Modelling management strategies for a disease including undetected sub-clinical infection: Bacterial kidney disease in Scottish salmon and trout farms

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ABSTRACT

Disease is a major constraint on animal production and welfare in agriculture and aquaculture. Movement of animals between farms is one of the most significant routes of disease transmission and is particularly hard to control for pathogens with subclinical infection. *Renibacterium salmoninarum* causes bacterial kidney disease (BKD) in salmonid fish, but infection is often sub-clinical and may go undetected with major potential implications for disease control programmes. A Susceptible-Infected model of *R. salmoninarum* in Scottish aquaculture has been developed that subdivides the infected phase between known and undetected sub-clinically infected farms and diseased farms whose status is assumed to be known. Farms officially known to be infected are subject to movement controls restricting spread of infection. Model results are sensitive to prevalence of undetected infection, which is unknown. However, the modelling suggests that controls that reduce BKD prevalence include improve biosecurity on farms, including those not known to be infected, and improved detection of infection. Culling appears of little value for BKD control. BKD prevalence for rainbow trout farms is less sensitive to controls than it is for Atlantic salmon farms and so different management strategies may be required for the sectors.

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Introduction

Food production and security in agriculture, whether animals or plant, can be undermined by diseases (Wilkinson et al., 2011). These diseases can be very expensive to society, with examples such as tuberculosis control from the United States at $3.5 BN and foot and mouth disease in Europe at €6 BN (Horan et al., 2010). Aquacultural production is similarly affected by disease (Murray and Peeler, 2005), and losses can also run into billions of dollars, for example those due to white spot disease of shrimp (Hill, 2002).

Human activity plays a major role in the introduction and spread of such diseases in agricultural systems (Wilkinson et al., 2011). One important activity for spreading disease is the movement of animals between farms (Fèvre et al., 2006), such movements are extensive in many production systems, both in terms of the numbers of and the distances that animals are moved (Green et al., 2011). Targeted controls on the spread of disease aim to prevent transmission from infected sites by imposing movement controls on them and, in more extreme cases, culling animals, which also prevents transmission to other farms through the environment. Uninfected farms may improve biosecurity and limit inputs when aware of the presence of a potential disease problem, conversely

farms whose operators are confident that risk is low, because probability or consequence of infection is low, may relax their biosecurity and welfare measures (Hennessy, 2007).

Imposition of targeted controls requires knowledge of the distribution of a pathogen. Diseased animals frequently exhibit clinical signs that indicate presence of the pathogen by visual inspection and so allow passive reporting of problems by farmers who are in daily contact with their animals. Confirmation of the pathogen usually requires laboratory diagnostic testing, but action can be taken immediately on suspicion if deemed necessary. However, infections generally go through an incubation phase during which the host appears healthy. This subclinical infection may be short lived (e.g. foot and mouth disease virus (FMDV)) or last for a prolonged period (e.g. *Myobacterium bovis* the agent of bovine tuberculosis). Detection of infection during this phase requires an active programme of field sampling, often carried out by vets or official health inspectors. Such farm visits can also detect animals with clinical signs that have not been reported and allow inspectors to interact with farmers to improve passive reporting rates. Active sampling is necessarily limited by resources (Cannon, 2009) and risk-based surveillance allows populations at the greatest risk of receiving or transmitting infection to be targeted (Stärk et al., 2006). A particularly useful form of risk-based surveillance is contact tracing of farms that have received or sent animals to a known infected farms (Eames and Keeling, 2003). Delays in detection of infection can be disastrous, even the relatively short period before movement controls were imposed allowed FMDV to become spread to regions

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throughout Great Britain (GB) as a result of the movement of animals (Green et al., 2006) and the control of bovine tuberculosis spread in England and Wales is problematic due to the prolonged subclinical infection (Gilbert et al., 2005).

In this paper we model a case study of subclinical spread of infection in an animal production system: the bacterial pathogen *Renibacterium salmoninarum* (Toranzo et al., 2005), the cause of both chronic subclinical infection and bacterial kidney disease in the farmed salmonid population of Scotland. The epidemiology of BKD in Scotland reviewed in detail by Murray et al. (2011) and Wallace et al. (2011) is summarised in the following text, and this epidemiology informs the basis of the model structure described subsequently. We use the modelling to explore the role of this subclinical infection on the response of BKD prevalence to alteration in model parameters; this analysis includes the effect of uncertainty as to the prevalence of subclinical infection on these responses. The model is used to investigate the effects of potential applied controls on BKD prevalence and thus identify strategies that control or reduce the current prevalence of disease. Ideally disease control strategies should be selected that balance costs of controls and impacts of disease (Peddie and Stott, 2003), unfortunately we lack systematic costings of these and the modelling outputs are of use to aid policy decisions rather than to directly confirm optimal controls.

Methods

The system: Scottish aquaculture and epidemiology of BKD

Scottish farmed Atlantic salmon (*Salmo salar*) production was 144,247 tonnes in 2009 (Walker, 2010) and industry figures show 2010 production to be worth £500 M at farm gate value and £1 BN retail value (SSPO, 2011); salmon was Scotland's largest single food export product. Scottish production of rainbow trout (*Oncorhynchus mykiss*) was also substantial at 6766 tonnes in 2009 (Walker, 2010). About 90% of Scottish salmonid fish farms are salmon and 10% trout (Walker, 2010); very small numbers of brown trout (*Salmo trutta*) and Arctic char (*Salvelinus alpinus*) are also farmed. Aquaculture is a major employer and investor both at the Scottish level, but more particularly in many regional communities where there are relatively few alternative sources of employment.

Scottish aquaculture has been affected by a range of disease problems and infectious diseases account for about a third of all the losses to production from marine salmon farms (Soares et al., 2011), other losses being to production processes, adverse environments and predators. One of the diseases infecting both salmon and trout farms is bacterial kidney disease (BKD) (Bruno, 2004; Murray et al., 2011). This disease is caused by the pathogen *R. salmoninarum*, which is found in Western Europe (including GB, but not Ireland), North America, Japan and Chile (Toranzo et al., 2005).

In Scotland *R. salmoninarum* is spread between farms primarily with the movement of fish (Austin and Rayment, 1985; Murray et al., 2011). Although bacteria are shed into the aquatic environment particularly from clinically diseased fish (McKibben and Pascho, 1999), they survive poorly in the water and so are unlikely to be transported except over short distances (Austin and Rayment, 1985). Outbreaks of BKD tend to reflect patterns of transport within companies (Murray et al., 2011). *R. salmoninarum* can also be transmitted vertically with eggs (Evelyn et al., 1986), however this requires the high infection loads associated with clinical disease and no Scottish broodstock farm has yet tested positive.

Both salmon and trout are moved extensively in a complex network of contacts between farms (Green et al., 2009; Jonkers et al., 2010). These movements occur throughout GB and ova are imported from sources worldwide, although imports of live

salmonid fish are limited to a few from BKD free areas of the EU (Walker, 2010) (mostly the Republic of Ireland). The movement of fish between farms is an essential requirement of the production cycle, both biologically and economically. Fish are moved from hatcheries to ongrowing farms, and all salmon, and some trout, are moved from freshwater farms to marine farms as they smolt. Movements of fish tend to involve large numbers and so even pathogens present at low levels within the population are likely to be transported (Fenichel et al., 2008).

BKD is notifiable within the United Kingdom (UK), so it is a legal requirement to report suspicion or confirmation of the presence of this disease (Munro, 2007). Suspicion also applies with contact tracing of farms that have received or deliver fish to the infected farm within 6 months or are in the same locality (subcatchment of a river or within tidal excursion distance at sea). On report of suspicion, official fish health inspectors (FHI) visit the farm; in addition FHI routinely inspect all farms annually. Under the control regime that applied up until 2010 the FHI took samples from 150 fish at suspect sites, and, every other year, 30 fish from sites visited for routine inspection. Recently the policy has changed (Richards, 2011), such that sampling only occurs if the FHI observe signs consistent with BKD when visiting farms whether for a routine or targeted inspection.

