Impact of parasites on salmon recruitment in the Northeast Atlantic Ocean

Martin Krkošek[1], Crawford W. Revie[2], Patrick G. Gargan[3], Ove T. Skilbrei[4], Bengt Finstad[5], and Christopher D. Todd[6]

[1] Department of Zoology, University of Otago, Dunedin, New Zealand, email:

martin.krkosek@otago.ac.nz; ph: +64 3 479 7991

[2] Atlantic Veterinary College, University of Prince Edward Island, Charlottetown, Canada

[3] Inland Fisheries Ireland, Dublin, Ireland

[4] Institute of Marine Research, Bergen, Norway.

[5] Norwegian Institute for Nature Research, Trondheim, Norway

[6] Scottish Oceans Institute, University of St Andrews, St Andrews, Scotland

ABSTRACT

Parasites may have large effects on host population dynamics, marine fisheries, and conservation but a clear elucidation of their impact is limited by a lack of ecosystem-scale experimental data. We conducted a meta-analysis of replicated manipulative field experiments concerning the influence of parasitism by crustaceans on the marine survival of Atlantic salmon (*Salmo salar* L.). The data include 24 trials in which tagged smolts (totaling 283,347 fish; 1996-2008) were released as paired control and parasiticide-treated groups into 10 areas of Ireland and Norway. All experimental fish were infection-free when released into freshwater, and a proportion of each group was recovered as adult recruits returning to coastal waters one or more years later. Treatment had a significant positive effect on survival to recruitment, with an overall effect size (odds ratio) of 1.29 that corresponds to an estimated loss of 39% (95% CI: 18% to 55%) of adult salmon recruitment. The parasitic crustaceans were likely acquired during early marine migration in areas that host large aquaculture populations of domesticated salmon, which elevate local abundances of ectoparasitic copepods – particularly *Lepeophtheirus salmonis*. These results provide experimental evidence from a large marine ecosystem that parasites can have large impacts on fish recruitment, fisheries, and conservation.

1. INTRODUCTION

Infectious diseases may threaten biodiversity conservation and food security [1,2]. Conceptually, a number of disease-associated mechanisms may elevate extinction risk, which include small pre-epidemic population size and the presence of a reservoir host population [3]. Furthermore, evolutionary similarity to domesticated animals may be a key factor associated with parasite-mediated population declines of wildlife [4]. For food security, disease threats to domesticated populations are associated with increased host density or emergence of novel pathogen strains [1,5]. More broadly, parasites are increasingly being recognized for their direct and indirect effects on host population dynamics and community structure [6-10].

However, clear experimental demonstrations of parasites regulating or limiting host population dynamics in field conditions are rare [11,12]. For marine fishes, uncertainty may be particularly high because fish recruitment is highly stochastic and non-linear [13,14], and analyses of recruitment are correlative with correlates often being ephemeral [15]. Nevertheless, there is a growing perception of the potential regulatory importance of parasites in marine fish populations [16-19]. Furthermore, parasites that are shared between wild marine fish populations and evolutionarily similar domesticated stocks in aquaculture may affect fish population dynamics, fisheries productivity, biodiversity conservation, and aquaculture productivity [5,20,21].

In coastal seas, domesticated populations in aquaculture are rapidly growing and these experience both incidental and persistent disease outbreaks [22-24]. Although disease and its control are costly for aquaculture producers, concerns also have emerged on the potential wider consequences for marine ecosystems and wild fisheries [20,21,25,26]. Perhaps nowhere is this more contentious than with Pacific (*Oncorhynchus* spp.) and Atlantic salmon (*Salmo salar* L.) and their native, specialist ectoparasitic copepod, the salmon louse *Lepeophtheirus salmonis* (Krøyer) [27-29]. In the North Atlantic, stocks of wild *S. salar*

3

show a marked and steady decline of ~45% since the 1980s, with variability among stocks [30], and correlations to salmon aquaculture have been drawn [31,32].

Lepeophtheirus salmonis is a marine ectoparasitic copepod of salmonids (*Salmo* spp., *Salvelinus* spp., *Oncorhynchus* spp.) that feeds on host surface tissues causing morbidity and mortality [27,28]. There is no intermediate host and the parasitic gravid female releases free-living larvae to the water column where they can be dispersed among wild and farmed populations [5,33]. *L. salmonis* is extremely unusual amongst macroparasites [34,35] in typically reaching 100% prevalence on wild one sea-winter (1SW) and two sea-winter (2SW) Atlantic salmon [36,37]. Persistent re-infestation of wild salmon at sea is apparent from the significantly higher mean abundance of *L. salmonis* on wild 2SW fish compared to 1SW adults [37]. Thus, *L. salmonis* must be viewed either as being exceptionally well adapted in locating the host fish or, more likely, the behaviour of salmon is such that they inevitably encounter the infective copepodid stage of *L. salmonis* both in coastal waters and in the open Atlantic ocean.

Numerous studies have associated salmon farming and sea louse infestations of wild juvenile salmon, but the impact on salmon recruitment remains contentious [20,38-44]. A primary reason is that many studies are correlative and results depend on modeling assumptions [32,38,39]. By contrast, manipulative field experiments provide an opportunity for strong inferences based on differential survival between paired releases of control and parasiticide-treated groups of emigrant juvenile salmon smolts [40,42,45,46]. The parasiticides affect crustaceans, which include other native salmon parasites, particularly *Caligus elongatus*, though *L. salmonis* remains the focus due to its prevalence and adverse lethal and sub-lethal effects [27,28]. Some of the field experiments have identified significant impacts on salmon survival [42,45] whereas others have claimed no significant effect at the population level [40,46].

We assembled and analyzed all the published results of large-scale, pair-wise field experiments of the marine survival of Atlantic salmon in the Northeast Atlantic Ocean. These studies were conducted in Ireland and Norway, and typically occurred in river systems discharging to near-shore marine waters that accommodated salmon farms in [40,42,45-47]. Figure 1 shows the location of coastal salmon farm sites adjacent to the named experimental release rivers in Norway and Ireland; however, not all farm sites were in active production in all years of experimental releases. The published studies all were substantial, involving the release of thousands of hatchery-raised juvenile salmon smolts into rivers. Prior to release, all fish were tagged (either coded wire or carlin tags) and approximately half the juveniles received a parasiticide treatment while the others were untreated controls. Targeted tag recovery programs and screening of commercial catches of return adult spawners allowed comparisons of marine survival between treatment and control groups. The large majority of the recovered fish spent one year at sea, and we focus on these so-called one sea-winter (1SW) fish in the main analysis. Further details, including comparative analyses of return adults of all sea ages (1SW, 2SW, and 3SW), and the data analyzed, are presented in the electronic supplementary material (ESM).

