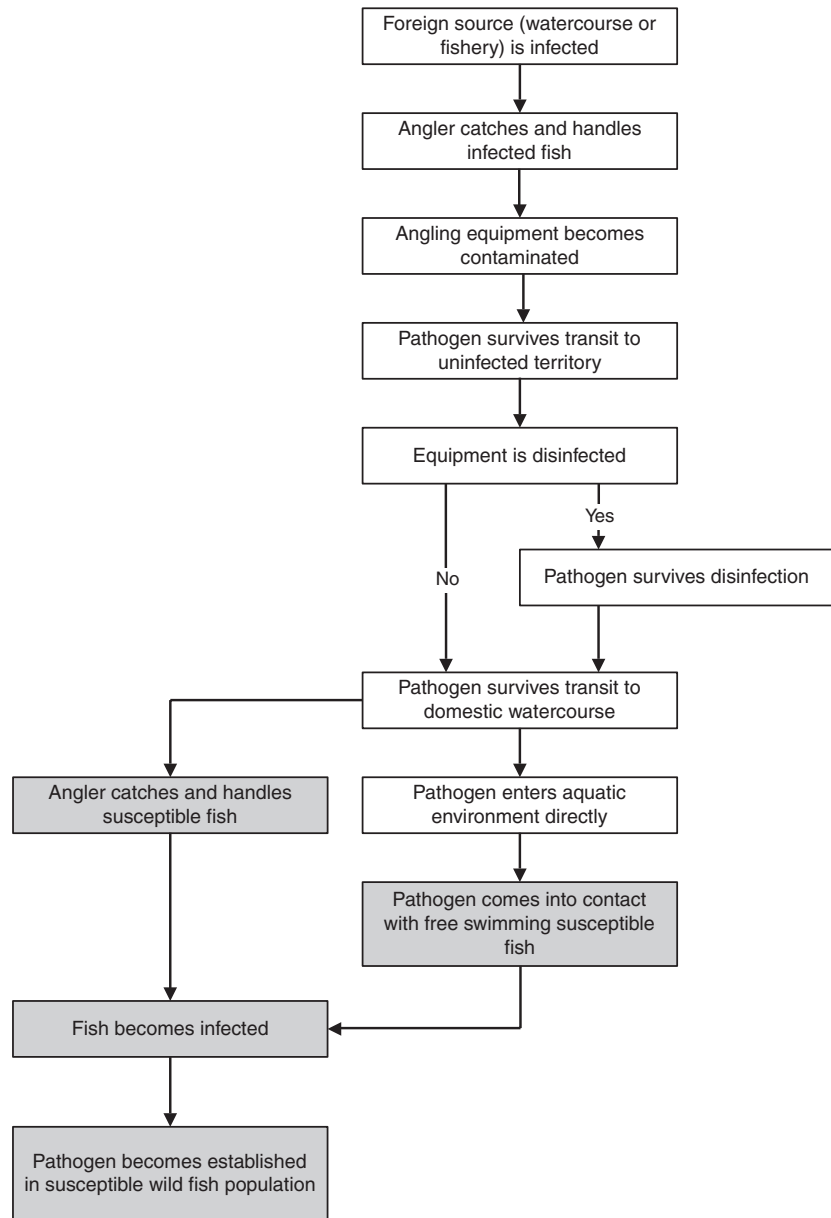
There are two main approaches to risk analysis: qualitative and quantitative (Vose, 2000). A qualitative analysis is based on descriptive terminology and

is essentially a systematic and logical discussion of relevant contributory factors of a hazard in which its likelihood and the magnitude of its consequence are expressed using non-numerical descriptors such as high, medium, low or negligible (Murray *et al.*, 2004), which often involve the aggregation of expert opinions. Occasionally, the definitions used in a qualitative risk analysis are given a numerical range (e.g. high is equivalent to greater than 50%) moving the assessment towards a quantitative approach and is sometimes referred to as a semiquantitative analysis (Peeler, Gardiner & Thrush, 2004). In quantitative analyses, all hazard risk components are expressed numerically (e.g. 'current levels of trade in commodity X will result in the introduction of disease Y once every 100 years'). The main advantage provided by quantitative methods is their ability to assess uncertainty (owing to imprecise knowledge of input parameters) and true variability inherent to all biological systems.

Initially, both approaches require the formulation of a clear risk question and the development of a scenario tree. A scenario tree is a visual representation of the pathway of all the physical and biological events required for the hazard to occur. Figure 1 (developed here as an example of a generic risk analysis) illustrates the specific pathway for the introduction of an unspecified pathogen via contaminated angling equipment. The scenario tree in itself provides a useful conceptual framework, which is a powerful tool for communicating the logic behind the risk assessment to stakeholders. The decision to adopt a qualitative or quantitative approach to a risk assessment is dependent on whether a qualitative result will provide an adequate conclusion for the analysis and whether resources and data are available to complete a quantitative assessment. Vose (2000) recommended that all risk analyses are first attempted qualitatively.

#### *Risk assessments of disease emergence*

Risk assessment of newly emerging diseases provides a logical and rigorous method to identify the most likely routes of spread and thus inform the development of policies to mitigate their impact. The risk assessment approach has been applied directly to examine the processes that underpin disease emergence in aquaculture. Murray & Peeler (2005) used the Covello-Merkhofer model to identify farm-level



**Fig. 1** An example scenario tree for a generic risk analysis: the introduction and establishment of an unspecified pathogen via the use of contaminated angling equipment, showing routes of release (pathways necessary for introduction) and exposure (pathways necessary for the exposure of aquatic species in the importing territory to the introduced exotic pathogen [shaded boxes]).

processes in aquaculture which drive the emergence and spread of disease. Others have adopted a similar approach at a higher level of organisation to identify broad industry-level factors that may favour disease emergence (Bridges *et al.*, 2007).

### Statistical models of disease

Statistical models use observations (historic data) to predict future trends without specific explanation (examples include regression and Poisson models). Statistical models have been used to describe macro-

parasite loads (Shaw & Dobson, 1995), as in the examples of generalised linear models identifying risk factors associated with sea lice loads on farmed Atlantic salmon (*Salmo salar*, L) (Revie *et al.*, 2003) or *Anisakis* loading in wild Baltic herring (*Clupea harengus membras*, L.) (Podolska & Horbowy, 2003). With respect to emerging disease, statistical models have been used to analyse databases of emerging human infectious disease events and identify non-random global patterns (Jones *et al.*, 2008). A similar approach could be employed to better understand at a global level drivers to the emergence of disease in

aquatic animal populations, although underreporting is likely to be a serious constraint.

### Mathematical models of disease

Mathematical models may be variously categorised. Generally, a distinction is made between deterministic and stochastic (probabilistic) models. Deterministic models use differential equations with fixed parameters to describe disease transmission. Every set of variable states is uniquely determined by parameters in the model and by sets of previous states of these variables. Therefore, there is a single outcome for any given set of initial conditions. By contrast, in a stochastic model, randomness (i.e. stochasticity) is present, and variable states are described by probability distributions. The probability distributions are sampled for each run (simulation) to generate the results, which themselves have distributions. Quantitative risk analyses generally use stochastic models (using Monte Carlo simulation) to control the probability components (uncertainty and variability) of a scenario, and a number of software packages may be used for this purpose, including @Risk (Palisade Corporation, NY, U.S.A) that operates as a spreadsheet add-on and Analytica (Lumina Decision Systems, CA, U.S.A) that provides a fully integrated risk analysis environment.

Both deterministic and simulation modelling may be used to predict the spread of disease in individual populations. SIR models for example divide populations into susceptible (S), infected (I) and removed (recovered or dead) (R) phases. Disease spreads to susceptible hosts by their interaction with infected individuals (Anderson & May, 1979). The application of basic principles from SIR-type modelling to aquatic ecosystems has been described by Reno (1998), and this approach has been successfully applied to predict the spread of disease between fish farms (Jonkers *et al.*, 2010; Taylor *et al.*, 2010). However, differences in transmission of pathogens in aquatic environments are likely to reduce the dependence on close direct contact between infected and susceptible hosts (McCallum *et al.*, 2004). This could lead to important functional differences, such as the absence of a threshold for infection and nonlinear relationships between infected population and infection pressure.