Until 2010 samples were tested using enzyme-linked immunosorbent assay (ELISA) and confirmed using bacterial culture; since 2011 quantitative polymerase chain reaction (qPCR) has been used as the sole test on animals with clinical signs. Analysis of these diagnostic methods indicated that although they are sensitive at detecting and specific at confirming *R. salmoninarum* in the presence of clinical BKD (Bruno et al., 2007), both ELISA and culture have relatively poor sensitivity for confirmation of subclinical infection (Hall et al., 2011) because bacterial colonies are few and localised in such fish (Austin and Rayment, 1985). However, the *R. salmoninarum* qPCR is a considerably more sensitive test for subclinical infection (Hall et al., 2011). When low test sensitivity is combined with low levels of infection within infected populations and further reduced sensitivity in pooled samples, analysis shows that the routine sampling as practiced in Scotland up until 2010 was of negligible value in detecting subclinical infection (Hall et al., 2011).

If a farm tests positive it is placed under movement restrictions (Munro, 2007), first a Thirty Day Notice (TDN) and then, if infection was confirmed, a Designated Area Order (DAO). DAOs are now called Confirmed Designation Notices (CDNs) but the term DAO will be used in this manuscript as it applied at the time for which data are presented. These TDNs and DAOs prohibited movement from the farm, except for the case of non-diseased fish to other similarly infected farms (Munro, 2007), restrictions have recently been lifted on movements to trout farms in areas containing no salmon farms (Richards, 2011). Movement of clinically disease fish is banned under welfare legislation. Previously, restrictions were lifted from a farm after 150 fish have tested negative on two occasions by ELISA by FHI, now only one sample of 150 fish by qPCR is required because of the greater sensitivity found for this test. Restrictions can also be lifted (now and under the old regime) if the farm has been depopulated, disinfected and fallowed.

The first ever report of BKD was in Scottish wild salmon and was referred to 'Dee disease' (Mackie et al., 1933; Smith, 1964), BKD is a significant cause of wild fish mortality in other countries to this day (Fenichel et al., 2009). However, BKD has not been reported from Scottish wild freshwater fish since the 1960s. Extensive ELISA screening of wild fish by FHI and researchers in Scotland since the 1960s has returned only negative results (for example 4520 wild freshwater fish were sampled between 1989 and 2004 alone (Wallace et al., 2011)). In 2003 an ELISA positive was obtained from a single herring (*Clupea harengus*) taken from within a cage
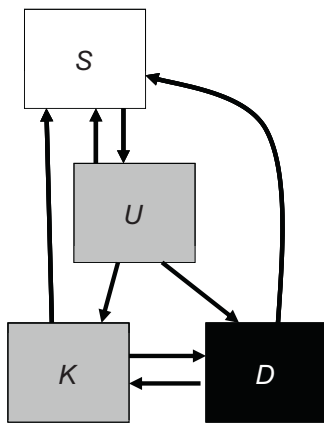
Fig. 1. Structure of the model: *S* = susceptible; *U* = unknown infected; *K* = known infected; *D* = clinically diseased with BKD.

Fig. 2. Percentage of Scottish salmonid farms with DAOs 2004–8: for all farms (thick solid line); for salmon (dashed line); or rainbow trout (thin solid line).

holding salmon with advanced clinical BKD (unpublished result). Recent qPCR sampling of 2703 Scottish freshwater fish gave positive results for two pools of stickleback (*Gasterosteus aculeatus*), one pool of minnow (*Phoxinus phoxinus*) and 3 (likely escaped) rainbow trout pools; the positive samples were obtained close to infected farms and none had signs of BKD (Wallace et al., 2011). Low levels of infection were also found in England and Wales (40 by qPCR and 2 by culture out of 946 fish sampled) by Chambers et al. (2008). These wild fish might sometimes act as a reservoir, particularly if *R. salmoninarum* were eradicated from farms. Given this low level of infection and its chronic nature it is reasonable to assume that BKD has little impact on Scottish wild fish populations and they have little role in BKD transmission between farms so it is reasonable not to include them explicitly in the model, although they may be relevant to parameter values concerned with transmission and persistence of infection and potential roles are noted when the model parameter values are considered.

Given the low level of *R. salmoninarum* infection in Scottish fish, we do not include these in the modelling. The situation in Scotland is in contrast to North America, where the dynamics of BKD in managed wild salmonid populations have been modelled for the Great Lakes by Fenichel et al. (2009) and the Snake River in Washington State by Hamel (2001).

Previous BKD control strategies in the UK were underpinned by European Union (EU) Addition Guarantees (AG) that banned imports of fish and ova to the UK from areas of the EU affected by BKD (Munro, 2007). However, these AG were dependent on an effective eradication programme and, while controls had kept the prevalence of BKD low, eradication was not occurring in GB (see Fig. 2 later), although Ireland (including Northern Ireland) retains AG for BKD. Furthermore a conflict of interest between salmon farmers, who supported the existing controls, and trout farmers, who did not, meant that alternative control strategies needed to be investigated (Richards, 2011) for their likely effect on the prevalence of BKD.

The model

A simple model is presented following the principles of Anderson and May (1979) in which the population is divided into uninfected susceptible (*S*) and infected farms. In this case the infected farms are subdivided into diseased (*D*) or sub-clinically infected farms. The sub-clinically infected farms are further divided into 'known' cases (*K*) and 'undetected' cases of infection (*U*) because targeted controls can only be imposed on known cases (Fig. 1). The unit of population in this model is the farm; a farm with 1% and a farm with 90% of fish infected are both considered
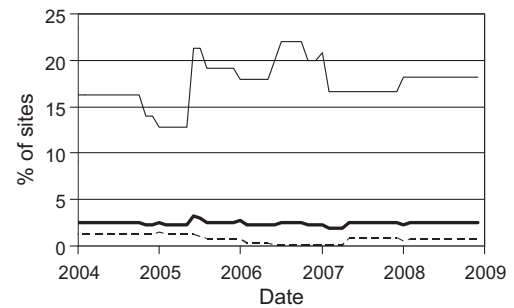
'infected' farms. 'Prevalence', thus here refers to proportion of farms and 'level' to proportion of fish within a population that are infected or diseased. The population modelling is density independent with the variables representing the proportions of farms in each category and so $S + U + D + K = 1$.

Fenichel et al. (2009) used similar categories (susceptible (*S*), exposed (*U*) and infectious (*D*)) to model wild fish with *R. salmoninarum* infection although these apply at the individual fish rather than the farm level. In their case there was no possibility of knowing the status of individual fish, nor any way to target management on infected fish should they be known, so they had no category equivalent to *K*.

Taylor et al. (2011) used a similar approach to our model of *S*, *I* and *C* when modelling koi herpesvirus (KHV) in English and Welsh carp (*Cyprinus carpio*). They divided their infected population into controlled *C* and uncontrolled *I* farms, with only the latter spreading infection to susceptible *S* farms, so $C = K + D$ in our model.

Our BKD model's variables each have a steady state value that they reach for baseline parameter values. For example U^* is the proportion of farms with undetected infection, *U*, at steady state and similarly D^*, K^* and S^* are the steady-state values of *D*, *K*, and *S* (ignoring the trivial solution $S^* = 1$, $U^* = K^* = D^* = 0$). When model parameters are changed this leads, with enough time, to a new steady-state. The new steady states under these scenarios are denoted as U^+, D^+, K^+ and S^+.

The model variables interact through processes of transmission of and recovery from infection and onset and abatement of clinical disease and unknown infection may become known through contact tracing or direct surveillance (Fig. 1). All these interactions are driven by model parameters described below and listed in Table 1.

Susceptible populations can develop infection through contact with any of the infected populations (*U*, *K* or *D*). Transmission follows the format $\beta_U US$, $\beta_K KS$ or $\beta_D DS$ a standard format for epidemiological models (Anderson and May, 1979) that has previously been used to model pathogen transmission between fish farms (Murray, 2006; Taylor et al., 2011). Pathogen transmission leads to transformation from *S* to *U* (i.e. the subclinical infection in these populations is initially unknown, but see later for contact tracing). In the case of *R. salmoninarum* most transmission is likely to be through movements of fish (Murray et al., 2011); movement controls, DAOs, are a key part of BKD controls (Munro, 2007), which are applied where infection is officially known (*K* or *D* farms). So while some transmission may occur from *D* farms by bacteria are shed into the water, transmission of this pathogen is largely halted for *D* or *K* farms by imposition of DAOs.