2. MATERIALS AND METHODS

(a) *Data sources*

The data spanned 24 trials between 1996 and 2008, and included a total of 283,347 smolts released into 10 rivers mostly in Ireland but also Norway (figure 1, table 1, and ESM). Most trials involved a single release of paired control-treatment groups into a river (or estuary [47]) during the spring emigration (typically April-May). In some trials there were multiple separate releases within an emigration season: for these, we summed the data across the multiple releases into a single observation for that annual trial. In 21 of 24 trials the in-feed

treatment emamectin benzoate (Slice™; Schering-Plough) was applied; this is a widely used parasiticide in salmon aquaculture [48]. For three trials, a different proprietary compound, Substance Ex (Alpharma), was used [47] (Table 1), which involves a topical bath treatment.

(b) *Analytical approaches*

We considered three independent but complementary analyses based on odds ratios, paired sample *t*-tests, and mixed effects models, each of which synthesize the data across studies to quantitatively assess sea louse-induced mortality of Atlantic salmon. The first approach is a standard survival analysis that leads to estimates of the odds ratio in survival between control-treatment data pairs, as well as an overall meta-analytic mean odds ratio [49]. The second analysis begins with the standard assumptions of survival analysis, and leads to a simple paired-sample *t*-test of survival estimates on a natural log scale. A key advantage of this approach is that it permits an estimation of the percent of adult salmon recruitment that is lost to parasites. The third analytical approach also begins with the standard assumptions of survival analysis but, relative to the second approach, differs subtly in how residual variation is distributed between control and treatment groups. This third approach leads to a mixed-effects model of survival estimates, again on a log scale, and also permits estimation of the percent of salmon recruitment lost to parasites.

Our initial standard meta-analysis is an approach which often is adopted when seeking to estimate the overall effect associated with a range of trials that report the same outcome variable. Because the outcomes were dichotomous an appropriate measure of association was the odds ratio. Given the degree of heterogeneity evident among the studies, a random effects meta-analysis [49] was adopted. The meta.DSL function from the rmeta package of the R statistical software was used to carry out the analysis.

The second and third approaches begin with a standard survival analysis where the probability of survival from time $t=0$ to time $t=T$ is

$$(1) \quad s = \exp\left(-\int_0^T \mu(t)\,dt\right)$$

and μ is known variously as the instantaneous mortality rate, hazard rate, or force of mortality [50].

The second analytical approach involves a model of the data according to

$$(2) \quad \begin{aligned} s_{C,i} &= \exp\left(-\int_0^T \mu_C(t)\,dt + \theta_i + \varepsilon_{C,i}\right) \\ s_{P,i} &= \exp\left(-\int_0^T \mu_P(t)\,dt + \theta_i + \varepsilon_{P,i}\right) \end{aligned}$$

where $s_{C,i}$ and $s_{P,i}$ are the proportions of fish that were recovered from the control group (C) and parasiticide treatment group (P) in trial i. The parameters μ_C and μ_P are the instantaneous mortality rates of Atlantic salmon from control (C) and parasiticide treatment (P) groups. The mortality rate then is integrated over the duration of the study from the time of release ($t=0$) to the average time of recapture ($t=T$). Variation in mortality rates among trials (but not between control and treatment groups within trials) is modeled as the normally distributed random variable, θ_i with a mean of zero; thus the treatment and control groups in the same release share the same environmental variability in mortality rate. The parameter θ_i also encompasses random variation in T among trials, but we assume that T does not vary between control and treatment groups within trials. The parameter $\varepsilon_{C,i}$ is a normally distributed random variable with a mean of zero that models random variation among trials in parasite exposure in control groups. The parameter $\varepsilon_{P,i}$ is a normally distributed random variable with a mean of zero that models random variation among trials in the level of protection conferred by parasiticide treatment.

Equations (2) can be simplified to

(3)
$$\ln(s_{C,i}) = b_C + q_i + e_{C,i}$$
$$\ln(s_{P,i}) = b_P + q_i + e_{P,i}$$

where

(4)
$$b_C = -\int_0^T m_C(t)\,dt$$
$$b_P = -\int_0^T m_P(t)\,dt$$
.

Equations (4) lead to an estimate of the average mortality due to parasites

(5) $M = 1 - \exp[-\varphi]$

where $\varphi = \beta_C - \beta_P$. It follows that φ can therefore be estimated as

(6) $\ln\left(S_{i,P}\right) - \ln\left(S_{i,C}\right) = \varphi + e_i$,

where $\varepsilon_i = \varepsilon_{P,i} - \varepsilon_{C,i}$ is a random normal variable with mean of zero and variance to be

estimated. Equation (6) indicates that statistical inference on φ, and therefore parasite-

induced mortality of Atlantic salmon, can be conducted as a simple paired-sample t-test

between paired survival estimates of control and treatment groups among trials on a natural

log scale.

The third model of the data we consider is

(7) $$s_{i,j} = \exp\left(-\int_0^T m_j(t)\,dt + q_i + e_{i,j}\right)$$

where j represents control (C) or parasiticide treatment (P) groups. Equation (7) is similar to

equations (2), except that $\varepsilon_{i,j}$ is a normally distributed random variable that is distributed over

control and treatment groups across the dataset. Here, it is assumed that mortality rates for

each individual group – be it control or treatment – vary among each other according to a

single random variable, whereas in equations (2) variation in mortality rate among trials

within treatment or control groups was modeled separately for control and parasiticide

treatment groups.

This third approach leads to a model for the log-transformed survival data

(8) $\ln(s_{i,j}) = b_j + q_i + e_{i,j}$,

which has the form of a mixed-effects model where θ_i is a random effect for shared environmental variability for control and treatment groups within trials and $\varepsilon_{i,j}$ is the residual variation. Here, statistical inference on whether parasiticide treatment has a significant effect on survival can be conducted by means of a likelihood ratio test between model (8) and its null version where β_j is constant ($\beta_j = \beta_0$). Estimation of φ, and therefore parasite-induced mortality (M) as defined above, can be conducted from the maximum likelihood estimate of the difference (and associated standard error) between the treatment and control fixed effects in the mixed model (equation 8).

3. RESULTS

Meta-analysis of differential survival between control and parasiticide-treatment groups indicated a consistent directionality of the effect of treatment among trials, albeit with variation among trials in effect size, and a significant protective effect of treatment (overall odds ratio 1.29 with 95% CI 1.18 to 1.42; figure 2). The paired sample t-test revealed significant differences in survival between treatment and control groups ($t = 3.37$, $df = 23$, p-value = 0.003). Similarly for our third (mixed model) analytical approach, treatment had a significant effect on survival (Likelihood ratio test; $\chi^2 = 9.64$, $df = 1$, $p = 0.002$). The estimated difference in log survival between paired treatment and control groups was $\varphi = 0.50$ from both the latter analyses. Uncertainty in φ was given by 95% confidence intervals of 0.19 to 0.80 in the paired sample t-test, and a range of two standard errors giving the interval 0.20 to 0.79 in the mixed model. These estimates of φ correspond to parasite-associated mortality of 1SW Atlantic salmon of $M = 1-\exp[-\varphi] = 39.3\%$ (95% CI from paired sample t-test, 17.5% to 55.3%; range of two standard errors from mixed model, 18.3% to 54.8%). The

complementary analysis (ESM) that included all sea ages (1-3SW) of returning adults gave a final estimate of $M = 39.9\%$.