### Population models

There is a long-established history of fish population modelling in both marine and freshwater ecosystems (Ricker, 1954; Beverton & Holt, 1957; Pelletier & Mahévas, 2005; Chu *et al.*, 2006; Nunn *et al.*, 2007; Hanson, 2009), and wider ecosystem dynamics have been studied using modelling systems such as ECO-SIM (Christensen & Walters, 2004). However, the specific role of disease in freshwater aquatic animal population dynamics has received little attention (Longshaw *et al.*, 2010). The net impact of disease on a population depends on direct pathogen-induced mortality and also on the compensatory response of the population to changes in mortality. Therefore, disease models, especially for chronic diseases, require embedding in host population models. There is scope also to extend this approach to study the potential impact of emerging diseases at the population level. Simple examples reviewing the interaction between disease and host dynamics exist for terrestrial populations (Anderson & May, 1979; May & Anderson, 1979). The behaviour of these models depends strongly on the functional nature of transmission (McCallum *et al.*, 2004), which may be substantially different in modelled population responses to aquatic disease (Murray, 2009). Aquatic examples exist; for example, a Ricker model was used by Fenichel, Tsao & Jones (2009) to model impacts of bacterial kidney disease (BKD) on populations of Chinook salmon (*Oncorhynchus tshawytscha*, Walbaum 1792) in Lake Michigan; and des Clers (1993) modelled impacts of disease-induced mortality on different life stages of wild salmonids.

Disease impacts interact with other mortality processes, for example diseases that are host density dependent will have a reduced impact in populations which have been depleted by fishing (Dobson & May, 1987). Disease reduces stock available to fisheries (Dobson & May, 1987; Patterson, 1996), but interaction with fishing has not been assessed using models specifically for freshwater fish populations. Conversely stocking may increase disease impacts, and this effect has been modelled, as described, for BKD in freshwater (Fenichel *et al.*, 2009). Mortality at different stages of a fish's life cycle may have different impacts. For example, des Clers (1993) found that diseases impacting the early freshwater stages of Atlantic

salmon had more impact on population size than did diseases that affected marine stages or those that had returned to fresh water. In the case of a short-lived epidemic, host populations do not have time to respond to losses; however, host population dynamics will still control the recovery of populations following mass mortality. This situation has been modelled for an epidemic in the marine environment (an outbreak of pilchard herpes virus that caused mass mortality of marine Australian pilchards (*Sardinops sagax*, Jenyns 1842) (Murray & Gaughan, 2003)), but there are no equivalent studies for freshwater ecosystems.

There are other approaches to modelling impacts on population. For example, modelling has been undertaken of the decline of wild brown trout (*Salmo trutta*, L) populations in Switzerland using a Bayesian probability network model (Borsuk *et al.*, 2006; Burkhardt-Holm, 2008) in which disease [proliferative kidney disease (PKD)] was one significant factor amongst many. Given that population models are in widespread use, the opportunity to include disease-specific components should be taken. The combination of disease and population modelling provides a unique tool for estimating the likely spread and impact of newly emerged diseases.

### Spatial and temporal analysis (risk mapping)

Spatial and temporal analysis can make an important contribution to our understanding of disease. The development of geographic information systems (GIS) and spatial statistics has allowed spatially distributed determinants of health and disease to be fully evaluated. Geographic information systems have been widely applied in terrestrial animal epidemiology, where mapping the distribution of vector species, for example, has identified areas susceptible to the introduction of tick-borne diseases (Lessard *et al.*, 1988, 1990; Perry *et al.*, 1990; Thompson *et al.*, 2006). Whilst GIS has been used to investigate the distribution of fish species (Creque, Rutherford & Zorn, 2005; Righton & Mills, 2006), its application has not been extended to any degree to the investigation into the spatial distribution of disease and its determinants (e.g. currents, water temperature, vector populations).

Spatially explicit hydrodynamic models, which model tidal and other currents, can be used to predict the likely passive spread of pathogens and parasites

(Amundrud & Murray, 2009; Viljugrein *et al.*, 2009; Jonkers *et al.*, 2010). Species distribution modelling may enhance the application of risk mapping, where knowledge of species distribution is limited or uncertain. This methodology uses a maximum entropy density estimation (Maxent) algorithm to estimate geographic distributions of species from presence-only locality point data, which is frequently all that may be available in areas where population surveys have not been undertaken (Phillips, Anderson & Schapire, 2006; Phillips & Dudík, 2008).

Risk mapping is directly relevant to the study of emerging diseases, and a principal area where this may be applied is in relation to climate change. To date, studies on the potential impact of climate change on emerging disease have focused on humans (Patz *et al.*, 2005), terrestrial livestock populations (Gale *et al.*, 2009) and especially vector-borne diseases of both humans and animals (Rogers & Packer, 1993; Rogers & Randolph, 2003; Rogers, 2006). Studies of aquatic animal disease emergence and climate change in fresh water are limited (Marcogliese, 2008; Marcos-López *et al.*, 2010) and have not employed spatial or temporal mapping methods. Diseases of aquatic animals generally become clinically apparent under certain temperature conditions, which may need to be higher or lower than a critical threshold for a specific time interval (permissive temperature profile). Information on disease-specific permissive temperature profiles and susceptible species distribution can be readily combined to provide risk maps for the likelihood of disease establishment in fresh waters. Mapping intermediate or alternate host populations will identify high-risk areas for parasite diseases. This approach could assist risk-based surveillance and help monitor and predict the impact of environmental changes on the prevalence and severity of emerging endemic diseases (i.e. increasing in prevalence or range). For example, PKD has recently increased its geographic distribution and impact in Switzerland and Norway (see Okamura *et al.*, 2010) and may serve as an example of increased disease vulnerability of wild fish populations to endemic pathogens in a warmer climate (Sterud *et al.*, 2007). Mapping bryozoans that are alternate hosts for *Tetracapsuloides bryosalmonae* (the causative agent of PKD) and water temperature data will support prediction of the extent of the spread of the disease under different climate change scenarios.

### Modelling disease interaction and pathogen exchange between wild and farmed fish

Disease interaction and pathogen exchange between wild and farmed fish underpin the emergence of many types of emerging diseases. Transfer of parasites both from wild to farmed and from farmed to wild fish is important in disease emergence. Interaction underpins the establishment of exotic pathogens in wild populations that have been introduced with imported live animals for aquaculture (see Peeler & Feist, 2011). A level of contact between the original host (of a known parasite or a commensal agent) and the new potential hosts may occur under a range of circumstances. The open design of many freshwater farming systems allows parasites to be exchanged between wild and farmed fish without direct contact (Kent, 2000). High host density, poor environment and intercurrent disease (occurring during the course of another disease) may undermine immunity in farmed stocks and thus reduce resistance to disease while also enhancing contact. Interaction between wild and farmed populations can also lead to disease emergence through parasite 'spillback'. This may occur when a non-native species is a competent host for a native pathogen, with the presence of the additional host increasing disease impacts in native species. In some freshwater ecosystems, farmed fish may constitute a significant proportion of the animal biomass and farming conditions (e.g. high stocking rates) allow for high levels of disease to build up and spill back into wild populations (Arkoosh *et al.*, 1998) (see Poulin *et al.*, 2010 for macro-parasite examples).

Models of such spillback impacts have been developed for impacts of marine farming on wild salmonids. Krkošek *et al.* (2007) used a model to predict a 99% collapse in local pink salmon (*Oncorhynchus gorbuscha*, Walbaum 1792) populations within four generations owing to exposure to sea lice (*Lepeophtheirus salmonis*) from farmed Atlantic salmon. A more general statistical modelling analysis indicated widespread effects of salmon farms on wild salmonids (Ford & Myers, 2008). Other modelling analyses that took into account currents and low salinity (Brooks, 2005; Brooks & Jones, 2008) predicted that sea lice would have a smaller impact on the same local salmonid populations.

Risk models for disease emergence have qualitatively assessed interaction between farmed and wild

populations and the influence of farming conditions on disease emergence (Murray & Peeler, 2005). Current mathematical modelling approaches that have been used to examine disease dynamics between wild and farmed terrestrial animals have not, to date, been applied to aquatic ecosystems. The conceptual framework for managing disease in multiple host populations set out by Haydon *et al.* (2002) can be applied to the emergence of disease in farmed and wild populations. Work on applying the principles of dynamic disease modelling to disease emergence in terrestrial wildlife populations (Real & Biek, 2007) could similarly be extended to aquatic animal species.

### Application of risk-based surveillance to improve detection of emerging diseases

Epidemiological knowledge and risk mapping are the basis of risk-based surveillance systems (Stärk *et al.*, 2006). Focusing the limited resources available for surveillance on the highest risk populations and animals will improve the efficiency of the system (Stärk *et al.*, 2006). In the context of emerging diseases, analysis of past disease emergence and an understanding of the processes underpinning emergence can be used to identify high-risk populations and geographic zones (i.e. where diseases are most likely to emerge). This analysis thus supports risk-based surveillance for emerging diseases.