The model does not explicitly include vertical transmission, although this can occur (Evelyn et al., 1986) there is no evidence of it doing so in Scotland (Murray et al., 2011). Should it occur, the existing model formulation would apply to vertical transmission within Scotland; imports might re-introduce infection from an external country should eradication occur.

Table 1

Model variables and parameters. Initial steady states are based on the current situation for the entire industry and values selected are described in the text. Calculated values refer to parameters calculated using formulae in Appendix 1 given the initial steady state. Modelled new steady-state values are model outputs after one or more parameters are altered and the model is run until stabilised.

Name	Default value	Description
S	Model variable	Proportion of farms uninfected (susceptible)
U	Model variable	Proportion of farms sub-clinically infected but not yet detected
K	Model variable	Proportion of farms known to be sub-clinically infected
D	Model variable	Proportion of farms with clinical BKD
S^*	$1 - U^* - K^* - D^*$	Initial steady-state value of S
U^*	Input	Initial steady-state value of U
K^*	0.005, 0.0125 or 0.1	Initial steady state value of K (salmon, all farms, trout)
D^*	K^*	Initial steady state value of $D = K^*$, half DAOs
S^+	Modelled	New steady-state S after parameter(s) altered
U^+	Modelled	New steady-state U after parameter(s) altered
K^+	Modelled	New steady-state K after parameter(s) altered
D^+	Modelled	New steady-state D after parameter(s) altered
β_U	0.2	Transmission coefficient from U
β_K	0	Transmission coefficient from K (controlled)
β_D	0.04	Transmission coefficient from D (controlled, except environmental transmission)
G	Calculated	Average removal rate of infection
g_U	Calculated	Removal rate of infection from U
g_K	Calculated	Removal rate of infection from K
g_D	Calculated	Removal rate of infection from D
y	2	Factor by which n_K and n_D are $>n_U$
x	Calculated	Rate of onset of disease
r	Calculated	Rate of recovery from disease
q	0	Background surveillance (not effective)
c	1	Contact tracing efficacy

Infection can be lost from infected farms at a rate g_U, g_K, or g_D (these parameters are evaluated in Appendix 1). Loss of infection could occur through infection self resolving, or by fallowing the farm either as part of ongoing biosecurity practices or specifically because infection is present; the fish could even be culled (giving high g_K and g_D values). In this case U, K or D will return to susceptible S. Infection removal rates may differ because targeted fallowing or culling may be applied to known infected farms. Infection on U farms is undetected, so any practices applied to increase g_U must also be applied to uninfected S farms.

Disease can develop on sub-clinically infected farms (U or K) at a rate x, while diseased farms can revert to sub-clinical K at a rate r (the presence of infection on these farms is known because of their past disease history).

Subclinical infection can be detected by contact tracing or by more general surveillance of the population and either form of detection converts U to K. Contact tracing is simulated as proportional to the rate of development of unexpected new cases of disease (cxU), i.e. from unknown infected farms U not from K. Parameter q is the rate at which sub-clinical infections are discovered through surveillance. This is dependent on the effort and methods used, but current methods appear ineffective at identifying sub-clinical infection (Hall et al., 2011).The resultant equations are:

$$\frac{dS}{dt} = -\beta_U SU - \beta_K SK - \beta_D SD + g_U U + g_K K + g_D D \qquad (1)$$

$$\frac{dU}{dt} = \beta_U SU + \beta_K SK + \beta_D SD - cxU - g_U U - xU - qU \qquad (2)$$

$$\frac{dK}{dt} = rD + cxU + qU - xK - g_K K \qquad (3)$$

$$\frac{dD}{dt} = xU + xK - g_D D - rD \qquad (4)$$

The model has been coded in R (R Development Core Team, 2009) and the code is provided in Appendix 2.

Parameterisation

If we take an approximate value for model variables D and K based on current prevalence of known infection and make some assumptions concerning the existing control policies we can estimate many of the basic parameters for the model (Table 1). The analytical solutions of key parameters are detailed in Appendix 1 and are based on the assumption that the system is in steady state.

The number of farms with DAOs has been fairly stable; this observed number gives the value of $D + K$ when divided by the number of active farms (Walker, 2010) (Fig. 2). Cases of BKD have occurred for decades in salmonid farms at a low prevalence (Bruno, 1986, 2004) so reasonable stability has existed for a long time. For the period 2004–8 approximately 2.5% of farms had DAOs, however there was considerable difference between the trout and salmon sectors with nearly 20% (17.6%) of trout but less than 1% (0.72%) of salmon farms under DAOs at any one time. Some of these farms had clinical BKD (D), but others did not (K). In this initial section analyses for the entire industry are described (i.e. 2.5% prevalence, $K^* = D^* = 0.0125$), later we describe the model's implications for control policies within salmon (1%, $K^* = D^* = 0.005$) and trout (20%, $K^* = D^* = 0.1$) industries. The difference in prevalence supports the generally weak connectivity between the salmon and trout industries in Scotland (Murray et al., 2011) and so it is reasonable to assume that salmon and trout can be managed as separate compartments (Zepeda et al., 2008).

We do not know the number of undetected cases of infection, U (this is not a tautology, because it is possible to know the prevalence of undetected infection without knowing the specific farms that are infected, if infection is dynamic). We therefore explore the full range of possible values of the prevalence of undetected infection (zero to one minus the proportion of farms known to be infected).

The model uses an arbitrary time step such that the transmission coefficient $\beta_U = 0.2$ over that time step (the value of β_U used to limit the time step is entirely arbitrary, but too large a value could induce numerical instability and too small a value increases computational overheads required to obtain steady-state). This use of an arbitrary time step means that we do not need to know the transmission coefficient over a given time, per day for example. As most transmission of *R. salmoninarum* appears to be associated with movement of fish between farms (Austin and Rayment, 1985; Murray et al., 2011) and current policy is to impose movement controls we assume there is no transmission from farms known to be infected but without disease, $\beta_K = 0$. Note that movements can occur between infected farms without spreading infection, so an outright movement ban is not necessarily implied by $\beta_K = 0$. Fish on clinically infected farms will shed bacteria into the water and so some transmission is possible (McKibben and Pascho, 1999), this transmission includes any due to wild or escaped fish acting as vectors, but as noted earlier prevalence is very low (Wallace et al., 2011). Under these movement controls water-borne transmission continues and to represent his $\beta_D = 0.04$, equal to 20% of the transmission rate due to the transport of fish between farms (in the absence of movement controls $\beta_D = 0.24$). Water-borne transmission is relatively weak for BKD, because *R. salmoninarum* does not survive well in water (Austin and Rayment, 1985) relative to
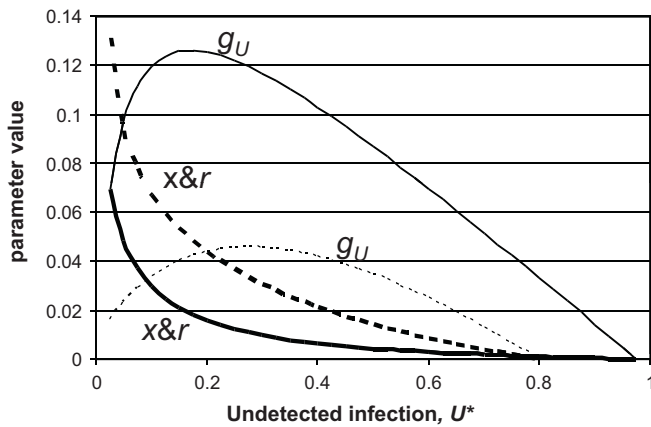
Fig. 3. Values of parameters, n_U, x and r as functions of prevalence of U^* for $D^* = K^* = 0.0125$ (solid lines) and for $D^* = K^* = 0.1$ (dashed lines, italic labels). Note that values of x and r are identical for the given scenarios.

other pathogens such as infectious pancreatic necrosis virus (IPNV) (McAllister and Bebak, 1997). The bacteria are associated with fish faeces (Balfry et al., 1996) that are liable to sink close to their source rather than be transmitted over long distances.

As the model variables represent proportions of the population ($S + U + K + D = 1$), the modelled transmission is density independent. Since transmission is mostly associated with movements of fish between farms, and there is no reason to assume these will increase if there are more farms, density independent transmission is a reasonable assumption. Density-independent transmission is also consistent with the steady-state of prevalence.