4. DISCUSSION

These results provide manipulative experimental evidence at a large spatial scale from the marine environment that parasitism is a significant limiting factor for the recruitment of Atlantic salmon. Treatment of smolts with parasiticide significantly improved their survival to adulthood relative to control untreated groups. The most common treatment in the trials, emamectin benzoate, has a half-elimination period of 9-12 days in Atlantic salmon smolts [51] and is effective for up to the first 1-2 months at sea [48]. The differential survival between control and treatment groups is therefore attributable to near-shore and coastal waters where the juvenile post-smolts transit from rivers to offshore waters. These near-shore waters typically host large domesticated salmon populations in aquaculture operations (figure 1), which represent a large – but not exclusive – source of sea lice. Potential wild sources of sea lice include sea trout (*Salmo trutta* L.), Arctic char (*Salvelinus alpinus* L.), and spring-returning adult *S. salar* [27].

Though we focus attention on *L. salmonis*, in view of its prevalence and known adverse effects on host salmon, it is likely that *C. elongatus*, which also is native and occurs both on wild and farmed salmon [27], contributes to mortality. In addition, it is not implausible that there may be other unknown effects of the treatments that improve survival. Another caveat is that the data are based on hatchery-reared smolts, which, among other differences with wild smolts, are larger: hatchery smolts are typically 18-19 cm whereas wild smolts are typically 11-14 cm in Ireland and Norway. The larger size of hatchery smolts can partially offset their typically low marine survivorship compared to wild smolts [52]. Nonetheless, due to the size-related effects of sea louse-induced stress on smolts [27,28],

wild salmon would likely experience higher mortality than we have estimated here for hatchery smolts.

We considered the possibility of a dose-dependent effect – i.e. including sea louse abundance on farms as a covariate – but proceeded otherwise. It was not possible to formally structure the analysis in this way because we lack sufficient farm data for all areas and years. Furthermore, local hydrodynamic processes that disperse the infective sea louse larval stage will be highly variable among locations [33,53], making it difficult to construct a covariate that is geographically comparable. Rather, we regard the variance in the data of differential survival as representative of the spatio-temporal variation of ectoparasite exposure that wild salmon experience in salmon-farming regions of the Northeast Atlantic.

While it is apparent that parasites have potential to be a significant source of mortality in wild fish populations [10,16,54], it is difficult to measure marine mortality associated with disease, and furthermore to evaluate whether such mortality scales up to a limiting or regulating factor of recruitment. Disease-associated mortality of fish in the marine environment often goes undetected or is observed sporadically, and parasite-induced mortality may be compensatory, for example due to predation [55]. Some examples include parasite-associated mortality of juvenile coho salmon (*Oncorhynchus kisutch*) with infestations of the digenean trematode *Apophallus* sp [56], mortality of European eels (*Anguilla anguilla*) infested with the nematode *Anguillicoloides (=Anguillicola) crassus* [57], and mortality of juvenile Pacific salmon (*Oncorhynchus* spp.) due to the trematode *Nonophyetus salmincola* [58].

However, none of the above example studies of parasite-related mortality have been able to establish if parasitism is linked with declines in host fish recruitment, or is otherwise offset by compensatory mechanisms. From meta-analysis of taxonomically diverse field- and laboratory-based experimental studies, parasitized hosts tend to be ~2.6 times more likely to

die compared to control groups, and that odds ratio is likely to be higher for fishes [10]. It has to be acknowledged, however, that variation in the odds ratio of host mortality is influenced both by taxon and latitude, and differs for (direct) parasite-associated effects and (indirect) predation-mediated influences of parasites on host survivorship [10]. Our analysis for one species of fish yielded a meta-analytic mean odds ratio of 1.29 (95% CI 1.18 to 1.42), which is relatively low compared to reported values [10], and yet which still implies a high proportion (39%) of host mortality attributable to a specialist ectoparasite.

In contrast to the foregoing [56-58], our analysis of experimental manipulations of emigrant Atlantic salmon smolts permitted an explicit, though indirect, quantitative test of the significance of host mortality attributable to a specialist ectoparasite. All experimental fish were known to be free of *L. salmonis* infection at the start of the experiment because the parasite is acquired only following seawater entry by the emigrant smolt. Fish in the control and treated groups all were identifiable by tags, and surviving adults which successfully completed the return marine migration in subsequent years could be recaptured because of the fidelity of salmon to their natal (or experimental release) river. Moreover, both the prophylactic experimental treatments applied have specific effects in controlling arthropod ectoparasites and emamectin benzoate is widely used in the aquaculture industry specifically to control *L. salmonis* infestations on cultured salmon.

The three analytical approaches we used reveal a key insight into interpreting the results of salmon and sea lice studies that formed the basis of our meta-analysis. While the assembled data indicate a clear consistency in direction of parasiticide effects on survival, the magnitude of the odds-ratio is relatively small. This is due to the very high marine mortality that naturally affects both control and treatment groups. This, perhaps, underlies the conclusions of some studies that the effect is biologically insignificant relative to the overall mortality within a salmon lifecycle [40,46]. However, our analyses based on paired sample *t*-

tests and mixed effects models allowed us to account for the high natural mortality and isolate the estimated loss of recruitment due to parasitism, revealing a large effect of parasites. Precisely because natural mortality rates are high, even a proportionally small additive mortality from parasites can amount to a large loss in salmon recruitment.

It is rare to identify and quantify the factors that affect population dynamics of marine fishes [15] as well as the role of infectious disease in conservation [59]. Our results indicate that parasite-associated mortality may cause the closure of some fisheries when conservation targets of return adult abundances are not being met. However, the implications of our results may be most acute for small populations in small river systems. Due largely to the fidelity to their natal rivers, populations of Atlantic salmon typically show substantial genetic structuring and variability that is considered adaptive [60]. Small river systems that support salmon populations of low effective population size [61] will be especially vulnerable. The concern therefore is not only for a 39% loss in salmon abundance, but also the loss of genetic variability and its associated potential for adaptation to other environmental changes. More broadly, and in contrast to the conclusions from two of the original studies [40,46], our results supply manipulative field experimental evidence at a large spatial scale that parasitism may be a significant limiting factor for marine fish, fisheries, and conservation.