Scenario tree modelling approaches have been developed to assess the sensitivity of a surveillance system (Martin, Cameron & Greiner, 2007). A key advantage of this method is that different sources of surveillance information, for example, routine testing, structured surveys, *ad hoc* and opportunistic observations etc. can be combined and compared. The models require the estimates of the likelihood that disease will be detected at each stage in the surveillance model (i.e. sensitivity). Scenario tree modelling approaches can be used to identify the most efficient surveillance system for detecting emerging diseases (Hadorn & Stärk, 2008). To achieve this for aquatic animal diseases, surveillance must include a range of sources of surveillance information: observations by anglers, fish farmers, fishery managers etc. together with structured surveys. This may enable the surveillance system to record unspecific mortality and reports on various macropathological findings. Regular and

systematic scanning of these data (i.e. syndromic surveillance) will allow early identification of possible emerging disease events, which could then be investigated in detail.

### Key examples of where epidemiological modelling has been applied

#### *Gyrodactylus salaris*

The monogenean parasite *Gyrodactylus salaris* emerged as a serious parasite of wild Atlantic salmon in Norway in the early 1970s, following its introduction to Norway from Sweden with imported Atlantic salmon smolts. It is now considered to be one of the most significant threats to the east Atlantic stock of the Atlantic salmon (Bakke, Cable & Harris, 2007). This strain of Atlantic salmon, has, in contrast to most Baltic stocks, proven highly susceptible to the parasite. Its introduction to areas inhabited by the east Atlantic stock (for example Norway) has proven devastating. The parasite is lethal to juvenile fish (parr), and infection may reduce the salmon production in a river to almost zero within about 5 years (Johnsen & Jensen, 1991). Currently, the only susceptible European populations declared free of *G. salaris* are in Great Britain, Eire, the Faroe Islands and Iceland.

A considerable body of biological knowledge for *G. salaris* exists in scientific literature, including information on susceptible and vector species and biophysical properties of the pathogen (survival under various environmental conditions, transmission characteristics etc.) (see review by Bakke *et al.* (2007)). This information has been vital for risk analyses and models to describe the potential for spread and to support contingency planning for early detection, containment and eradication of the parasite should it be introduced. *G. salaris* may be spread by live or dead infected fish, by fomites (physical objects that transmit infections agents) or through water as free-living parasites. The importance of these transmission routes for spread between river catchments in England and Wales has been ranked (Peeler *et al.*, 2004). Their risk assessment concluded that the anthropogenic movement of live salmonids (for restocking and the supply of fingerlings for table production) showed the highest potential for spread from infected to non-infected areas, followed by the

anthropogenic movement of live vector species. Other routes (wild fish migration and transmission by fomites) would be influential only for local spread (within catchments or between neighbouring river systems). Stochastic simulation models have been developed to study the risk of transmission of *G. salaris* by live salmonid movement between specific locations (Paisley *et al.*, 1999) and to demonstrate the potential magnitude of geographical spread of the parasite on a national scale (Thrush & Peeler, 2006). These studies were important for establishing proper regulations and prioritising surveillance measures.

Anthropogenic activities may be controlled; however, the behaviour of wild fish cannot. In 1987, the river Drammenselva in southeast Norway became infected with *G. salaris*. Following protracted debate about the complexity of treating this river system and the aspiration of the local community to maintain salmon production, a restocking programme was established in spite of possible increased risk of spread to neighbouring rivers from the endemically infected Drammenselva population. A quantitative risk analysis was conducted to assess the infection pressure this source could pose on three adjacent non-infected river catchments (Høgåsen & Brun, 2003). Incorporation of parameters including swimming behaviour and speed, water salinity and temperature profiles, in addition to knowledge of the parasite into a simulation model, enabled a risk estimate for each river to be calculated. These estimates were important for the continuation of the restocking work and establishing a surveillance programme in surrounding areas.

A key factor for parasite dispersal between catchments is the salinity profile of brackish water between rivers. Smolt migration occurs in spring during a period of seasonal flooding and associated reduced salinity. These conditions increase the probability of parasites remaining viable and attached to smolts migrating between rivers. The effect has been mathematically modelled for several river-fjord systems in Norway (Jansen, Matthews & Toft, 2007), demonstrating that the natural migration of fish during high river flows has most likely been responsible for the majority of the transmission of *G. salaris* in Norway.

The presence of *G. salaris* in some infected Norwegian rivers may not be explained by migration and may be the result of anthropogenic actions other than the movement of live fish, for example movement of



contaminated substrate or transfer of water containing free-living *G. salaris* from an infected to a non-infected river. Small amounts of water (enough to keep parasites viable) may be transferred between rivers by fishing gear, boots, canoes, boats, water bottles, etc. Risk assessment has been used to quantify the probability that a given water volume taken randomly from a known infected river would contain free-living parasites (Høgåsen, Brun & Jansen, 2009). Uncertainties associated with assumptions made as well as the inherent variability in biological systems were accounted for by Monte Carlo simulation and sensitivity analysis. The authors concluded that the risk of inter-river dispersal owing to the transfer of contaminated water through common river activities is low.

The focus of the majority of work on *G. salaris* has been on estimating probabilities for transmitting parasites from infected to non-infected rivers, relatively little attention has been given to the risk of establishment following introduction. Because this parasite is viviparous, an introduction of even a small number of viable parasites attached to a susceptible host may pose a high risk of establishment, ultimately determined by the distribution and density of other susceptible hosts (discussed by Peeler *et al.* (2004) and Høgåsen *et al.* (2009)). On the other hand, the probability of establishment if only free-living parasites are introduced will be much reduced, as these will need to find a susceptible host within a reasonable time to initiate reproduction. Using geophysical, water chemistry and land use data and the distribution of other (endemic) salmonid gyrodactylid species, Morris *et al.* (2009) have taken a GIS approach to identify environmental factors that are good predictors for the establishment of *G. salaris* should it be introduced into the United Kingdom.

#### *Infectious pancreatic necrosis virus (IPNV)*

Infectious pancreatic necrosis (IPN) is a viral disease of marine and freshwater fish (Ariel & Olesen, 2002). The disease has emerged in most salmonid farming areas. The causal virus (IPNV) was notifiable in farmed Scottish Atlantic salmon until 2006 (i.e. was required by law to be reported to government authorities) and is still notifiable in Irish salmon farms. As a result, the emergence of IPNV in farmed salmon in both freshwater and marine sites was well documented. A statistical model of emergence in

salmon farms was derived for Scotland (Murray, Busby & Bruno, 2003), and process models of emergence were derived for both Scottish (Murray, 2006) and Irish (Ruane *et al.*, 2009) salmon farms.

The process models were SIR models, and the units of population were individual farms. Fish were transferred from fresh water to marine farms, carrying any infection with them. Although a much higher proportion of marine than freshwater salmon farms were infected, these models showed that the epidemiology of the virus was much more sensitive to intervention in fresh water (Murray, 2006) and that inputs to freshwater from outside the system (imports, transfer from other species, new emergence) had far more impact on the early stages of emergence than did similar events affecting marine farms (Ruane *et al.*, 2009).

Although early IPN outbreaks occurred only in fresh water (Munro, Liveredge & Elson, 1976), IPN is now generally considered a disease of marine farmed salmon. Even so, modelling has shown that the freshwater component of its epidemiology played a critical role in its emergence in aquaculture. To be effective, controls should be applied where they have most effect, not where the consequences of disease manifest themselves. This may apply to other diseases that affect farmed and wild salmonids in both their marine and freshwater phases.

Infectious pancreatic necrosis virus spreads from farms to adjacent wild fish populations (Munro *et al.*, 1976). A statistical model was developed demonstrating the association of IPNV in wild marine fish with distance from infected marine fish farms (Wallace *et al.*, 2008). In addition, samples of surface water and sediment were taken at measured distances from these sites, and this highlighted the short- to medium-term persistence of IPNV temporally and spatially with respect to these facilities (Gregory *et al.*, 2007). Because IPNV is shed into the aquatic environment (Urquhart *et al.*, 2008) and may be transported long distances, for example in rivers (McAlister & Bebak, 1997), infection may spread to adjacent wild fish populations. The spread of IPNV by hydrodynamics around farms was modelled by Murray, Amundrud & Gillibrand (2005).