Under the assumption that prevalence of infection is in steady state, the rate of recovery from infection equals the rate of infection. The overall removal rate of infection from all infected farms is G and this is subdivided into g_U, g_K and g_D, rates for removal of infection from the different farm types. The algebra to determine these parameters, while not complex, is involved, and so is detailed in Appendix 1. We assume known infected or diseased farms are twice as likely ($y = 2$) to have infection cleared by targeted improved biosecurity practices relative to undetected farms subject to standard practices. The value of the removal of infection from undetected infected farms, g_U, is calculated as a function of prevalence of undetected infection U^* (Fig. 3), and $g_K = g_D = yg_U$. Wild fish might act as a reservoir of infection, if so this might limit the ability to increase G but does not affect the default value because it is calculated over the arbitrary time step.

Similarly, the rate of development of, x, and recovery from, r disease can be derived for the steady state (Appendix 1) with values calculated for the full range of prevalence of undetected infection U^* (Fig. 3).

We assume that contact tracing for each new case of BKD reveals on average one subclinical case ($c = 1$). Sometimes contact tracing leads to several cases being confirmed (Bland, 2007) and on other occasions no source or new infections are detected. The background rate of detection of sub-clinical cases is currently very low ($q = 0$) because of poor testing sensitivity (Hall et al., 2011), owing to the small number and restricted distribution of bacterial colonies present in subclinical fish (Austin and Rayment, 1985), and due to low levels of infection on sub-clinically infected farms. We include q in the model to enable us to assess potential new management scenarios based on improved sampling.

Models sensitivity analysis

We assess model sensitivity to our assumptions of parameter values by varying these values and determining their effects on the

steady-state values of the model variables. The default approach is to vary parameters over the range of values of between -50% and $+50\%$ of the values either specified (β_U, y, c) or calculated for steady state assumptions for a given scenario (G, r, x). However, some parameters are by default zero (β_K, q) or very low (β_D). Two special sensitivity analyses are carried out involving these low value parameters. In one β_K varies from 0 to 0.2 (β_U) while β_D varies from 0.04 to 0.24 ($\beta_U + 0.04$); this represents a range of 100–0% effective movement controls with the remaining 0.04 of β_D representing transmission through the environment which is not affected by movement controls. The other special sensitivity analysis allows the surveillance parameter q to vary from its default zero value up to 0.1. The values of D^+/D^* as they vary in response to the parameter changes, are plotted to give the relative change in the prevalence of clinical disease the key output of the sensitivity analysis.

Management scenarios

Scenarios are derived to assess the potential impacts of management policy changes. The scenarios are evaluated for each of the initial assumptions of base-line prevalence (entire industry 2.5%, salmon 1%, or trout 20%). The scenarios are listed in Table 2. The standard output is the change in relative prevalence of disease ($[D^+/D^*] - 1$), but changes for other outputs are presented for scenarios III and IV.

The first scenario is to abandon existing movement controls so that transmission from infected farms is increased to that from uncontrolled farms. This scenario is simulated by setting $\beta_K = \beta_U$ and $\beta_D = \beta_U + 0.04$ since this low-level water-borne transmission from farms with clinical disease remains.

The second scenario is to improve the rate of removal of infection. This can be done using a general improvement in biosecurity practice such as fallowing farms regularly, irrespective of the known infection status. This is simulated by doubling G (i.e. g_U, g_K and g_D) so removal of infection is increased from all farms regardless of knowledge of their infection status.

A third scenario of stamping out infection is also based on removal of infected farms, but to specifically and heavily target known infected farms, so that g_K and g_D are increased by a factor of 5, while g_U remains unchanged. Stamping out will reduce the number of BKD cases since these are targeted for destruction, however more important is the incidence of new cases $x[U+K]$, because this will reflect the ongoing impact of infection.

The fourth scenario is to enhanced surveillance effort such that background surveillance $q = 0.02$. This value of q is 10% of transmission rate when all farms are susceptible, $S = 1$, (i.e. $R0$) and is chosen to illustrate a moderately powerful level of surveillance. Sensitivity analysis indicates higher values of q are likely to lead to eradication, but these would require the frequent testing of large samples with highly sensitive diagnostic methods. Increased surveillance works by putting more farms under movement restriction, and this has a significant (although unquantified) impact on industry profitability therefore the change in the relative number of farms with DAOs ($K+D$) is presented as well as the change in prevalence of disease.

Results

Model sensitivities

Model sensitivity of changed disease prevalence to parameter change is highly dependent on the initial prevalence of undetected infection, U^* (Fig. 4). The new disease prevalence, D^+, is divided by the pre-change disease prevalence, D^*, to make the sensitivity responses comparable for trout and salmon. These results are presented on a log scale, because otherwise limited areas of parameter

Table 2
Management scenarios investigated.

Number	Description	Parameters changed	Output relative change in:
I	Abandon movement controls	$\beta_K = 0.2$, $\beta_D = 0.24$	Disease prevalence
II	Improve general biosecurity	$g_U \times 2$, $g_K \times 2$, $g_D \times 2$	Disease prevalence
III	Targeted culling	$g_K \times 5$, $g_D \times 5$	Disease incidence
IV	Improve surveillance	$q = 0.02$	Disease prevalence and DAOs

space exhibiting extreme changes can obscure smaller changes. Generally sensitivity of $\ln(D^+/D^*)$ is far higher if the prevalence of undetected infection (U^*) is low rather than high (Fig. 4).

The model is sensitive to transmission from undetected farms β_U (Fig. 4I) and rate of removal of infection, G (Fig. 4III). These are parameters that alter the amount of disease spread from undetected infected farms which cannot be subject to targeted controls. At low prevalence of undetected infection a small decrease in β_U or increase in G could lead to eradication of $R.$ $salmoninarum$. In spite of sensitivity to β_U, the model shows little sensitivity to transmission from known sub-clinical or diseased farms β_K or β_D (Fig. 4II), except at very low prevalence of undetected infection, because of the relatively high transmission from these undetected farms, β_U. The model shows relatively little sensitivity to the factor by which removal from known sub-clinically infected or diseased farms is faster than removal from undetected farms, y (Fig. 4IV). The values

of β_K, β_D and y are our modelling assumptions, so the model's lack of sensitivity is reassuring.

The model shows little sensitivity to the rate of onset of disease, x, and sensitivity unlike other parameters increases with the prevalence of undetected infection, except when this is very low where this pattern reverses (Fig. 4V). At low prevalence an increasing rate of onset of disease, x, can counter-intuitively cause disease to decline, this is because of faster detection and hence imposition of movement controls as disease occurs. There is very little sensitivity in disease prevalence, $\ln(D^+/D^*)$, to r (recovery from disease, Fig. 4VI) because removal rates via removal of disease, g_D, are much higher than via removal of infection, r (Fig. 3). This may be a reasonable approximation of the condition in salmon where disease once started generally continues until fallowing (Murray et al., 2011).