REFERENCES

1. Daszak, P., Cunningham, A. A. & Hyatt, A. D. 2000 Emerging infectious diseases of wildlife - Threats to biodiversity and human health. *Science* **287**, 443-449. (doi:10.1126/science.287.5452.443)
2. Ferguson, N. M., Donnelly, C. A. & Anderson, R. M. 2001 Transmission intensity and impact of control policies on the foot and mouth epidemic in Great Britain. *Nature* **413**, 542-548. (doi:10.1038/35097116)
3. de Castro, F. & Bolker, B. 2005 Mechanisms of disease-induced extinction. *Ecol. Lett.* **8**, 117-126. (doi:10.1111/j.1461-0248.2004.00693.x)
4. Pedersen, A. B., Jones, K. E., Nunn, C. L. & Altizer, S. 2007 Infectious diseases and extinction risk in wild mammals. *Conserv. Biol.* **21**, 1269-1279. (doi:10.1111/j.1523-1739.2007.00776.x)
5. Jansen, P. A., Kristoffersen, A. B., Viljugrein, H., Jimenez, D., Aldrin, M. & Stien, A. 2012 Sea lice as a density-dependent constraint to salmonid farming. *Proc. R. Soc. B* **279**, 2330-2338. (doi:10.1098/rspb.2012.0084)
6. Hatcher, M. J., Dick, J. T. A. & Dunn, A. M. 2012 Diverse effects of parasites in ecosystems: linking interdependent processes. *Front. Ecol. Env.* **10**, 186-194. (doi:10.1890/110016)
7. Fenton, A. & Brockhurst, M. A. 2008 The role of specialist parasites in structuring host communities. *Ecol. Res.* **23**, 795-804. (doi:10.1007/s11284-007-0440-6)
8. Hudson, P. J., Rizzoli, A., Grenfell, B. T., Heesterbeek, H. & Dobson, A. P. 2001 *The Ecology of Wildlife Diseases*. Oxford, Oxford University Press.
9. Thomas, F., Renaud, F. & Guegan, J. F. 2005 *Parasitism and Ecosystems*. Oxford, Oxford University Press.
10. Robar, N., Burness, G. & Murray, D. L. 2010 Tropics, trophics and taxonomy: the determinants of parasite-associated host mortality. *Oikos* **119**, 1273-1280. (doi:10.1111/j.1600-0706.2009.18292.x)
11. Hudson, P. J., Dobson, A. P. & Newborn, D. 1998 Prevention of population cycles by parasite removal. *Science* **282**, 2256-2258. (doi:10.1126/science.282.5397.2256)
12. Redpath, S. M., Mougeot, F., Leckie, F. M., Elston, D. A. & Hudson, P. J. 2006 Testing the role of parasites in driving the cyclic population dynamics of a gamebird. *Ecol. Lett.* **9**, 410-418. (doi:10.1111/j.1461-0248.2006.00895.x)
13. Fogarty, M. J., Sissenwine, M. P. & Cohen, E. B. 1991 Recruitment variability and the dynamics of exploited marine populations. *Trends Ecol. Evol.* **6**, 241-246. (doi:10.1016/0169-5347(91)90069-a)
14. Anderson, C. N. K., Hsieh, C. H., Sandin, S. A., Hewitt, R., Hollowed, A., Beddington, J., May, R. M. & Sugihara, G. 2008 Why fishing magnifies fluctuations in fish abundance. *Nature* **452**, 835-839. (doi:10.1038/Nature06851)
15. Myers, R. A. 1998 When do environment-recruitment correlations work? *Rev. Fish Biol. Fisher.* **8**, 285-305. (doi:10.1023/a:1008828730759)
16. Dobson, A. P. & May, R. M. 1987 The effects of parasites on fish populations - theoretical aspects. *Int. J. Parasitol.* **17**, 363-370. (doi:10.1016/0020-7519(87)90111-1)
17. Lafferty, K. D., Porter, J. W. & Ford, S. E. 2004 Are diseases increasing in the ocean? *Annu. Rev. Ecol. Evol. Syst.* **35**, 31-54. (doi:10.1146/annurev.ecolsys.35.021103.105704)
18. 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 Ecol. Evol.* **19**, 585-591. (doi:10.1016/j.tree.2004.08.009)

19. Wood, C. L., Lafferty, K. D. & Micheli, F. 2010 Fishing out marine parasites? Impacts of fishing on rates of parasitism in the ocean. *Ecol. Lett.* **13**, 761-775. (doi:10.1111/j.1461-0248.2010.01467.x)

20. 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. (doi:10.1126/science.1148744)

21. Diana, J. S. 2009 Aquaculture production and biodiversity conservation. *Bioscience* **59**, 27-38. (doi:10.1525/bio.2009.59.1.7)

22. Toranzo, A. E., Magarinos, B. & Romalde, J. L. 2005 A review of the main bacterial fish diseases in mariculture systems. *Aquaculture* **246**, 37-61. (doi:10.1016/j.aquaculture.2005.01.002)

23. Johnson, S. C., Treasurer, J. W., Bravo, S., Nagasawa, K. & Kabata, Z. 2004 A review of the impact of parasitic copepods on marine aquaculture. *Zool. Stud.* **43**, 229-243.

24. Asche, F., Hansen, H., Tveteras, R. & Tveteras, S. 2009 The salmon disease crisis in Chile. *Mar. Res. Econom.* **24**, 405-411.

25. Ward, T. M., Hoedt, F., McLeay, L., Dimmlich, W. F., Kinloch, M., Jackson, G., McGarvey, R., Rogers, P. J. & Jones, K. 2001 Effects of the 1995 and 1998 mass mortality events on the spawning biomass of sardine, *Sardinops sagax*, in South Australian waters. *ICES J. Mar. Sci.* **58**, 865-875. (doi:10.1006/jmsc.2001.1077)

26. Heuch, P. A., Bjørn, P. A., Finstad, B., Holst, J. C., Asplin, L. & Nilsen, F. 2005 A review of the Norwegian 'National Action Plan Against Salmon Lice on Salmonids': The effect on wild salmonids. *Aquaculture* **246**, 79-92. (doi:10.1016/j.aquaculture.2004.12.027)

27. Costello, M. J. 2006 Ecology of sea lice parasitic on farmed and wild fish. *Trends Parasitol.* **22**, 475-483. (doi:10.1016/j.pt.2006.08.006)

28. Pike, A. W. & Wadsworth, S. L. 1999 Sealice on salmonids: Their biology and control. *Adv. Parasitol.* **44**, 233-337. (doi:10.1016/S0065-308X(08)60233-X,)

29. Jones, S. R. M. & Beamish, R. J. 2011 *Salmon Lice: An Integrated Approach to Understanding Parasite Abundance and Distribution*. Oxford, UK, Wiley-Blackwell.

30. Hindar, K., Hutchings, J. A., Diserud, O. H. & Fiske, P. 2010 Stock, recruitment, and exploitation. In *Atlantic Salmon Ecology* (eds. Aas Ø., Einum S., Klemetsen A., Skurdal J.). Oxford, Wiley-Blackwell.