#### *Viral haemorrhagic septicaemia (VHSV IVb)*

A recently emerged new genotype of viral haemorrhagic septicaemia (VHSV IVb) in the Great Lakes

region of the United States and Canada (Elsayed *et al.*, 2006; Lumsden *et al.*, 2007) poses a significant threat to wild fish populations, potentially impacting important commercial bait fish and sport fishing industries. The Great Lakes basin is one of the largest freshwater systems in the world and further spread of the virus to wild fish and introduction to the aquaculture industry in surrounding regions in North America currently free of disease would lead to widespread trade restrictions in addition to direct losses from disease. The situation is exacerbated by the extensive taxonomic host range compared with previous genotypes of VHSV and the difficulty of controlling disease in an open environment.

To monitor the distribution of the emergent virus and mitigate the risk of spread outside the regulated area, the U.S. and Canadian governments have developed a bilateral risk-based approach to coordinate surveillance in the region. To facilitate this, a list of risk factors perceived important to the spread of VHSV IVb were generated by an expert panel (VHSV Expert Panel and Working Group, 2010). This information was used to create an evidence aggregation model that provides a quantitative framework for combining historical surveillance results with contextual evidence for the likelihood of disease presence (including for example, hydrographic and environmental parameters, wild fish distribution and anthropogenic activities) (Gustafson *et al.*, 2010) to determine the surveillance intensity required in different watersheds. This is a comprehensive example of risk-based surveillance that may be used as a model for the surveillance for other emerging diseases.

#### *Chytridiomycosis*

Amphibian chytridiomycosis is an emerging infectious disease caused by the chytrid fungus *Batrachochytrium dendrobatidis*. This pathogen infects over 350 species globally (Fisher, Garner & Walker, 2009) and is associated with the decline of many amphibian populations and species extinctions (Berger *et al.*, 1998). *Batrachochytrium dendrobatidis* is considered to be the most significant threat to biodiversity in vertebrates (Skerratt *et al.*, 2007); however, the principal drivers that have led to the emergence of the disease remain unclear. Fisher & Garner (2007) reviewed the role of international trade in amphibians for the long-range spread of chytridiomycosis and

highlighted the need for national risk identification and mitigation measures, but to date no formal IRAs have been completed for this disease.

Rödder *et al.* (2009) used known biophysical characteristics of *B. dendrobatidis* and climate information coupled with species distribution modelling to predict the distribution of the pathogen and identify amphibian populations most at risk from emerging disease globally. A similar approach was taken by Puschen-dorf *et al.* (2009) at a regional level to identify areas that would be suitable as refuges for endangered species in conservation planning in Costa Rica. Examples of population-level modelling are limited: Boykin & McDaniel (2008) included infection with chytrid fungus with other ecological variables in a scenario-based population model for the Chiricahua leopard frog (*Rana chiricahuensis*, Platz & Mecham 1979); however, to date no other studies have been published.

#### **Potential future epidemiological modelling of emerging freshwater diseases**

##### *Epizootic ulcerative syndrome*

Epizootic ulcerative syndrome (EUS) has a complex aetiology that has been associated with a variety of parasitic, bacterial, viral and fungal infectious agents (Lilley *et al.*, 1998). It is now characterised by the presence of *Aphanomyces invadans*, a peronomycete fungus (O.I.E., 2009). It is a disease of wild and farmed, fresh- and brackish-water fish that first appeared in Japan in 1971 (Egusa & Masuda, 1971) and has become widely distributed in Asia, Australia and the east coast of the United States and has recently become established in the Zambezi river system in southern Africa (FAO, 2009). It has been reported in over 100 species (EFSA, 2007) including a wide range of ornamental fish. Over a billion ornamental fish are traded annually between over 100 countries. In an appraisal of the effectiveness of Australia's stringent risk assessment and quarantine controls for ornamental imports to Australia, Whittington & Chong (2007) concluded that an acceptable level of protection from exotic diseases introduction was not being achieved. This shows EUS to be a major hazard of uninfected susceptible populations globally. However, this disease has attracted very little attention from epidemiologists (Morgan, 2001), and to date

no specific risk assessment or modelling work has been undertaken for EUS.

#### *Ranaviruses*

Systemic iridoviruses (ranaviruses) are a recently emerged group of viruses that infect fish, amphibians and reptiles. Examples include epizootic haematopoietic necrosis virus (EHNV) that has caused widespread mortalities of perch (*Perca fluviatilis*, L) in Australia (Langdon & Humphrey, 1987) and the closely related, but distinct, European sheatfish and European catfish viruses (ESV, ECV) (Marsh *et al.*, 2002). Very similar ranaviruses have been associated with mortality events in amphibians in Europe, Asia, Australia, North and South America and are infectious for both amphibians and fish (Moody & Owens, 1994; Ahne *et al.*, 1998). Historically, there have been no legal requirements for health certification for the import of amphibians and reptiles (although the recent listing of ranavirus infection by the OIE provides a basis for future legislation), so the lack of host specificity demonstrated by these pathogens and common anthropogenic mechanisms of spread for finfish and amphibians (i.e. trade in ornamental aquatic animals) makes virulent ranaviruses a serious threat to aquatic animals. In the United Kingdom, for example, the pattern of ranaviral infections indicates that disease is relatively new, and it is likely to have been introduced with imported non-native amphibians or freshwater fish (Cunningham *et al.*, 2007). The possibility of emergence from unknown reservoir hosts associated with environmental change is also a potential risk (Whittington, Becker & Dennis, 2010). The consequences of the introduction of emerging ranavirus diseases to fish and amphibian stocks and to aquatic ecosystems and the development of appropriate protective measures to prevent incursions and spread should provide a focus for risk assessment and disease modelling.

#### *Whirling disease*

Whirling disease is principally a disease of farmed salmonids. Caused by the myxosporean parasite *Myxobolus cerebralis*, it was first described in Germany in 1893 and has been spread, by anthropogenic activities, to many European countries and to other continents (Bartholomew & Reno, 2002). The parasite

can be effectively managed in regions where it has become endemic to levels below which clinical disease occurs in culture; however, massive mortalities may result from infection in naïve populations, and clinical disease may also have a significant impact in wild fish populations (Nehring & Walker, 1996). Experience with *M. cerebralis* in the United States has highlighted that the impact of the parasite in culture and the likelihood of establishment in wild fish may depend on environmental factors (for example hatcheries in California can manage the disease, whereas those in Utah experience losses on the order of 90% (Modin, 1998)). Krueger *et al.* (2006) used regression analysis to determine correlations among environmental characteristics to assess the risk of *M. cerebralis* infection in rainbow trout in Montana, and Bartholomew *et al.* (2005) used a comprehensive risk assessment approach to assess factors associated with the risks of introduction and establishment of the parasite and identify effective mitigation actions. Clearly, there is further scope for risk assessment and mathematical models to support future management of this disease.

#### **Limitations to methodologies and future development**

Current IRA methods are designed to assess existing pathogens. They do not take into account the likelihood that, for example, movement of non-native species may introduce a previously unknown pathogen and thus drive disease emergence. A move away from the current pathogen-centric approach to IRA has been suggested to address this problem (Whittington & Chong, 2007; Jones & Perera, 2009). Clearly, forecasting in advance the effects of even a known pathogen introduced into a new ecosystem is challenging. Data gathered from regions where disease is endemic may be used to inform risk assessments of exotic pathogens; however, the uncertainty associated with their results will be increased if environmental conditions in the different areas are not similar. Peeler *et al.* (2009) encountered this problem assessing the risk of establishment of EHNV resulting from the import of carp (*Cyprinus carpio*, L) to the United Kingdom from Australia.

The methodology for consequence analysis (quantification of the impact of a pathogen following introduction and establishment) in particular is not well developed, and guidance on consequence

assessment for aquatic animal IRAs is very limited. As a result, consequence assessment is frequently not completed in IRA (only 5 of 17 IRAs reviewed by Peeler *et al.* (2007) attempted a consequence assessment, and these were the weakest elements of the analyses). The process is generally constrained by lack of data which will make the application of consequence analysis to emerging diseases, where data availability will be minimal, particularly prob-

lematic (Rodgers, 1997). The overall consequence of an emerging disease event will have economic and environmental components, but the completed analysis needs to be expressed in monetary terms. It is difficult to derive a value for an environmental resource which, for a stock of wild salmon for example, may include recreational value. Methodologies exist that attempt to address this issue through the establishment 'user' and 'non-user' values (Olsen,

**Table 1** Summary of risk and disease modelling approaches used to study disease emergence and spread in aquatic environments. See text for details and explanation of abbreviations