The model suggests the prevalence of BKD is highly sensitive to the effectiveness of surveillance (and hence impose targeted
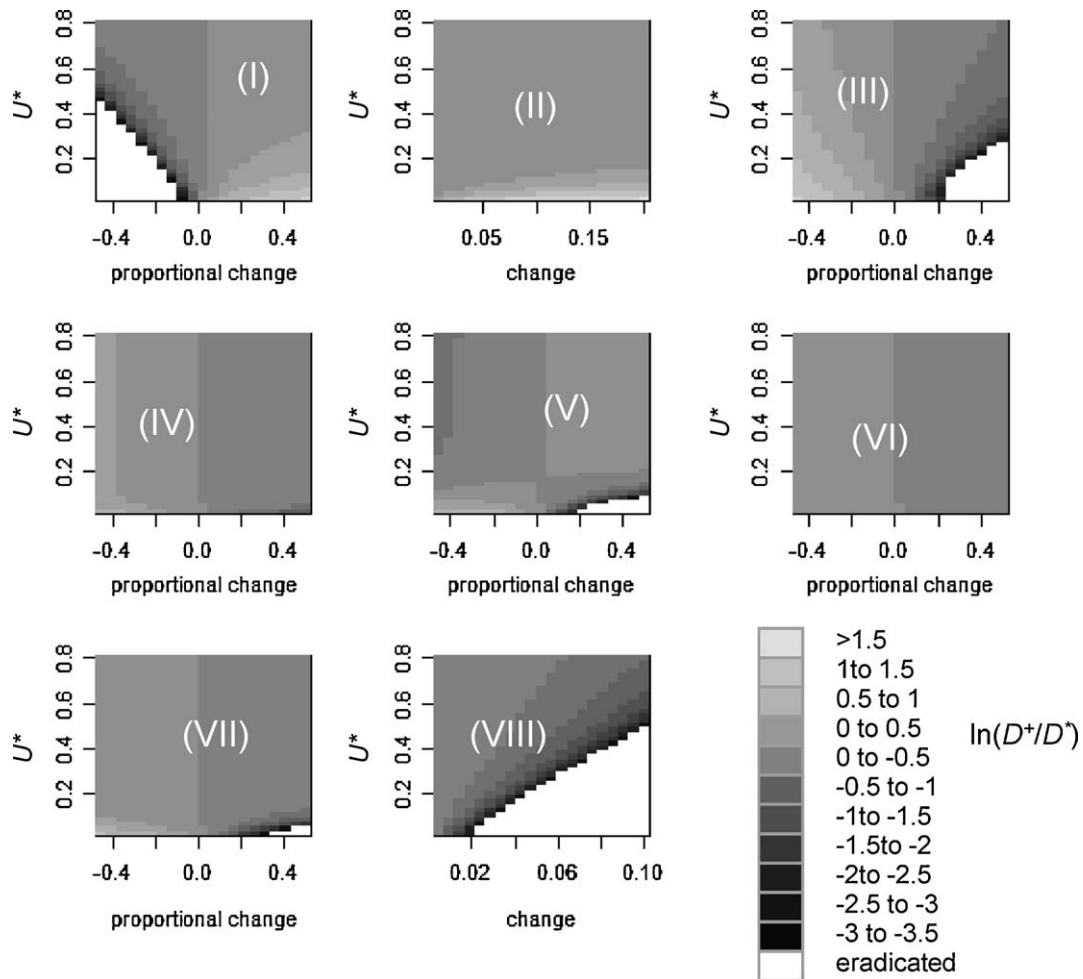

Fig. 4. Sensitivity analysis results for the model in terms of the value of $\ln(D^+/D^*)$ under changing parameter value for $K^* = D^* = 0.0125$. Panels are: (I) β_U (uncontrolled transmission); (II) β_K and β_D (efficacy of movement controls); (III) G (change in g_U, g_K, and g_D); (IV) y (value of g_K and g_D relative to g_U); (V) x (onset of disease); (VI) r (recovery from disease); (VII) c (contact tracing); (VIII) q (background surveillance). Most parameters are altered over the range -50% to $+50\%$ of the default value (-0.5 to $+0.5$) but two analyses (II and VIII) are over specific value ranges. Under II β_K is varied over the range 0–0.2 and β_D over the range 0.04–0.24 (representing perfect control to no control of anthropogenic spread) and under VIII the value of q is varied from 0 to 0.1.
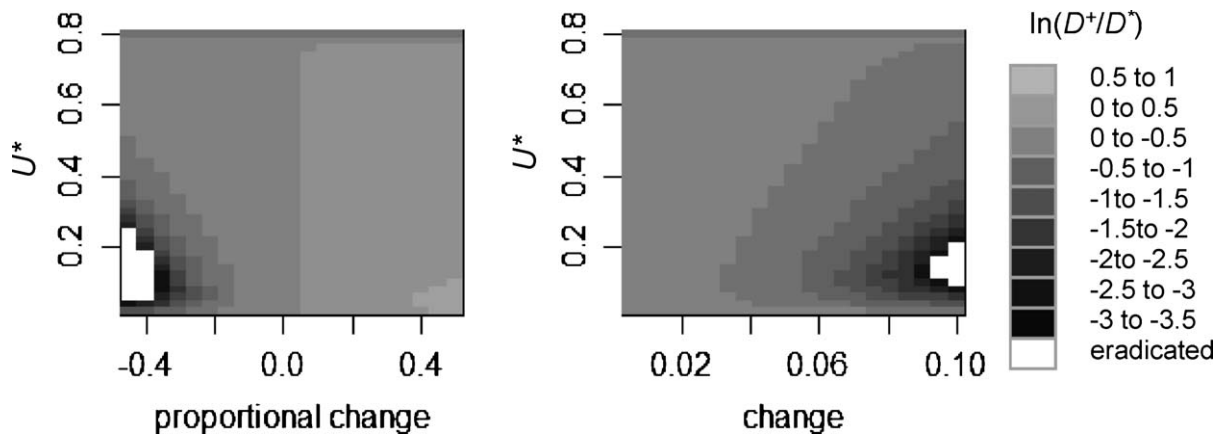
Fig. 5. Sensitivity analysis for the trout model for two most sensitive parameters: (I) β_U and (II) q. Parameter β_U is varied from -50% to $+50\%$ of default value (0.2) while q varies from 0 to 0.1 (scale as in Fig. 4, but two categories are excluded as the range of change is less).

controls); it is more sensitive to the level of background surveillance q (Fig. 4VIII) than to contact tracing c (Fig. 4VII).

Differential responses of the salmon and trout sectors

DAOs in the salmon sector cover <1% of salmon farms, while >17% of trout farms have DAOs. If the model is run using assumptions for known subclinical infection and disease prevalence of $K^* = D^* = 0.005$ for salmon or $K^* = D^* = 0.1$ for trout the outcomes are substantially different.

The salmon model gives similar sensitivity results to the industry average model but is biased towards low prevalence responses, unless a very high prevalence of undetected infection U^* is assumed. A high value of U^* is improbable because the salmon production cycle takes longer than that for trout and they may be more likely, over this longer time, to develop clinical BKD if infected. These results are similar to those displayed in Fig. 4, so they are not presented.

The prevalence of known infection in trout is much higher than in salmon and there is no reason to believe that undetected infection is relatively rarer. This high prevalence makes the model more stable for trout, indicating prevalence of BKD is less likely to change in response to either enhanced or relaxed controls. The two parameters that disease prevalence [$\ln(D^+/D^*)$] for trout is most sensitive to are transmission coefficient β_U and surveillance q (Fig. 5), but even to these BKD in trout is considerably less sensitive than the industry average (Fig. 4I and VI).

When prevalence of undetected infected farms = 0.8 there appears to be a drop in $\ln(D^+/D^*)$ for trout (Fig. 5). This is because at this point the prevalence of susceptible farms = 0 and the model is stable at $g_U = 0$, $r = 0$, $x = 0$ (Fig. 3), i.e. when there is no turnover in the model. The value in the output is thus that the post change prevalence of disease is the value set by the initial conditions, which are arbitrary and so the result is unrealistic.

Management scenarios

Results are presented for four examples (Table 2) of management scenarios (Fig. 6). Standard output is relative change in disease prevalence, but scenarios III presents change in incidence, while IV additionally presents change in farms with DAOs, as described in methods. We do not use a log scale for plotting scenario outcomes, since absolute changes are of interest for selection of management strategies.

The abandonment of existing movement controls (Fig. 6I) has far more effect on salmon than on trout. Increases in the number

of cases of clinical diseases of an order of magnitude are possible if prevalence of undetected infection, U^*, is small for salmon. Assuming U^* for trout is similar to or has greater prevalence than the known infection the number of cases is unlikely to increase by much. The abandonment of movement controls saves this considerable regulatory burden and reduces the sampling and diagnostic costs since there would be no practical point in knowing which farms were infected in the absence of clinical BKD.

The policy of improved general removal of infection is highly effective (Fig. 6II) and leads to the eradication of *R. salmoninarum* under the salmon model, unless the prevalence of undetected infection is very large. This policy leads to major drops in prevalence in trout, although not to eradication. Drops in the proportion of farms under DAOs are similar (not shown).

If moderately increased removal of infection from all farms is effective then perhaps a more aggressive stamping out of known cases of infection might also be expected to be effective. It turns out that this is a surprisingly poor policy in this case (Fig. 6III). Stamping out does lead to a very large drop in relative prevalence of disease and DAOs by reducing both the new prevalence of disease and known subclinical infection, D^+ and K^+, (not shown) as these farms are being targeted. Stamping out can lead to the eradication of BKD from trout (unlike scenario II), but only if prevalence of undetected infection is low. The incidence of new disease cases, however, can actually increase, especially for trout, if prevalence of undetected infection is large, because following culling controls are removed and the previously controlled farm can again spread infection if re-infected.