31. Ford, J. S. & Myers, R. A. 2008 A global assessment of salmon aquaculture impacts on wild salmonids. *PLoS Biol.* **6**, e33. (doi:10.1371/journal.pbio.0060033)

32. Otero, J., Jensen, A. J., L'Abée-Lund, J. H., Stenseth, N. C., Storvik, G. O. & Vøllestad, L. A. 2011 Quantifying the ocean, freshwater and human effects on year-to-year variability of one-sea-winter Atlantic salmon angled in multiple Norwegian rivers. *PLoS ONE* **6**, e24005. (doi:10.1371/journal.pone.0024005)

33. Murray, A. G. & Gillibrand, P. A. 2006 Modelling salmon lice dispersal in Loch Torridon, Scotland. *Mar. Poll. Bull.* **53**, 128-135. (doi:10.1016/j.marpolbul.2005.09.013)

34. Poulin, R. 2007 Are there general laws in parasite ecology? *Parasitology* **134**, 763-776. (doi:10.1017/s0031182006002150)

35. Poulin, R. 2011 The many roads to parasitism: A tale of convergence. *Adv. Parasitol.* **74**, 1-40. (doi:10.1016/b978-0-12-385897-9.00001-x)

36. Todd, C. D., Whyte, B. D. M., MacLean, J. C. & Walker, A. M. 2006 Ectoparasitic sea lice (*Lepeophtheirus salmonis* and *Caligus elongatus*) infestations of wild, adult, one sea-winter Atlantic salmon *Salmo salar* returning to Scotland. *Mar. Ecol. Progr. Ser.* **328**, 183-193. (doi:10.3354/meps328183)

37. Todd, C. D., Walker, A. M., Hoyle, J. E., Northcott, S. J., Walker, A. F. & Ritchie, M. G. 2000 Infestations of wild adult Atlantic salmon (*Salmo salar* L.) by the ectoparasitic copepod sea louse *Lepeophtheirus salmonis* Krøyer: prevalence, intensity and the spatial distribution of males and females on the host fish. *Hydrobiologia* **429**, 181-196.

38. Marty, G., Saksida, S. & Quinn, T. J. 2010 Relationship of farm salmon, sea lice, and wild salmon populations. *Proc. Natl Acad. Sci. USA* **107**, 22599-22604. (doi:10.1073/pnas.1009573108)

39. Krkošek, M., Connors, B. M., Morton, A., Lewis, M. A., Dill, L. M. & Hilborn, R. 2011 Effects of parasites from salmon farms on productivity of wild salmon. *Proc. Natl Acad. Sci. USA* **108**, 14700-14704. (doi:10.1073/pnas.1101845108)

40. Jackson, D.*, et al.* 2011 An evaluation of the impact of early infestation with the salmon louse *Lepeophtheirus salmonis* on the subsequent survival of outwardly migrating Atlantic salmon, *Salmo salar* L., smolts. *Aquaculture* **320**, 159-163. (doi:10.1016/j.aquaculture.2011.03.029)

41. Beamish, R. J., Jones, S., Neville, C. E., Sweeting, R., Karreman, G., Saksida, S. & Gorden, E. 2006 Exceptional marine survival of pink salmon that entered the marine environment in 2003 suggests that farmed Atlantic salmon and Pacific salmon can coexist successfully in a marine ecosystem on the Pacific coast of Canada. *ICES J. Mar. Sci.* **63**, 1326-1337. (doi:10.1016/j.icesjms.2006.04.011)

42. Gargan, P., Forde, G., Hazon, N., Russell, D. J. F. & Todd, C. D. 2012 Evidence for sea lice-induced marine mortality of Atlantic salmon (*Salmo salar*) in western Ireland from experimental releases of ranched smolts treated with emamectin benzoate. *Can. J. Fish. Aquat. Sci.* **69**, 343-353. (doi:10.1139/f2011-155)

43. Gargan, P., Tully, O. & Poole, W. R. 2002 The relationship between sea lice Infestation, sea lice production and sea trout survival in Ireland, 1992-2001. In *Salmon on the Edge* (ed. Mills D.), pp. 119-135. Edinburgh, Atlantic Salmon Trust/Atlantic Salmon Federation.

44. Costello, M. J. 2009 How sea lice from salmon farms may cause wild salmonid declines in Europe and North America and be a threat to fishes elsewhere. *Proc. R. Soc. B* **276**, 3385-3394. (doi:10.1098/rspb.2009.0771)

45. Skilbrei, O. T. & Wennevik, V. 2006 Survival and growth of sea-ranched Atlantic salmon, *Salmo salar* L., treated against sea lice before release. *ICES J. Mar. Sci.* **63**, 1317-1325. (doi:10.1016/j.icesjms.2006.04.012)

46. Jackson, D.*, et al.* 2011 Impact of early infestation with the salmon louse *Lepeophtheirus salmonis* on the subsequent survival of outwardly migrating Atlantic salmon smolts from a number of rivers on Ireland's south and west coasts. *Aquaculture* **319**, 37-40. (doi:10.1016/j.aquaculture.2011.06.042)

47. Hvidsten, N. A., Finstad, B., Kroglund, F., Johnsen, B. O., Strand, R., Arnekleiv, J. V. & Bjørn, P. A. 2007 Does increased abundance of sea lice influence survival of wild Atlantic salmon post-smolt? *J. Fish. Biol.* **71**, 1639-1648. (doi:10.1111/j.1095-8649.2007.01622.x)

48. Stone, J., Sutherland, I. H., Sommerville, C., Richards, R. H. & Varma, K. J. 2000 Commercial trials using emamectin benzoate to control sea lice *Lepeophtheirus salmonis* infestations in Atlantic salmon *Salmo salar. Dis. Aquat. Org.* **41**, 141-149. (doi:10.3354/dao041141)

49. DerSimonian, R. & Laird, N. 1986 Meta-analysis in clinical trials. *Control. Clin. Trials* **7**, 177–188.

50. Klein, J. P. & Moeschberger, M. L. 2003 *Survival Analysis*. New York, Springer.

51.   Skilbrei, O. T., Glover, K. A., Samuelsen, O. B. & Lunestad, B. T. 2008 A laboratory study to evaluate the use of emamectin benzoate in the control of sea lice in sea-ranched Atlantic salmon (*Salmo salar* L.). *Aquaculture* **285**, 2-7. (doi:10.1016/j.aquaculture.2008.07.055)

52.   Jonsson, N., Jonsson, B. & Hansen, L. P. 2003 The marine survival and growth of wild and hatchery-reared Atlantic salmon. *J. Appl. Ecol.* **40**, 900-911.