Subject of assessment	Approach	Examples	Reference [notes/ inter-related approaches]
Disease emergence	Risk analysis	Emergence of disease in aquaculture	Murray & Peeler (2005); Bridges <i>et al.</i> (2007)
Transboundary disease spread	Import risk analysis (IRA)	Introduction of EHNV into the United Kingdom Introduction of <i>G. salaris</i> into the United Kingdom Introduction of VHSV into Chile	Peeler <i>et al.</i> (2009) [qualitative assessment] Peeler & Thrush (2004) [semi-quantitative assessment] Hervé-Claude <i>et al.</i> (2008) [quantitative assessment; uses Monte Carlo simulation]
Disease spread between populations	Risk analysis	Transmission of <i>G. salaris</i> from a farm to wild population of Atlantic salmon  Inter-river transmission of <i>G. salaris</i> by migrating Atlantic salmon smolts  Inter-river transmission of <i>G. salaris</i> by transfer of contaminated water by anthropogenic activities	Paisley <i>et al.</i> (1999) [quantitative assessment; uses Monte Carlo simulation] Høgåsen & Brun (2003) [quantitative assessment; uses Monte Carlo simulation] Høgåsen <i>et al.</i> (2009) [quantitative assessment; uses Monte Carlo simulation]
	Statistical modelling SIR modelling	Spread of IPNV in Scotland Spread of IPNV in Ireland Spread of exotic salmonid pathogens in England and Wales	Murray <i>et al.</i> (2003) Ruane <i>et al.</i> (2009) Jonkers <i>et al.</i> (2010) [includes hydrodynamic component]
	Monte Carlo simulation Hydrodynamic modelling	Spread of exotic salmonid pathogens in England and Wales Spread of pancreas disease  Spread of sea lice	Thrush & Peeler (2006)  Viljugrein <i>et al.</i> (2009) [uses statistical modelling] Amundrud & Murray (2009) [uses statistical modelling]
	Bayesian models	Spread of VHSV between water catchments	VHSV Expert Panel and Working Group (2010)
Likelihood of establishment	Risk mapping	Use of multiple variables to assess the risk of establishment of <i>G. salaris</i>	Morris <i>et al.</i> (2009) [uses statistical modelling]
Impact of disease on populations	Population modelling	Study of the impact of BKD on wild chinook salmon populations Disease impacts on wild salmonid populations	Fenichel <i>et al.</i> (2009)  des Clers (1993)
	SIR modelling	Disease impacts of viral disease on pilchard populations	Murray <i>et al.</i> (2001)
	Bayesian models	PKD included as a factor in brown trout population model	Burkhardt-Holm (2008)

Richards & Scott, 1991; Krokan & Mørkved, 1994). Payno Morant (2009) developed a standardised methodology for assessing consequences of aquatic disease outbreaks; this assessed economic and environmental components separately by quantitative and semiquantitative approaches, respectively. Research in this area and the development of standardised guidelines would have direct application to emerging diseases.

Mathematical models may be used to provide input for risk analysis where data are limited. This approach is particularly important in generating a range of feasible scenarios, as response to the control of emerging diseases must be proportionate to their likely impact, and these predictions must be soundly based. However, the usefulness of quantitative methods is again ultimately constrained by data availability. High levels of uncertainty require input parameters with wide confidence intervals (modelled by large probability distributions). The output will consequently also have a wide confidence interval, and this range may be no more useful for decision-making than a qualitative result. The application of sensitivity analysis to mathematical models provides a key tool for assessing elements of input that have the greatest impact on their results and may be used to identify research priorities for emerging diseases.

## Conclusion

Whilst risk assessment and disease modelling employ distinctive and different approaches, both are *ex-ante* attempts to predict the spread and impact of disease. Therefore, both are done for the same reason: to support the development of aquatic animal health policies to minimise the likelihood of emergence and impact of disease. A summary of how different methods have been used to study various aspects of disease emergence and spread in the aquatic environment is provided in Table 1. Some risk work has explicitly attempted to investigate the processes that underpin emergence and thus inform policies that will reduce the rate of emergence (Murray & Peeler, 2005; Bridges *et al.*, 2007). Pathogen interaction between wild and farmed populations was identified as a key driver for emergence. The validity of the outputs of risk and disease models needs to be discussed on a case by case basis. However, it is clear that both risk and disease modelling offer transparent and rigorous methods to maximise the use of the

available information and to identify key data gaps in the study of disease emergence. Similarly, risk mapping provides a tool that allows geographically referenced information to be used to predict the likely distribution of new and emerging disease. *G. salaris* offers the best case study of the application of modelling work to support measures to minimise the spread of the pathogen in countries where the parasite is endemic (e.g. Norway) and to minimise the likelihood of entry, establishment and spread in areas currently free of the pathogen (e.g. the United Kingdom). There are fewer examples in the literature of similar approaches being so widely applied to other more recently emerged pathogens (e.g. EUS and chytrid fungus). The application of modelling approaches extends from examining spread of emerging disease to improved early detection through the application of risk approaches to disease surveillance. Anthropogenic drivers for disease emergence are likely to remain and intensify; for this reason, investigations into newly emerged diseases should be designed to generate the data necessary to run models of their spread and impact, so that appropriate measures can be identified and tested.

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## References

- Ahne W., Bearzotti M., Bremont M. & Essbauer S. (1998) Comparison of European systemic piscine and amphibian iridoviruses with epizootic haematopoietic necrosis virus and frog virus 3. *Journal of Veterinary Medicine B*, **45**, 373–383.
- Alderman D.J. (1996) Geographical spread of bacterial and fungal diseases of crustaceans. *Revue Scientifique et Technique, Office International des Epizooties* **15**, 603–632.
- Amundrud T.L. & Murray A.G. (2009) Modelling sea lice dispersion under varying environmental forcing in a Scottish sea loch. *Journal of Fish Diseases*, **32**, 27–44.
- Anderson R.M. & May R.M. (1979) Population biology of infectious diseases: Part 1. *Nature*, **280**, 361–367.

- Anon (1983) *Risk Assessment in the Federal Government: Managing the Process*, National Academy Press, Washington, 191 pp.
- Ariel E. & Olesen N.J. (2002) Finfish in aquaculture and their diseases – a retrospective view on the European Community. *Bulletin of the European Association of Fish Pathologists*, **22**, 72–83.
- Arkoosh M.R., Casillas E., Huffman P., Clemons E., Evered J., Stein J.E. *et al.* (1998) Increased susceptibility of juvenile chinook salmon from a contaminated estuary to *Vibrio anguillarum*. *Transactions of the American Fisheries Society*, **127**, 360–374.
- Bakke T.A., Cable J. & Harris P.D. (2007) The biology of gyrodactylid monogeneans: the “Russian-doll killers”. *Advances in Parasitology*, **64**, 161–376.
- Bartholomew J.L. & Reno P.W. (2002) The history and dissemination of whirling disease. In: *Whirling Disease: Reviews and Current Topics*. American Fisheries Society Symposium, 29. (Eds J.L. Bartholomew & J.C. Wilson), pp. 3–24. American Fisheries Society, Bethesda.
- Bartholomew J.L., Kerans B.L., Hedrick R.P., Macdiarmid S.C. & Winton J.R. (2005) A risk assessment based approach for the management of whirling disease. *Reviews in Fisheries Science*, **13**, 205–230.
- Berger L., Speare R., Daszak P., Green D.E., Cunningham A.A., Goggin C.L. *et al.* (1998) Chytridiomycosis causes amphibian mortality associated with population declines in the rain forests of Australia and Central America. *Proceedings of the National Academy of Sciences of the United States of America*, **95**, 9031–9036.
- Beverton R.J.H. & Holt S.J. (1957) *On the Dynamics of Exploited Fish Populations*. Chapman and Hall, London.
- Borsuk M.E., Reichert P., Peter A., Schager E. & Burkhardt-Holm P. (2006) Assessing the decline of brown trout (*Salmo trutta*) in Swiss rivers using a Bayesian probability network. *Ecological Modelling*, **192**, 224–244.
- Boykin K.G. & McDaniel K.C. (2008) Simulated potential effects of ecological factors on a hypothetical population of Chiricahua leopard frog (*Rana chiricahuensis*). *Ecological Modelling*, **218**, 175–181.
- Bridges V.E., Akkina J., Grannis J., Johnson C., Johnson R. & Tuszynski C. (2007) A qualitative assessment tool for the potential of infectious disease emergence and spread. *Preventive Veterinary Medicine*, **81**, 80–91.
- Brooks K.M. (2005) The effects of water temperature, salinity, and currents on the survival and distribution of the infective copepodid stage of sea lice (*Lepeophtheirus salmonis*) originating on Atlantic salmon farms in the Broughton Archipelago of British Columbia, Canada. *Reviews in Fisheries Science*, **13**, 177–204.
- Brooks K.M. & Jones S.R.M. (2008) Perspectives on pink salmon and sea lice: scientific evidence fails to support the extinction hypothesis. *Reviews in Fisheries Science*, **16**, 403–412.
- Brown C. (2000) Emerging diseases of animals – an overview. In: *Emerging Diseases of Animals*. (Eds C. Brown & C. Bolin), pp. 1–12. American Society for Microbiology, Washington.
- Burkhardt-Holm P. (2008) Decline of brown trout (*Salmo trutta*) in Switzerland – How to assess potential causes in a multi-factorial cause-effect relationship. *Marine Environmental Research*, **66**, 181–182.
- Christensen V. & Walters C.J. (2004) Ecopath with Ecosim: methods capabilities and limitations. *Ecological Modelling*, **172**, 109–139.
- Chu C., Collins N.C., Lester N.P. & Shuter B.J. (2006) Population dynamics of smallmouth bass in response to habitat supply. *Ecological Modelling*, **195**, 349–362.
- des Clers S. (1993) Modelling the impact of disease induced mortality on the population size of wild salmonids. *Fisheries Research*, **17**, 237–248.
- Codex Alimentarius Commission (1997) Proposed draft principles and guidelines for the conduct of microbiological risk assessment. *ALINORM*, **97/13A**, 42–46. (Appendix IV).
- Coutant C.C. (1998) What is normative for fish pathogens? A perspective on the controversy over interactions between wild and cultured fish *Journal of Aquatic Animal Health*, **10**, 101–106.
- Covello V.T. & Merkhofer M.W. (1993) *Risk Assessment Methods: Approaches for Assessing Health and Environmental Risks*. Plenum Publishing, New York.
- Creque S.M., Rutherford E.S. & Zorn T.G. (2005) Use of GIS-derived landscape-scale habitat features to explain spatial patterns of fish density in Michigan rivers. *North American Journal of Fisheries Management*, **25**, 1411–1425.
- Cunningham A.A., Hyatt A.D., Russell P. & Bennett P.M. (2007) Emerging epidemic diseases of frogs in Britain are dependent on the source of ranavirus agent and the route of exposure. *Epidemiology and Infection*, **135**, 1200–1212.
- Daszak P., Cunningham A.A. & Hyatt A.D. (2003) Infectious disease and amphibian population declines. *Diversity and Distributions*, **9**, 141–150.
- Dobson A.P. & May R.M. (1987) Effects of parasites on fish populations – theoretical aspects. *International Journal of Parasitology*, **17**, 363–370.
- EFSA (2007) Scientific Opinion of the Panel on Animal Health and Welfare on a request from the European Commission on possible vector species and live stages of susceptible species not transmitting disease as