Improved surveillance (Fig. 6IV) allows infected farms to be placed under movement controls faster, and this does lead to a major decline in D^+ (i.e. clinical BKD). However, if this is not sufficient for eradication or serious reduction in D^+, this policy can lead to a permanent increased numbers of farms being subject to movement control if prevalence of undetected infection is large enough (Fig. 6).

Transient model responses

The model has been run until it becomes stable, visually assessed as beyond the point at which variables reach equilibrium. However, the model has transient responses that are of importance for management so two examples are presented (Fig. 7). If movement restrictions are lifted from known sub-clinically infected farms this means an immediate drop in the number of farms under movement restrictions, but disease prevalence increases only slowly. In the long term the proportion of farms under movement restrictions
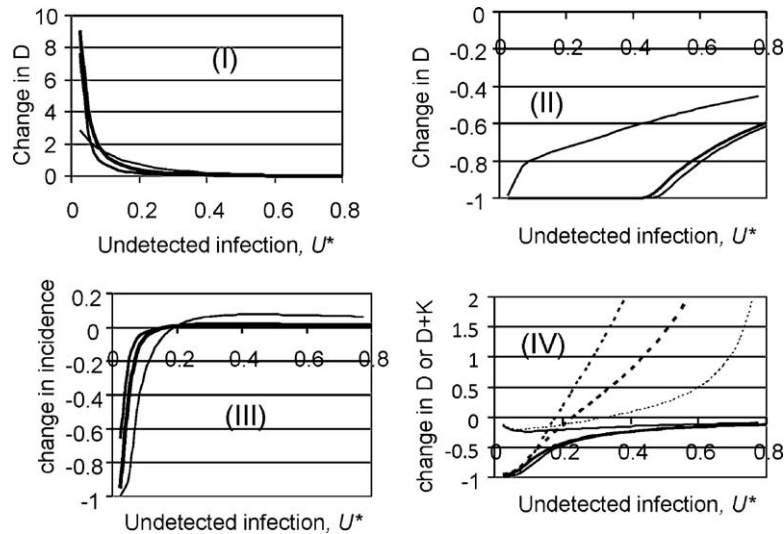
Fig. 6. Responses of the model to potential control policies given the initial value of U^* before policy is introduced; outputs changes are relative to pre-policy values. Thin line = trout ($D^* = K^* = 0.1$) medium line = salmon ($D^* = K^* = 0.005$) and thick line = both ($D^* = K^* = 0.0125$). Policies are: (I) abandon movement controls on infected farms ($\beta_K = 0.2$, $\beta_D = 0.024$); (II) improve infection removal generally, $2 \times g_U$, $2 \times g_K$, $2 \times g_D$); (III) stamp out infection where known ($5 \times g_K$, $5 \times g_D$); (IV) increase surveillance ($q = 0.02$). In panels I, II and IV results are a change in the proportion of farms with clinical disease ($[D^+/D^*] - 1$) and in III the result is proportional change in the incidence of disease ($[U^+ + K^+]/[U^* + K^*] - 1$). Panel IV also displays proportional change in farms under movement controls, ($[K^+ + D^+]/[K^* + D^*] - 1$) (dashed lines).
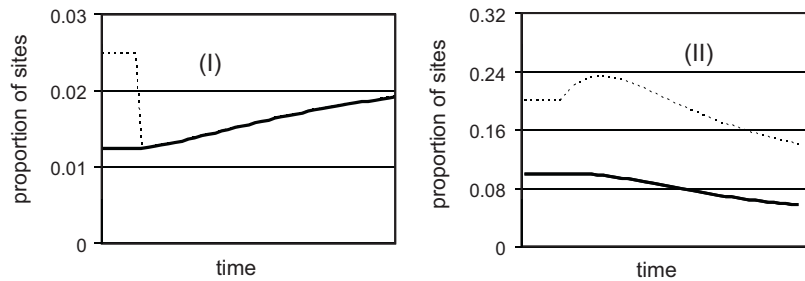

Fig. 7. Transient response in the proportion of farms under movement restrictions (dotted line) and with disease (solid line) under: (I) removal of movement restrictions from K and low prevalence of infection ($S^* = 0.875$, $U^* = 0.1$, $K^* = 0.0125$, $D^* = 0.0125$); (II) improved surveillance under the trout model ($S^* = 0.6$, $U^* = 0.2$, $K^* = 0.1$, $D^* = 0.1$).

pre- and post-policy change is similar (only 12% drop); but after the change these controlled farms are all diseased (as opposed to 50% before the change). However, the benefits of reduced controls are immediate and the costs of increased disease are delayed so discounting reduces these long-term costs (Hennessy, 2007). Alternatively, if more effective surveillance is introduced (the scenarios under which c increased from 1 to 2 and q from 0 to 0.02), this reduces both the numbers of farms under movement restrictions and the numbers with disease. However, in the short term there is a transient increase in the number of farms under movement restrictions because farms with undetected infection are converted to farms with known infection.

The model time step is arbitrarily fitted to the fixed transmission coefficient β_U value of 0.2 per time step. Therefore the duration of the transient response is not defined in the model.

Discussion

Control strategies

The model can be used to illustrate that the outcomes of particular control strategies (Table 2), these depend strongly on the prevalence of undetected infection. This means a strategy that may be effective if the prevalence of undetected infection is low might be quite ineffective if this is high. The model indicates that more effective disease control policies include untargeted removal

of infection (increased g_U, g_K and g_D) and improved surveillance (increased q).

Relaxing existing movement controls may have minimal effect on cases of disease, if prevalence of undetected infection is high, although it does remove the costs of these controls. However, if prevalence of undetected infection is low the consequence of removing controls may be a large increase in cases of disease as spread from the known sub-clinically infected farms becomes relatively more important. A knowledge of the background prevalence of infection is needed to asses the consequences of relaxing existing controls.

Increased untargeted removal of infection, increased G, is effective at reducing prevalence of BKD and could be achieved by more effective or frequent fallowing, regardless of a farm's official infection status. Since this or any other untargeted policy includes farms that are not known to be infected it has to be applied to all farms, not just the small number known to be infected, therefore any practical infection removal policy must impose minimal costs. However fallowing would require that sites be emptied for harvest over a relatively short period at the end of a production cycle as opposed to a model of continuous input and output of fish (Wallace et al., 2011). This episodic production could both flood local markets and might lead to cash flow problems for trout companies with relatively few farms, but is not a problem for salmon companies generally with many farms and a global market. The salmon industry already incorporates fallowing periods at the end of each production cycle

and BKD does not generally appear to persist on salmon farms post fallowing (Murray et al., 2011). As it is already widely applied to salmon farms it may be difficult to improve on this to a significant extent. Fallowing of trout farms is less regular and so there may be room for improvement here and, since it is not targeted, could also improve control of other diseases (Wallace et al., 2011).

Stamping out policies appear to be surprisingly ineffective at preventing new cases of clinical BKD. This is likely due to the fact that after infection is eradicated from a farm the movement controls are lifted, so the farm may become re-infected and again a source of uncontrolled infection (Wallace et al., 2011). The low R. salmoninarum transmission rate from infected farms subject to movement controls, even in the presence of disease, means they are effectively removed as infection sources, so even a small increase in uncontrolled farms can have a big impact on infection pressure and hence new cases. In the case of diseases that do spread more strongly through the environment, such as infectious salmon anaemia in Scotland (Murray et al., 2010), stamping out may be important as a control measure as infection can continue to spread from farms under movement controls.