53.   Gillibrand, P. A. & Kate, J. W. 2007 Dispersal of sea lice larvae from salmon farms: A model study of the influence of environmental conditions and larval behaviour. *Aquat. Biol.* **1**, 63-75. (doi:10.3354/ab00006)

54.   Bakke, T. A. & Harris, P. D. 1998 Diseases and parasites in wild Atlantic salmon (*Salmo salar*) populations. *Can. J. Fish. Aquat. Sci.* **55(S1)**, 247-266. (doi:10.1139/d98-021)

55.   Krkošek, M.*, et al.* 2011 Fish farms, parasites, and predators: Implications for salmon population dynamics. *Ecol. Appl.* **21**, 897-914. (doi:10.1890/09-1861.1)

56.   Ferguson, J. A., Koketsu, W., Ninomiya, I., Rossignol, P. A., Jacobson, K. C. & Kent, M. L. 2011 Mortality of coho salmon (*Oncorhynchus kisutch*) associated with burdens of multiple parasite species. *Int. J. Parasitol.* **41**, 1197-1205. (doi:10.1016/j.ijpara.2011.07.005)

57.   Kennedy, C. R. 2007 The pathogenic helminth parasites of eels. *J. Fish Dis.* **30**, 319-334. (doi:10.1111/j.1365-2761.2007.00821.x)

58.   Jacobson, K. C., Teel, D., Van Doornik, D. M. & Casillas, E. 2008 Parasite-associated mortality of juvenile Pacific salmon caused by the trematode *Nanophyetus salmincola* during early marine residence. *Mar. Ecol. Progr. Ser.* **354**, 235-244. (doi:10.3354/meps07232)

59.   Smith, K. F., Sax, D. F. & Lafferty, K. D. 2006 Evidence for the role of infectious disease in species extinction and endangerment. *Conserv. Biol.* **20**, 1349-1357. (doi:10.1111/j.1523-1739.2006.00524.x)

60.   Garcia de Leaniz, C. G.*, et al.* 2007 A critical review of adaptive genetic variation in Atlantic salmon: implications for conservation. *Biol. Rev.* **82**, 173-211. (doi:10.1111/j.1469-185X.2006.00004.x)

61.   Nikolic, N., Butler, J. R. A., Baglinière, J.-L., Laughton, R., McMyn, I. A. G. & Chevalet, C. 2009 An examination of genetic diversity and effective population size in Atlantic salmon populations. *Genet. Res.* **91**, 395-412. (doi:10.1017/s0016672309990346)

Table 1. Summary of the data, giving the year, country, and river of release as well as the numbers of smolts released (N) and of one sea-winter (1SW) adults recovered (R) for treatment groups receiving parasiticides (t) and controls (c). Also shown are the total number of smolts released (N_{total}) and sources of the data (Ref), those studies with multiple within-season releases that were grouped (*), and the studies that used the proprietary Substance Ex as treatment (¶) rather than emamectin benzoate. Note that numbers of recaptured salmon for Refs [40] and [46] are their survival estimates that incorporated raising factors applied to the raw data (tags recovered), and may therefore be inflated relative to the other data.

| Year	Country	River	N_t	R_t	N_c	R_c	N_{total}	Ref
1996	Norway	Agdenes	3000	53	2985	43	5985	[47]¶
1997	Norway	Agdenes	2935	16	2936	12	5871	[47]¶
1998	Norway	Agdenes	2966	37	2977	14	5943	[47]¶
2002	Norway	Dale	5086	56	4859	40	9945	[45]*
2004	Ireland	Erriff	4325	44	4229	34	8554	[42]
2005	Ireland	Erriff	4659	37	4689	2	9348	[42]
2003	Ireland	Invermore	4589	17	4594	9	9183	[42]
2004	Ireland	Invermore	4653	37	4671	26	9324	[42]
2005	Ireland	Invermore	4716	31	4750	17	9466	[42]
2003	Ireland	Owengowla	4955	35	4822	3	9777	[42]
2004	Ireland	Owengowla	4655	51	4699	22	9354	[42]
2005	Ireland	Owengowla	4583	54	4735	53	9318	[42]
2001	Ireland	Burrishoole	5496	565	10039	992	15535	[40]
2002	Ireland	Burrishoole	5960	544	5989	545	11949	[40]
2003	Ireland	Burrishoole	4755	472	4587	374	9342	[40]
2004	Ireland	Burrishoole	4437	402	4369	398	8806	[40]
2005	Ireland	Burrishoole	3793	253	3867	182	7660	[40]
2006	Ireland	Burrishoole	8716	508	12779	549	21495	[40] *
2007	Ireland	Burrishoole	6746	492	6795	435	13541	[40]
2008	Ireland	Burrishoole	10132	163	10224	125	20356	[40] *
2001	Ireland	Bundorragha	12787	2056	12753	1873	25540	[46] *
2006	Ireland	Erne	5752	70	10357	68	16109	[46]
2006	Ireland	Lee	5207	10	5131	10	10338	[46]
2006	Ireland	Screebe	10990	157	9618	121	20608	[46]

Figure 1
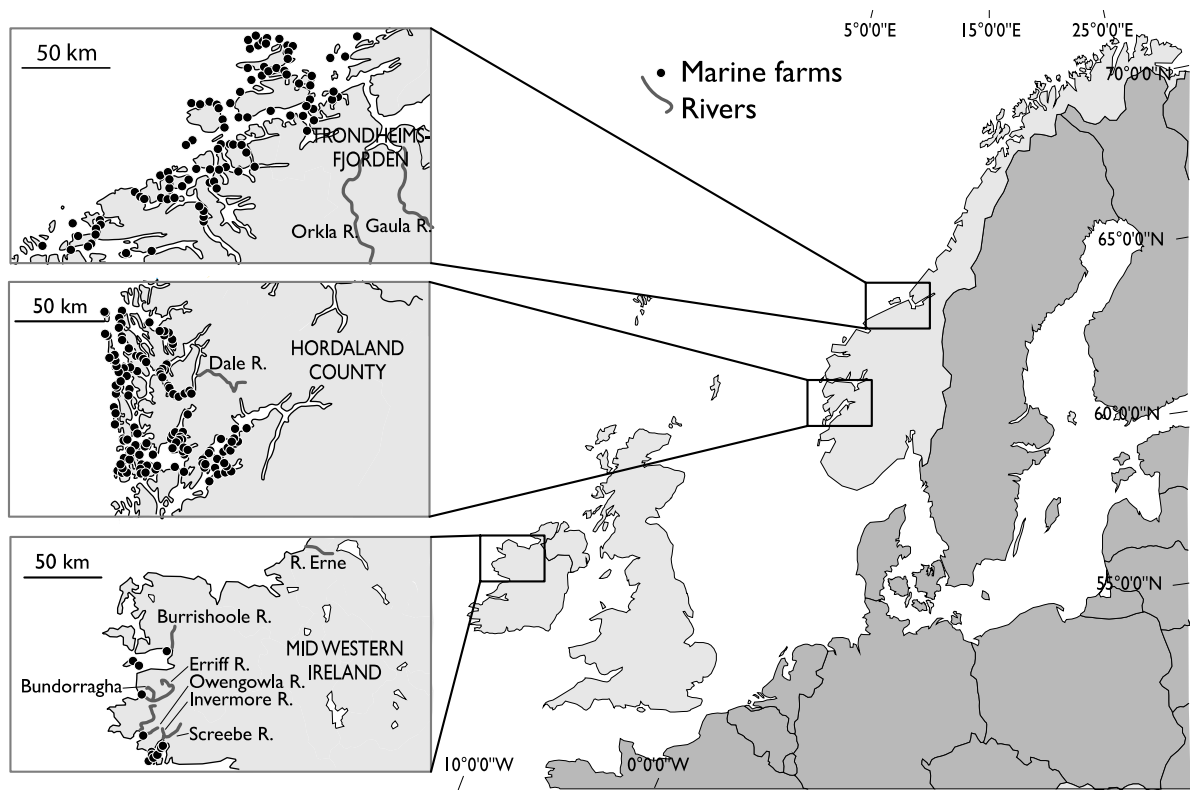
Figure 1. Map of the study regions showing rivers where salmon smolts were released and salmon farm locations (black circles). Interpretation of farming activities over the course of the study period should be made with caution because the distributions of farms, stocking levels, parasite levels, and management approaches have varied over the years.