- regards certain fish diseases. *The EFSA Journal* **584**, 1–163.
- Egusa S. & Masuda N. (1971) A new fungal disease of *Plecoglossus altivelis*. *Fish Pathology*, **6**, 41–46.
- Elsayed E., Faisal M., Thomas M., Whelan G., Batts W. & Winton J. (2006) Isolation of viral haemorrhagic septicemia virus from muskellunge, *Esox masquinongy* (Mitchill), in Lake St Clair, Michigan, USA reveals a new sublineage of the North American genotype. *Journal of Fish Diseases*, **29**, 611–619.
- FAO (2007) *Framework For Pest Risk Analysis. Vol. ISPM No. 02*. United Nations Food and Agriculture Organisation, Rome.
- FAO (2009) Report on the international emergency disease investigation task force on a serious fish disease in South Africa. p. 70. Rome.
- Fenichel E.P., Tsao J.L. & Jones M.L. (2009) Modeling fish health to inform research and management: *Renibacterium salmoninarum* dynamics in Lake Michigan. *Ecological Applications*, **19**, 747–760.
- Fisher M.C. & Garner T.W.J. (2007) The relationship between the emergence of *Batrachochytrium dendrobatidis*, the international trade in amphibians and introduced amphibian species. *Fungal Biology Reviews*, **21**, 2–9.
- Fisher M.C., Garner T.W.J. & Walker S.F. (2009) Global emergence of *Batrachochytrium dendrobatidis* and amphibian chytridiomycosis in space, time, and host. *Annual Review of Microbiology*, **63**, 291–310.
- Ford J.S. & Myers R.A. (2008) A global assessment of salmon aquaculture impacts on wild salmon. *PLoS Biology*, **6**, 411–417.
- Gale P., Drew T., Phipps L.P., David G. & Wooldridge M. (2009) The effect of climate change on the occurrence and prevalence of livestock disease in Great Britain: a review. *Journal of Applied Microbiology*, **106**, 1409–1423.
- Gregory A., Munro L.A., Wallace I.S., Bain N. & Raynard R.S. (2007) Detection of infectious pancreatic necrosis virus IPNV, from the environment in the vicinity of IPN infected salmon farms in Scotland. *Journal of Fish Diseases*, **30**, 621–630.
- Gustafson L., Klotins K., Tomlinson S., Karreman G., Cameron A., Wagner B. et al. (2010) Combining surveillance and expert evidence of viral hemorrhagic septicemia freedom: a decision science approach. *Preventive Veterinary Medicine*, **94**, 140–153.
- Hadorn D.C. & Stärk K.D.C. (2008) Evaluation and optimization of surveillance systems for rare and emerging infectious diseases. *Veterinary Research*, **39**, 57, DOI: 10.1051/vetres:2008033.
- Hanson N. (2009) Population level effects of reduced fecundity in the fish species perch (*Perca fluviatilis*) and the implications for environmental monitoring. *Ecological Modelling*, **220**, 2051–2059.
- Harvell C.D., Kim K., Burkholder J.M., Colwell R.R., Epstein P.R., Grimes D.J. et al. (1999) Emerging marine diseases – climate links and anthropogenic factors. *Science*, **285**, 1505–1510.
- Haydon D.T., Cleaveland S., Taylor L.H. & Laurenson M.K. (2002) Identifying reservoirs of infection: a conceptual and practical challenge. *Emerging Infectious Diseases*, **8**, 1468–1473.
- Hervé-Claude P.L., Carpenter T.E. & Hedrick R.P. (2008) Risk of introducing viral hemorrhagic septicemia virus (VHSV) to the Chilean South Pacific via sardine imports from Europe. *Diseases of Aquatic Organisms*, **78**, 199–207.
- Høgåsen H.R. & Brun E. (2003) Risk of inter-river transmission of *Gyrodactylus salaris* by migrating Atlantic salmon smolts, estimated by Monte Carlo simulation. *Diseases of Aquatic Organisms*, **57**, 247–254.
- Høgåsen H.R., Brun E. & Jansen P.A. (2009) Quantification of free-living *Gyrodactylus salaris* in an infected river and consequences for inter-river dispersal. *Disease of Aquatic Organisms*, **87**, 217–223.
- Jansen P.A., Matthews L. & Toft N. (2007) Geographic risk factors for inter-river dispersal of *Gyrodactylus salaris* in fjord-systems in Norway. *Disease of Aquatic Organisms*, **74**, 139–149.
- Johnsen B.O. & Jensen A.J. (1991) The *Gyrodactylus* story in Norway. *Aquaculture*, **98**, 289–302.
- Jones J.N. & Perera R.P. (2009) Moving away from the pathogen-centric approach to aquatic animal disease risk analysis. In: *EAFP XIV International Conference*. (Ed Anon.), p. 23. European Association of Fish Pathologists.
- Jones K.E., Patel N.G., Levy M.A., Storeygard A., Balk D., Gittleman J.L. et al. (2008) Global trends in emerging infectious diseases. *Nature*, **451**, 990–993.
- Jonkers A.R.T., Sharkey K.J., Thrush M.A., Turnbull J.F. & Morgan K.L. (2010) Epidemics and control strategies for diseases of farmed salmonids: A parameter study. *Epidemics*, DOI:10.1016/j.epidem.2010.1008.1001.
- Kent M.L. (2000) Marine netpen farming leads to infections with some unusual parasites. *International Journal for Parasitology*, **30**, 321–326.
- Krkošek M., Ford J.S., Morton A., Lele S., Myers R.A. & Lewis M.A. (2007) Declining wild salmon populations in relation to parasites from farm salmon. *Science*, **318**, 1772–1775.
- Krokan P.S. & Mørkved O.J. (1994) *Nytte-Kostanalyse av Innsatsen for å Bekjempe Lakseparasitten Gyrodactylus Salaris i Perioden 1981–1998*. VESO, Oslo.
- Krueger R.C., Kerans B.L., Vincent E.R. & Rasmussen C. (2006) Risk of *Myxobolus cerebralis* infection to rainbow