Improved surveillance is an effective strategy for reducing BKD prevalence; a similar result has been found for KHV, another pathogen with subclinical infection in aquaculture (Taylor et al., 2011). Improved surveillance allows imposition of more movement controls. This may be short-term with a transient increase followed by a long-term decline in the number of DAOs (possibly eradication of infection) or it may be that the surveillance leads to a permanent increase in the number of farms under DAOs, but always with a reduction in the number of disease outbreaks. An increase in the number of farms with DAOs is likely to occur if the prevalence of undetected infection was large prior to the increased surveillance and the proportion of these infected farms that is detected and controlled is not enough to prevent high levels of transmission. Surveillance could be improved by increasing sampling effort or by the use of quantitative real-time polymerase chain reaction (qPCR) as the screening method as this appears to be considerably more sensitive in detecting sub-clinical infection than the enzyme-linked immunosorbent assay (ELISA) screening that was previously used (Hall et al., 2011). Surveillance could also be improved by increasing incentives for faster reporting (Horan et al., 2010); as BKD is notifiable a failure to report can result in prosecution, however positive incentives might improve reporting (Hennessy, 2007), particularly of low level disease.

The control strategies illustrated are examples of model response to parameter changes, the sensitivity analysis showed the modelled BKD prevalence is also sensitive reduced transmission from farms not under movement controls (β_U) and, providing the prevalence of undetected infection (U^*) is small, to the rate of onset of disease (x) and contact tracing (c). We will briefly discuss the implications of these results for other potential BKD control strategies. Reduced transmission from farms with undetected infection might be achieved by simply reducing the total number of inter-farm movements, and relatively low numbers of movements occur between marine salmon farms specifically to reduce the risk of spreading ISA (Murray et al., 2010). However risk of transmission of disease through fish movements can also be reduced by relatively subtle changes to contact network structure (Green et al., 2009), and such changes are likely to be less disruptive than simply reducing the total number of movements. The effect of change in the rate of onset of disease, x, is interesting, slower onset can lead to there being more disease. This might mean less virulent strains of R. salmoniarum could actually result in more diseased farms (although perhaps such less virulent strains would cause less mortality per outbreak) or that good farmers might spread infection more than farmers who stress their fish. Contact tracing is a good way of reducing BKD if prevalence of undetected infection is low, but not if it is high; this contrasts with general surveillance (q) that is effective even if this prevalence is reasonable high. This difference occurs because contact tracing roots out a smaller proportion of the undetected infected farms, while q identifies more cases, the larger the prevalence of undetected farms is.

Salmon and trout

The known prevalence of BKD in trout farms is about 20 times higher than that in salmon farms in Scotland (Fig. 2). It is unlikely that salmon have a much higher relative prevalence of undetected infection, since the longer production time gives more time for disease to be expressed. We therefore suspect that salmon have a low prevalence of undetected infected farms and this low prevalence suggests that changes in controls may have a stronger effect on salmon than trout. This response applies to reduced infection control with a large increase in the cases of disease in salmon, but in trout the effect may be quite small. Conversely improved disease controls such as fallowing, reduced transmission or increased surveillance (leading to more farms being placed under movement restriction) could lead to eradication of infection from salmon, but could be costly and of limited effectiveness for trout. Existing practices in salmon production in Scotland include regular fallowing after each production cycle, which is rarely the case on trout farms where farms are in continuous production. As such, the different fallowing and biosecurity practices between the two industries may explain, at least in part, the existing difference in prevalence. Conversely, these practices can be seen as a result of the lack of incentive to invest in controls effective for BKD if consequence is low and probability of re-infection relatively high as appears to be the case for trout (Hennessy, 2007).

The low prevalence of known infection in Scottish salmon is quite unstable in the model (Fig. 4). This suggests that (unless there is a high prevalence of undetected infection U^*) small improvements in removal or prevention of spread (including small improvement in surveillance to allow targeted movement controls) could lead to a situation where infection is eradicated ($R0 < 1$). Indeed there was a period in 2006–7 when there was no known infection in salmon (Fig. 2), although this does not mean there were no undetected infected salmon farms. Although most cases of R. salmoninarum infected salmon farms in Scotland appear to be associated with other cases in salmon and therefore probably are due to spread from other salmon farms (Murray et al., 2011) it is possible that occasional inputs from wild reservoirs (Wallace et al., 2011), or imported ova (Walker, 2010), or trout farms (Fig. 2) are maintaining infection (Ruane et al., 2009; Taylor et al., 2010) and preventing eradication from the salmon industry. As risk of infection becomes perceived to be low the incentive to invest in controls is reduced thereby increasing that risk of re-emergence (Hennessy, 2007). Given its existing relatively high BKD prevalence, occasional external inputs are unlikely to have significant effects on R. salmoninarum epidemiology within the trout industry. The Scottish trout industry is closely coupled with that in England and Wales (Murray et al., 2011); so policy change to trout must be applied at the GB level. Ireland is BKD free, even though wild salmon and sea trout can easily cross from GB and there is extensive contact with Scottish aquaculture (Ruane et al., 2009); thus it is possible to have a BKD free salmon aquaculture industry in an environment similar to Scotland's. The conditions under which reservoirs prevent eradication of pathogens from populations targeted for control are discussed by Haydon et al. (2002). Reservoirs of coronavirus present at low levels in wildlife are believed to be the source of SARS (Guan et al., 2003), but did not play a role in its spread once in the human population.

If prevalence increases for trout farms then the risk of transmission to salmon may increase; if the existing prevalence of

undetected infection in trout farms is already high then risk to salmon will not change under any reduced internal controls in the trout industry. This risk can be controlled by ensuring or improving the separation of the two sectors of the industry. This compartmentalisation (Zepeda et al., 2008) seems to be potentially possible as farms in the two sectors are largely in separate networks and geographical areas (Murray et al., 2011); indeed the very different prevalence in the two sectors is evidence of an existing separation.

Costs and conflicts of controls

Control policies for BKD impose four different cost types: surveillance; movement restrictions; farm depopulation and the direct losses to disease. Costs may vary depending on the nature of the farm, for example a production farm may be relatively little affected by movement controls, but these could be devastating for a hatchery that depends on selling fish to ongrowing farms. BKD is believed to cause far greater losses to the salmon industry; these have not been systematically evaluated, but at the worst case a single farm ascribed 130 tonnes of salmon as lost to BKD (Murray et al., 2011).

Farmers will seek a point where increased investment in controls and surveillance balance reduced losses due to disease (Peddie and Stott, 2003). Hennessy (2007) has shown that cost imposed on farms by the state, even from epidemiologically ineffective controls, may help disease control by increasing the incentive on farmers to avoid infection. This incentive might be particularly important in the case of trout farms for which the direct costs of disease are believed to be minimal for BKD, but for which movement restrictions can be expensive. Loss of incentive by weakening of official controls might therefore lead to reduced incentive to invest in biosecurity.

Farms on which sub-clinical *R. salmoninarum* is detected can still develop BKD and have the additional cost of movement controls, yet this is the most effective way of controlling disease at the industry level. There is a conflict between the farm level and the industry level as to the benefits of rapid detection of infection (Horan et al., 2010). Furthermore the costs are fully borne by the infected farm as there is no official compensation for imposition while the benefits are a slightly reduced risk of infection to all uninfected farms.

Transient responses could impose costs that may discourage practices that would be beneficial in the long-term, or may encourage practices that are counter-productive in the long term. Since we do not know the prevalence of undetected infection, U^*, the possible long-term cost/benefit is difficult to balance against short term (and apparent) cost/benefit. Even if U^* is known and so long-term effects can be quantified, the benefits of their adoption will depend on the discount rate and time-scale of the effects (Hennessy, 2007). The model uses an arbitrary time step to fix transmission coefficient $\beta_U = 0.2$, so we cannot say how long the transient effects will last. However, these could be found if an independent estimate of any of the time dependent parameters were made.

Transient response and individual interests of farmers may combine to discourage improved practice. For example, in the early stages of improved fallowing practices the farms that first clear infection are likely to be re-infected from the many other farms that are still infected, even if improved practice is universal. Worse, any individual farm pioneering improved practice without a general improvement in the industry will remain indefinitely vulnerable to the high risk of re-infection. Conversely, the reduced infection pressure may be a benefit to other farms where fallowing is not practiced, which may discourage future fallowing of these facilities.

The control of BKD requires a long-term and collective approach to gain any benefits. This requires policies to be developed by Government and/or industry bodies rather than the operators of individual farms or companies (Hennessy, 2007). The salmon and trout sectors appear to have different interests in controls and so must either agree a suitable compromise or be operated as separate compartments.