Figure 2
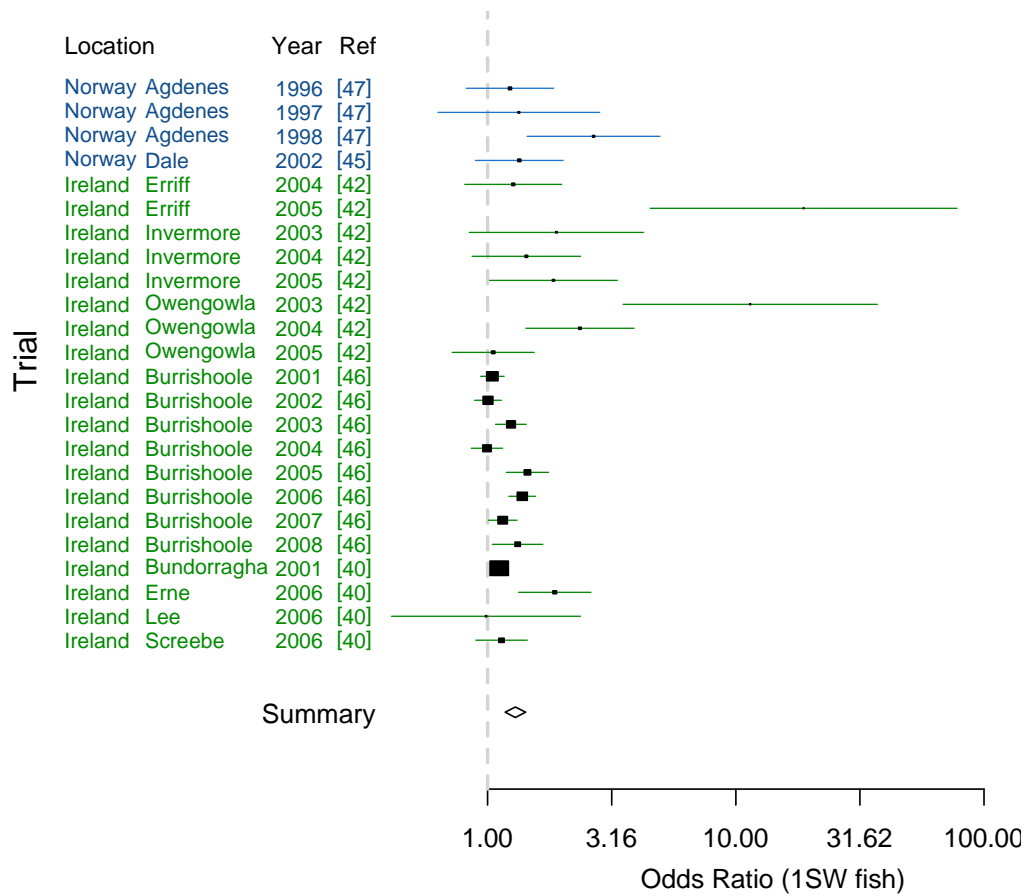
Figure 2. Forest plot displaying a random-effects meta-analysis of the effect of treatment on the likelihood of a one sea winter (1SW) adult salmon returning. Horizontal lines represent the 95% confidence intervals of the effect size in each trial, and the relative sizes of solid squares reflect the percentage weighting (based on standard errors of effect sizes) of each trial in the meta-analysis (range 0.42 - 8.12%). The open diamond shows the overall meta-analytic effect across all studies, with its width corresponding to the 95% confidence interval. Results are given by trial, identified by Location (country and river of release of smolts), Year (year when smolts were released), and Ref (the reference where the data were published).

Electronic Supplementary Material

The present analyses focused on all the available published literature pertaining to control and parasiticide-treated experimental releases of Atlantic salmon smolts. The process by which the data were identified was mainly by our knowledge of their existence – some co-authors were directly involved in the original studies and it is a relatively small research community. However, we also checked on the ISI Web of Science that we did not miss any studies by searching under the keyword "salmon AND lice", which produced 789 records from which we searched separately for the following further keywords: "tag" and "release". The publications providing the original data are listed in table 1. In all instances, with the exception of Refs [40] and [46], we included in our analyses the raw counts of control and treatment (parasiticide) tags retrieved from return adult migrant salmon. Refs [40] and [46] provide only the numbers of smolts released at each trial and the "raised" numbers, and estimated percent marine survival, of recaptured fish. Ideally, we would have included the raw tag counts from the trials in Refs [40] and [46] but the authors declined to provide those numbers, or the "raising factors" applied in deriving the percent estimates of marine survival. Multiple raising factors were applied to the tags retrieved in Refs [40] and [46], depending upon the source of tag retrieval. Thus, for example, in monitoring tags from commercial landings in the six Irish coastal fishery areas, the raising factor applied to a specific tag was dependent upon the proportion of an area's catch sampled and the frequency with which those catches were inspected by fishery scientists. As detailed in Ref [42], in order to estimate percent marine survivorship, the total number of tagged salmon actually taken in these various net fisheries would have been derived by multiplying the number of tagged salmon caught in each area by the ratio of the total declared salmon catch to sample size. It would therefore have been necessary to apply a different raising factor for each area because of the different proportions of the catch examined. In the absence of the specific raising factors applied to each tag retrieved for Refs [40] and [46] we make the assumption that each control-treatment data pairing received the same adjustments, and therefore the scaling factor is not needed for present purposes. From inspection of the numbers of smolts released across all experiments (table 1, table S1), and their reported range of percent marine survival [40, 46], there is no reason to suspect that the numbers of tags retrieved in Refs [40] and [46] will exert undue influence on the overall meta-analytical results presented here. Moreover, because we are interested in the difference in log survival between paired control-treatment groups, φ, the unknown scaling factors applied in Refs [40] and [46] have no

effect: if Z is the scaling factor, N_t and N_c are the number of treatment and control smolts released, and R_t and R_c are number of treatment and control adult recoveries, then an observation of φ is $\ln(ZR_t/N_t) - \ln(ZR_c/N_c) = \ln(Z) - \ln(Z) + \ln(R_t/N_t) - \ln(R_c/N_c) = \ln(R_t/N_t) - \ln(R_c/N_c)$.