- trout in the Madison River, Montana, U.S.A. *Ecological Applications*, **16**, 770–783.
- Langdon J.S. & Humphrey J.D. (1987) Epizootic haematopoietic necrosis, a new viral disease in redfin perch, *Perca fluviatilis* L., in Australia. *Journal of Fish Diseases*, **10**, 289–297.
- Lessard P., Leplatténier R., Norval R.A.I., Perry B.D., Dolan T.T., Burrill A. *et al.* (1988) The use of geographical information-systems in estimating East coast fever risk to African livestock. *Acta Veterinaria Scandinavica* **84**(suppl), 234–236.
- Lessard P., Leplatténier R., Norval R.A.I., Kundert K., Dolan T.T., Croze H. *et al.* (1990) Geographical information-systems for studying the epidemiology of cattle diseases caused by *Theileria-parva*. *Veterinary Record*, **126**, 255–262.
- Lilley J.H., Callinan S., Chinabut S., Kanchanakhan S., Macrae I.H. & Phillips M.J. (1998) *Epizootic Ulcerative Syndrome (EUS) Technical Handbook*, The Aquatic Animal Health Reserach Institute, Bangkok.
- Longshaw M., Frear P.A., Nunn A.D., Cowx I.G. & Feist S.W. (2010) The influence of parasitism on fish population success. *Fisheries Management and Ecology*, **17**, 426–434.
- Lumsden J.S., Morrison B., Yason C., Russell S., Young K., Yazdanpanah A. *et al.* (2007) Mortality event in freshwater drum *Aplodinotus grunniens* from Lake Ontario, Canada, associated with viral haemorrhagic septicemia virus, Type IV. *Disease of Aquatic Organisms*, **76**, 99–111.
- Marcogliese D.J. (2008) The impact of climate change on the parasites and infectious diseases of aquatic animals. *Revue Scientifique et Technique, Office International des Epizooties*, **27**, 467–484.
- Marcos-López M., Gale P., Oidtmann B.C. & Peeler E.J. (2010) Assessing the impact of climate change on disease emergence in freshwater fish in the United Kingdom. *Transboundary and Emerging Diseases*, **57**, 293–304.
- Marsh I.B., Whittington R.J., O'Rourke B., Hyatt A.D. & Chisholm O. (2002) Rapid differentiation of Australian, European and American ranaviruses based on variation in major capsid protein gene sequence. *Molecular and Cellular Probes*, **16**, 137–151.
- Martin P.A.J., Cameron A.R. & Greiner M. (2007) Demonstrating freedom from disease using multiple complex data sources. 1: a new methodology based on scenario trees. *Preventive Veterinary Medicine*, **79**, 71–97.
- May R.M. & Anderson R.M. (1979) Population biology of infectious diseases: Part 2. *Nature*, **280**, 455–461.
- McAlister P.E. & Bebak J. (1997) Infectious pancreatic necrosis virus in the environment: relationship to effluent from aquaculture facilities. *Journal of Fish Diseases*, **20**, 201–207.
- McCallum H.I., Kuris A., Harvell C.D., Lafferty K.D., Smith G.W. & Porter J. (2004) Does terrestrial epidemiology apply to marine systems? *Trends in Ecology and Evolution*, **19**, 585–591.
- Modin J. (1998) Whirling disease in California: a review of its history, distribution, and impacts, 1965–1997. *Journal of Aquatic Animal Health*, **10**, 132–142.
- Moody N.J.G. & Owens L. (1994) Experimental demonstration of the pathogenicity of a frog virus, Bohle iridovirus, for a fish species, barramundi *Lates calcarifer*. *Disease of Aquatic Organisms*, **18**, 95–102.
- Morgan K.L. (2001) Epizootic ulcerative syndrome: an epidemiological approach. In: *Risk analysis in aquatic animal health*. (Ed C.J. Rodgers), pp. 209–214. Office International des Epizooties, Paris.
- Morris D.J., Taylor N.G.H., Turnbull J.F. & Shinn A.P. (2009) Development of a risk evaluation system for *Gyrodactylus salaris* in English and Welsh river systems. In: *EAFP XIV International Conference*. (Ed Anon), P. 153. European Association of Fish Pathologists.
- Munro A.L.S., Liveredge J. & Elson K.G.R. (1976) The distribution and prevalence of infectious pancreatic necrosis virus in wild fish in Loch Awe. *Proceedings of the Royal Society of Edinburgh, B* **75**, 223–232.
- Murray A.G. (2006) A model of the emergence of infectious pancreatic necrosis virus in Scottish salmon farms 1996–2003. *Ecological Modelling*, **199**, 64–72.
- Murray A.G. (2009) Using simple models to review the application and implications of different approaches used to simulate transmission of pathogens among aquatic animals. *Preventive Veterinary Medicine*, **88**, 167–177.
- Murray A.G. & Gaughan D.J. (2003) Using an age-structured model to simulate the recovery of the Australian pilchard (*Sardinops sagax*) population following epidemic mass mortality. *Fisheries Research*, **60**, 415–426.
- Murray A.G. & Peeler E.J. (2005) A framework for understanding the potential for emerging diseases in aquaculture. *Preventive Veterinary Medicine*, **67**, 223–235.
- Murray A.G., O'Callaghan M. & Jones B. (2001) A model of transmission of a viral epidemic among schools within a shoal of pilchards. *Ecological Modelling*, **144**, 245–259.
- Murray A.G., Busby C.D. & Bruno D. (2003) Infectious pancreatic necrosis virus in Scottish Atlantic salmon farms, 1996–2001. *Emerging Infectious Diseases*, **9**, 455–460.
- Murray N., MacDiarmid S.C., Wooldridge M., Gummow B., Morley R.S., Weber S.E. *et al.* (2004) *Handbook on Import Risk Analysis for Animals and Animal Products – Introduction and Qualitative Risk Analysis*. Office International des Epizooties, Paris, pp 59.