Conclusions

The modelling provides specific conclusions concerning the control of BKD and more general conclusions that may be applicable for other diseases affecting aquaculture and agriculture. The effectiveness of potential BKD controls depends on the existing prevalence of infection in farmed salmon and trout, and in particular on the number of farms with undetected infection. Policies that are likely to work are either those that lead to improved general farm biosecurity, regardless of official DAO status, or those that increase the efficacy of detection. Additionally, improved biosecurity is likely to give general benefits in the control of a range of diseases. Industry level benefits may be acquired at the cost of specific restrictions to the individual farms. Epidemiological separation of salmon and trout production is likely to be economically beneficial, since different optimal control strategies appear to apply to these industries.

Other diseases affecting agricultural or aquacultural systems may be difficult to detect if they occur asymptomatically and if so they may be spread with the movement of animals. Examples include bovine tuberculosis (Gilbert et al., 2005), Jaagsiekte in sheep (Palmarini et al., 1999), and Johne's Disease (Whittington and Sergeant, 2007) from agriculture and KHV (Taylor et al., 2010) and oyster herpesvirus (Arzul et al., 2002) from aquaculture. Even cases of clinical disease may go unnoticed if producers consider the condition is 'normal', e.g. bovine fasciolosis in Indonesia (Tisdell et al., 1999). Similar modelling methods to those described here may be useful for investigating controls on these diseases (Taylor et al., 2011). The modelling approach developed here allows parameters to be estimated for endemic diseases in steady-state by using the arbitrary time-step approach. If the prevalence of unknown infection is known (quite possible if farms change infection status frequently) the model parameters values can be strongly constrained. The approach here may be of particular use for modelling systems with relatively poor knowledge of their epidemiology and in which resources for surveillance for infection are particularly limited. This can be the case for many agricultural diseases in less developed countries and even for aquaculture in developed countries. In systems for which there is more epidemiological knowledge these simple models can be replaced with more sophisticated models that have greater predictive power, although even in these cases the simple modelling approach can give useful initial results. The value of robust surveillance programme to improve disease control policies, and to evaluate their effectiveness, is strongly emphasised.

Acknowledgments

Appendix A. The analytical evaluation of parameters, g_U, g_K, g_D, x and r

The values of the model parameters and variables can be used to constrain each other, especially if we set the values of the variables to reflect the current situation and assume the prevalence of *R. salmoninarum* is approximately in steady state. This is a reasonable assumption for *R. salmoninarum* infection because the number

of new cases has been fairly constant in recent years and there is a long history of persistent low-prevalence infection. We use simple algebra on these equations, assuming the variables are at steady state and therefore constants, to solve the implied values of these parameters.

The number of farms actually affected by clinical BKD is very low and the number with DAOs (or CDNs) (i.e. known infection with or without BKD) is also low, so we set steady-state $K^* = D^* = 0.0125$ for the industry as a whole, 0.005 for salmon and 0.1 for trout (Fig. 2). We do not know the value of U, almost by definition, so we use U^* over a range of values to assess parameters (Fig. 3).

If infection is at steady state then $\beta_U S^* U^* + \beta_D D^* S^* = G(1 - S^*)$ where G is the removal rate and for this first step we assume this is equal for all infected components $G = g_U = g_K = g_D$. From this,

$$G = \frac{[\beta_U S^* U^* + \beta_D D^* S^*]}{(1 - S^*)}$$

If removal of known infection is faster than it is for undetected infection ($g_K = g_D > g_U$) then the weighted average value of G must reflect this balance. If removal of infection from known infected farms is faster by a factor y then (g_K or g_D) = yn_U then,

$$G = \frac{g_U[U^* + y(D^* + K^*)]}{[U^* + K^* + D^*]} \quad \text{so :}$$

$$gU = \frac{G(D^* + U^* + K^*)}{(yD^* + U^* + yK^*)}$$

$$g_K = g_D = g_U \times y$$

The turnover of D^* and the effectiveness of contact tracing from infection (spread from U^* is not observed and so no contact tracing is undertaken) will determine the value of x (onset of disease). From the equation for U^* we see $\beta_U S^* U^* + \beta_K S^* K^* + \beta_D S^* D^* - crU^* - g_U U^* - xU^* - qU^*$, which dropping the zero q term leaves $\beta_U S^* U^* + \beta_D S^* D^* - U^*(cr + n_U + r)$, so

$$x = \frac{[\beta_U S^* U^* + \beta_3 S^* D^* - g_U U^*]}{[(c + 1)U^*]}$$

Having defined x we can find r (recovery rate from disease) using $rD^* = x(U^* + K^*) - D^* n_D$

$$r = \frac{x(U^* + K^*)}{D^*} - g_D$$

The solution to x and r turn out to be identical for the scenarios investigated (see Fig. 3). We have not analytically derived why this is so as it is not relevant to our model analysis.

Appendix B. Model code

R code to run BKD SI model with detected and undetected infection
Alexander G Murray, Marine Scotland Science, Aberdeen, April 2011

```
par(mfrow = c(2,2))

# steady state variable values
Kx <- 0.005    # 0.005 salmon, 0.0125 whole industry, 0.1 trout
Dx <- Kx
Ux <- 0.0

# array to store model output
rr <- trunc(40 - 2 * Kx/0.025)    # max 40 runs but exclude where K + D + U > 1
xx <- 1:(4 * rr)
dim(xx) <- c(rr,4)

for(j in 1:rr) {    # model loop for each prevalence scenario
    Ux <- Ux + 0.025    # update I and S for each scenario
    Sx <- 1 - Ux - Dx - Kx

    betaU <- 0.2    # transmission coefficient from I
    betaK <- 0.0    # transmission coefficient from K
    betaD <- 0.04    # transmission coefficient from D
    ctr <- 1    # contact tracing
    y <- 2    # factor by which gK and gD > gU
    q <- 0.0    # surveillance rate

# calculate parameters dependent on U*
    G <- (betaU * Sx * Ux + betaD * Dx * Sx)/(1 - Sx)

    gU <- G*(Ux + Kx + Dx)/(y*(Dx + Kx) + Ux)    # loss of infection from U
    gK <- gU * y    # loss of infection from K
    gD <- gU * y    # loss of infection from D

    x <- (betaU * Sx * Ux + betaD * Dx * Sx - gU * Ux)/((ctr + 1) * Ux)    # rate of onset of disease
    r <- x*(Kx + Ux)/Ux - gD    # rate of recovery from disease to K

# modification of parameter values for model management scenarios
#q <- 0.02
#gU <- gU * 2
#gK <- 5 * gK    #2
#gD <- 5 * gD    #2
#betaK = 0.2
#betaD = 0.24

    S <- numeric(400)    # uninfected populations
    U <- numeric(400)    # infected non-diseased not detected
    K <- numeric(400)    # known infected, non-diseased
    D <- numeric(400)    # disease population

    S[1] <- 0.99
    U[1] <- 0.01
    K[1] <- 0
    D[1] <- 0

    for(t in 2:400) {    # run model

        trasm <- S[t - 1] * (betaU * U[t - 1] + betaK * K[t - 1] + betaD * D[t - 1])
        cont <- ctr * x * U[t - 1]

        S[t] <- S[t - 1] + gU * U[t - 1] - trasm + gK * K[t - 1] + gD * D[t - 1]
        U[t] <- U[t - 1] + trasm - cont - x * U[t - 1] - gU * U[t - 1] - q * U[t - 1]
        K[t] <- K[t - 1] + r * D[t - 1] + cont - gK * K[t - 1] - x * K[t - 1] + q * U[t - 1]
        D[t] <- D[t - 1] + x * (U[t - 1] + K[t - 1]) - r * D[t - 1] - gD * D[t - 1]
    }
    plot(1:400,S,type = "l",ylim = c(0,1),ylab = "population",xlab = "time",main = "S")

    plot(1:400,U,type = "l",ylim = c(0,1),ylab = "population",xlab = "time",main = "U")

    plot(1:400,D,type = "l",ylim = c(0,1),ylab = "population",xlab = "time",main = "D")

    plot(1:400,K,type = "l",ylim = c(0,1),ylab = "population",xlab = "time",main = "K")

# new stabilised values of parameters
    xx[j,1] = S[400]
    xx[j,2] = U[400]
    xx[j,3] = K[400]
    xx[j,4] = D[400]
}
```

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