Ref. [42] presented and analyzed only the numbers of adults returning after one winter at sea – so-called one sea-winter (1SW) adults. A small number of the juveniles tagged in these trials in Ireland returned two years after release as 2SW adults. In the analyses of the main text, we used only 1SW fish. Refs [40] and [46] provided no information on the sea ages of retrieved adult salmon, but the fish released into the Burrishoole system [40] all were of a line-bred grilse (= 1SW) strain so the presumption is made that all return adults were 1SW fish. We make the same presumption for the fish released to the Rivers Erne, Lee and Screebe [46]. With specific reference to the trials in Ireland [40,42,46], it is relevant to note that the west coast Ireland commercial drift net fishery for wild salmon was closed after summer 2006. Scientific monitoring of catches landed from this fishery provided a large number of tag returns for these experiments. For all of the trials in Ref [42], which involved juvenile releases in 2003, 2004 and 2005, all return 1SW adults (and tags) were available to be sampled by that fishery in a comparable manner over the time series. For the releases documented in [40] and [46], and which occurred from spring 2006 onwards, this fishery source of tag retrieval was no longer available and this may have implications for low estimates of marine survival from the retrieved tag numbers.

Table S1 shows the numbers of control and treatment smolts released and the tags successfully retrieved from all returning adults, of varying sea ages, which we also analyzed and report in the results presented below. Just as for the Irish recaptures, the return adults recorded from the Norwegian releases [45,47] included primarily 1SW adults, but also there were some numbers both of 2SW and even 3SW return adults. Again, in the analyses reported in the main text, only 1SW fish were included in the analysis. Ref [47] included 526 smolts (276 treated, 250 control) in the total of 10,471 fish released in their summed trial, and that were precociously mature male parr which had undergone smoltification. Of these 526 fish, 6 treated and 3 control tags were retrieved, and these were included in the analyses reported in this ESM below. Exclusion of the precociously mature male parr from the data in Table S1 yielded almost identical results to those reported below.

To ascertain the robustness of the results, we also analyzed the data for fish of all sea ages at recovery (including precociously mature male parr in ref [47] and the data from Refs

[40] and [46] as originally reported in their paper; table S1). Meta-analysis of odds ratios (figure S1) indicated very similar results to those reported in the main text. Analysis with a paired sample t-test revealed significant differences in survival between treatment and control groups ($t = 3.40$, $df = 23$, p-value = 0.002). Similarly for the mixed model, treatment had a significant effect on survival (Likelihood ratio test; $\chi^2 = 9.80$, $df = 1$, $p = 0.002$). The estimated difference in log survival between paired treatment and control groups was $\varphi = 0.51$ from both analyses – that is, for the mixed models analyzing 1SW fish only and for fish of pooled sea ages. Uncertainty in φ was given by 95% confidence intervals of 0.20 to 0.82 in the paired sample t-test, and a range of two standard errors of 0.21 to 0.81 in the mixed model. These estimates of φ correspond to parasite-associated mortality of Atlantic salmon of $M = 39.9\%$ (95% CI from paired sample t-test, 18.1% to 55.9%; range of two standard errors from mixed model, 18.9% to 55.4%).

Table S1. Summary of the data, giving the year, country, and river of release as well as the numbers of smolts released (N) and adults of all sea-ages (1SW-3SW incl.) that were recovered (R) for treatment groups receiving parasiticides (t) and controls (c). Also shown are sources of the data (Ref), studies with multiple within-season releases that were grouped (*), and studies that used the proprietary Substance Ex as treatment ([¶]) rather than emamectin benzoate. Note that recaptured salmon for Refs [40] and [46] are of un-reported sea age and numbers here are derived from their survival estimates that applied raising factors to the raw data (tags recovered): these numbers may therefore be inflated relative to the other data sources.

Year	Country	River	N_t	R_t	N_c	R_c	Ref
1996	Norway	Agdenes	3000	66	2985	51	[47][¶]
1997	Norway	Agdenes	2935	20	2936	15	[47][¶]
1998	Norway	Agdenes	2966	42	2977	17	[47][¶]
2002	Norway	Dale	5362	93	5109	53	[45]*
2004	Ireland	Erriff	4325	49	4229	34	[42]
2005	Ireland	Erriff	4659	38	4689	2	[42]
2003	Ireland	Invermore	4589	19	4594	11	[42]
2004	Ireland	Invermore	4653	37	4671	27	[42]
2005	Ireland	Invermore	4716	33	4750	17	[42]
2003	Ireland	Owengowla	4955	38	4822	3	[42]
2004	Ireland	Owengowla	4655	51	4699	24	[42]
2005	Ireland	Owengowla	4583	55	4735	55	[42]
2001	Ireland	Burrishoole	5496	565	10039	992	[40]
2002	Ireland	Burrishoole	5960	544	5989	545	[40]
2003	Ireland	Burrishoole	4755	472	4587	374	[40]
2004	Ireland	Burrishoole	4437	402	4369	398	[40]
2005	Ireland	Burrishoole	3793	253	3867	182	[40]
2006	Ireland	Burrishoole	8716	508	12779	549	[40]*
2007	Ireland	Burrishoole	6746	492	6795	435	[40]
2008	Ireland	Burrishoole	10132	163	10224	125	[40]*
2001	Ireland	Bundorragha	12787	2056	12753	1873	[46]*
2006	Ireland	Erne	5752	70	10357	68	[46]
2006	Ireland	Lee	5207	10	5131	10	[46]
2006	Ireland	Screebe	10990	157	9618	121	[46]

Fig S1. Forest plot displaying a random-effects meta-analysis of the effect of treatment on the likelihood of all sea ages (1SW-3SW incl.) of adult salmon returning. Horizontal lines represent the 95% confidence intervals of the effect size in each trial and the relative sizes of solid squares reflect the percentage weighting (based on standard errors of effect sizes) of each trial in the meta-analysis (range 0.42 - 8.12%). The diamond at the bottom represents the effect across all studies, with its width corresponding to the meta-analytic 95% confidence interval on the overall effect size. Results are given by trial, identified by Location (country and river of release of smolts), Year (year when smolts were released), and Ref (the reference where the data were published).

Location		Year	Ref
Norway	Agdenes	1996	[47]
Norway	Agdenes	1997	[47]
Norway	Agdenes	1998	[47]
Norway	Dale	2002	[45]
Ireland	Erriff	2004	[42]
Ireland	Erriff	2005	[42]
Ireland	Invermore	2003	[42]
Ireland	Invermore	2004	[42]
Ireland	Invermore	2005	[42]
Ireland	Owengowla	2003	[42]
Ireland	Owengowla	2004	[42]
Ireland	Owengowla	2005	[42]
Ireland	Burrishoole	2001	[46]
Ireland	Burrishoole	2002	[46]
Ireland	Burrishoole	2003	[46]
Ireland	Burrishoole	2004	[46]
Ireland	Burrishoole	2005	[46]
Ireland	Burrishoole	2006	[46]
Ireland	Burrishoole	2007	[46]
Ireland	Burrishoole	2008	[46]
Ireland	Bundorragha	2001	[40]
Ireland	Erne	2006	[40]
Ireland	Lee	2006	[40]
Ireland	Screebe	2006	[40]

Trial

Summary

Odds Ratio

1.00   3.16   10.00   31.62   100.00