- Murray A.G., Amundrud T.L. & Gillibrand P.A. (2005) Models of hydrodynamic pathogen dispersal affecting Scottish salmon production: modelling shows how Scotland eradicated ISA, but not IPN. *Bulletin of the Aquaculture Association of Canada*, **105**, 79–86.
- Nehring R.B. & Walker P.G. (1996) Whirling disease in the wild: the new reality in the Intermountain West. *Fisheries*, **21**, 28–31.
- Nokes D.J. & Anderson R.M. (1988) The use of mathematical models in the epidemiological study of infectious diseases and in the design of mass immunization programmes. *Epidemiology and Infection*, **101**, 1–20.
- Nunn A.D., Harvey J.P., Britton J.R., Frear P.A. & Cowx I.G. (2007) Fish, climate and the Gulf Stream: the influence of abiotic factors on the recruitment success of cyprinid fishes in lowland rivers. *Freshwater Biology*, **52**, 1576–1586.
- O.I.E. (2001) Risk analysis in aquatic animal health. In: *OIE International Conference on Risk Analysis in Aquatic Animal Health*. (Ed C.J. Rodgers ). Office International des Epizooties, Paris, 346pp.
- O.I.E. (2009) *Aquatic Animal Health Code*. World Organisation for Animal Health, Paris.
- Okamura B., Hartikainen H., Schmidt-Posthaus H. & Wahli T. (2010) Life cycle complexity, environmental change and the emerging status of salmonid proliferative kidney disease. *Freshwater Biology*, **56**, 735–753.
- Olsen D., Richards J. & Scott R.D. (1991) Existence and sport values for doubling the size of Columbia River basin salmon and steelhead runs. *Rivers*, **2**, 44–56.
- Paisley L.G., Karlsen E., Jarp J. & Mo T.A. (1999) A Monte Carlo simulation model for assessing the risk of introduction of *Gyrodactylus salaris* to the Tana river, Norway. *Diseases of Aquatic Organisms*, **37**, 145–152.
- Patterson K.R. (1996) Modelling the impact of disease-induced mortality in an exploited population of the fungal parasite *Ichthyophonus hoferi* in the North Sea herring (*Clupea harengus*). *Canadian Journal of Fisheries and Aquatic Sciences*, **53**, 2870–2877.
- Patz J.A., Campbell-Lendrum D., Holloway T. & Foley J.A. (2005) Impact of regional climate change on human health. *Nature*, **438**, 310–317.
- Payno Morant M. (2009) *Consequence Assessment for Exotic Fish Disease Incursions in England and Wales*. M.Sc., Cranfield University, 99pp.
- Peeler E.J. & Feist S.W. (2011) Human intervention in freshwater ecosystems drives disease emergence. *Freshwater Biology*, **56**, 705–716.
- Peeler E.J. & Thrush M.A. (2004) Qualitative analysis of the risk of introducing *Gyrodactylus salaris* into the United Kingdom. *Diseases of Aquatic Organisms*, **62**, 103–113.
- Peeler E.J., Gardiner R. & Thrush M.A. (2004) Qualitative risk assessment of routes of transmission of the exotic fish parasite *Gyrodactylus salaris* between river catchments in England and Wales. *Preventive Veterinary Medicine*, **64**, 175–189.
- Peeler E.J., Murray A.G., Thebault A., Brun E., Giovannini A. & Thrush M.A. (2007) The application of risk analysis in aquatic animal health management. *Preventive Veterinary Medicine*, **81**, 3–20.
- Peeler E.J., Afonso A., Berthe F., Brun E., Rodgers C.J., Roque A. et al. (2009) Epizootic haematopoietic necrosis virus – An assessment of the likelihood of introduction and establishment in England and Wales. *Preventive Veterinary Medicine*, **9**, 241–253.
- Pelletier D. & Mahévas S. (2005) Spatially explicit fisheries simulation models for policy evaluation. *Fish and Fisheries*, **6**, 307–349.
- Perry B.D., Lessard P., Norval R.a.I., Kundert K. & Kruska R. (1990) Climate, vegetation and the distribution of *Rhipicephalus appendiculatus* in Africa. *Parasitology Today*, **6**, 100–104.
- Phillips S.J. & Dudík M. (2008) Modeling of species distributions with Maxent: new extensions and a comprehensive evaluation. *Ecography*, **31**, 161–175.
- Phillips S.J., Anderson R.P. & Schapire R.E. (2006) Maximum entropy modeling of species geographic distributions. *Ecological Modelling*, **190**, 231–259.
- Podolska M. & Horbowy J. (2003) Infection of Baltic herring (*Clupea harengus membras*) with *Anisakis simplex* larvae, 1992–1999: a statistical analysis using generalized linear models. *ICES Journal of Marine Science*, **60**, 85–93.
- Poulin R., Paterson R.A., Townsend C.R., Tomkins D.M. & Kelly D.W. (2010) Biological invasions and the dynamics of endemic diseases in freshwater ecosystems. *Freshwater Biology*, **56**, 676–688.
- Puschendorf R., Carnaval A.C., Vanderwal J., Zumbado-Ulate H., Chaves G., Bolaños F. et al. (2009) Distribution models for the amphibian chytrid *Batrachochytrium dendrobatidis* in Costa Rica: proposing climatic refuges as a conservation tool. *Diversity and Distributions*, **15**, 401–408.
- Real L.A. & Biek R. (2007) Infectious disease modeling and the dynamics of transmission In: *Wildlife and Emerging Diseases: The Biology, Circumstances and Consequences of Cross-Species Transmission*. (Eds J.E. Childs, J.S. Mackenzie & J.A. Richt ), pp. 33–49. Springer, Berlin.
- Reno P.W. (1998) Factors involved in the dissemination of disease in fish populations. *Journal of Aquatic Animal Health*, **10**, 160–171.
- Revie C.W., Gettinby G., Treasurer J.W. & Wallace C. (2003) Identifying epidemiological factors affecting sea

- lice *Lepeophtheirus salmonis* abundance on Scottish salmon farms using general linear models. *Diseases of Aquatic Organisms*, **57**, 85–89.
- Ricker W.E. (1954) Stock and recruitment. *Journal of the Fisheries Research Board of Canada*, **11**, 559–623.
- Righton D. & Mills C. (2006) Application of GIS to investigate the use of space in coral reef fish: a comparison of territorial behaviour in two Red Sea butterflyfishes. *International Journal Of Geographical Information Science*, **20**, 215–232.
- Rödder D., Kielgast J., Bielby J., Schmidtlein S., Bosch J., Garner T.W.J. *et al.* (2009) Global amphibian extinction risk assessment for the panzootic chytrid fungus. *Diversity*, **1**, 52–66.
- Rodgers C.J. (1997) Risk assessment in aquaculture report on a workshop held at the VIII EAFF international conference. in: *EAFF VIII International Conference*. (Ed Anon), pp. 229–233. European Association of Fish Pathologists.
- Rogers D.J. (2006) Models for vectors and vector-borne diseases. *Advances in Parasitology*, **62**, 1–35.
- Rogers D.J. & Packer M.J. (1993) Vector-borne diseases, models, and global change. *Lancet*, **342**, 1282–1284.
- Rogers D.J. & Randolph S.E. (2003) Studying the global distribution of infectious diseases using GIS and RS. *Nature Reviews. Microbiology*, **1**, 231–237.
- Ruane N.M., Murray A.G., Geoghegan F. & Raynard R.S. (2009) Modelling the spread of infectious pancreatic necrosis virus (IPNV) in the Irish salmon farming industry: the role of inputs. *Ecological Modelling*, **220**, 1369–1374.
- Shaw D.J. & Dobson A.P. (1995) Patterns of macro-parasite abundance and aggregation in wildlife populations: a quantitative review. *Parasitology*, **111**, S111–S133.
- Skerratt L.F., Berger L., Speare R., Cashins K.R., McDonald K.R., Phillott A.D. *et al.* (2007) Spread of chytrid-omycosis has caused the rapid global decline and extinction of frogs. *EcoHealth*, **4**, 125–134.
- Stärk K., Regula G., Hernandez J., Knopf L., Fuchs K., Morris R. *et al.* (2006) Concepts for risk-based surveillance in the field of veterinary medicine and veterinary public health: review of current approaches. *Biomedical Central Health Service Research*, **6**, DOI:10.1186/1472-6963-6-20.
- Sterud E., Forseth T., Ugedal O., Poppe T.T., Joergensen A., Bruheim T. *et al.* (2007) Severe mortality in wild Atlantic salmon *Salmo salar* due to proliferative kidney disease (PKD) caused by *Tetracapsuloides bryosalmonae* (Myxozoa). *Diseases of Aquatic Organisms*, **77**, 191–198.
- Taylor N.G.H., Norman R.A., Way K. & Peeler E.J. (2010) Modelling the koi herpesvirus epidemic highlights the importance of active surveillance within a national control policy. *Journal of Applied Ecology*, DOI: 10.1111/j.1365-2664.2010.01926.x.
- Thompson G.R., Perry B.D., Catley A., Leyland T.J., Penrith M.L. & Donaldson A.I. (2006) Certification for regional and international trade in livestock commodities: the need to balance credibility and enterprise. *Veterinary Record*, **159**, 53–57.
- Thrush M. & Peeler E. (2006) Stochastic simulation of live salmonid movement in England and Wales to predict potential spread of exotic pathogens. *Diseases of Aquatic Organisms*, **72**, 115–123.
- Urquhart K.L., Murray A.G., Gregory A., O’Dea M., Munro L.A., Smail D.A. *et al.* (2008) Estimation of infectious dose and viral shedding rates for infectious pancreatic necrosis virus in Atlantic salmon, *Salmo salar* L., post-smolts. *Journal of Fish Diseases*, **31**, 879–887.
- VHSV Expert Panel and Working Group (2010) Viral hemorrhagic septicemia virus (VHSV) IVb) risk factors and association measures derived by expert panel. *Preventive Veterinary Medicine*, **94**, 128–139.
- Viljugrein H., Staalstrøm A., Molvær J., Urke H. & Jansen P. (2009) Integration of hydrodynamics into a statistical model on the spread of pancreas disease (PD) in salmon farming. *Disease of Aquatic Organisms*, **88**, 35–44.
- Vose D. (2000) *Risk Analysis – A Quantitative Guide*. John Wiley & Sons, Chichester, pp. 418.
- Walker S.F., Bosch J., James T.Y., Litvintseva A.P., Oliver Valls J.A., Piña S. *et al.* (2008) Invasive pathogens threaten species recovery programs. *Current Biology*, **18**, R853–R854.
- Wallace I.S., Gregory A., Murray A.G., Munro E.S. & Raynard R.S. (2008) Distribution of infectious pancreatic necrosis virus (IPNV) in wild marine fish from Scottish waters with respect to clinically infected aquaculture sites producing Atlantic salmon, *Salmo salar* L. *Journal of Fish Diseases*, **31**, 177–186.
- Whittington R.J. & Chong R. (2007) Global trade in ornamental fish from an Australian perspective: the case for revised import risk analysis and management strategies. *Preventive Veterinary Medicine*, **81**, 92–116.
- Whittington R.J., Becker J.A. & Dennis M.M. (2010) Iridovirus infections in finfish – critical review with emphasis on ranaviruses. *Journal of Fish Diseases*, **33**, 95–122.

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