INTRODUCTION

Fifty-eight percent of the infectious diseases affecting humans are zoonotic, passing from animals to people (Woolhouse & Gowtage-Sequeria, 2005). Among the parasites that cause these zoonotic diseases, many have complex life cycles that connect disparate host species across a sprawling food web (Figure 1). People have interrupted most of these transmission cycles in the developed world by disentangling human activities from nature: our water is purified, our sewers direct waste away from water and food sources, and our food is processed. But some activities...
keep humans intimately connected with ecosystems, and therefore risk ensnaring people in parasite life cycles.

As one of the few zoonoses that can be transmitted to humans from marine animals, anisakidosis is contracted through consumption of raw, pickled, smoked, undercooked, or improperly frozen wild marine seafood (Deardorff, Kayes, & Fukumura, 1991). The disease is caused by nematode parasites in the family Anisakidae (hereafter, anisakids), most commonly the genera Anisakis ("herring worm"
or "whale worm"; Mattiucci et al., 1997) and Pseudoterranova ("cod worm" or "seal worm"; Paggi et al., 1991), which are globally distributed and ubiquitous in the flesh of marine fishes (Figure 1a). Eggs from the adult worms are released in the feces of their marine mammal definitive hosts (i.e., cetaceans for Anisakis, pinnipeds for Pseudoterranova), and infect small crustaceans that consume the parasite eggs or larvae (Anderson, 2000; McClelland, 2002; Figure 1b,c). These first-intermediate crustacean hosts are then consumed by fishes, cephalopods, or other crustaceans, where they encyst and await trophic transmission, either to another intermediate host, to a paratenic (i.e., "transport") host, or to a marine mammal definitive host—and where they may then be incidentally ingested by humans (Figure 1b,c; Acha & Szyfres, 2003). The worms cannot successfully reproduce in the human intestinal tract, but they can survive there temporarily and cause substantial pathology (Bouree, Paugam, & Petithory, 1995).

Human seafood consumers often discover their infection status when they find live worms in their phlegm, mucus, vomit, or feces (Acha & Szyfres, 2003), and in serious cases, symptoms include acute abdominal pain, nausea, vomiting, and diarrhea, which can persist for months (Acha & Szyfres, 2003; Bouree et al., 1995). Misdiagnosis is common, as symptoms resemble those of many gastrointestinal ailments (Acha & Szyfres, 2003; Khan & Williams, 2016; Shibata, Ueda, Akaile, & Saïda, 2014; Shrestha et al., 2014). Restaurants and supermarkets in the United States are required to comply with regulations in the US Food and Drug Administration's Food Code, which stipulates that fishery products must be frozen to kill anisakids before raw product can be sold or served to the public (FDA, 2009). Similar regulations are in effect in the European Union (European Commission, 2011). Nonetheless, existing evidence suggests that anisakid exposure is substantial on a global scale among individuals who consume raw fish (Bao, Pierce, Pascual, et al., 2017; Garcia-Palacios et al., 1996; Uga, Ono, Kataoka, & Hasan, 1996). Even after worms have been killed by freezing, they can elicit gastrointestinal symptoms if consumed (Audicana, Ansegotui, Corres, & Kennedy, 2002; Audicana & Kennedy, 2008; Daschner, Alonso-Gomez, Cabanas, Suarez-de-Parga, & Lopez-Serrano, 2000) and respiratory or dermatological symptoms through nonconsumptive exposure, as in fishermen and fish-processing workers (Armentia et al., 1998; Nieuwenhuizen et al., 2006; Purello-D'Ambrosio et al., 2000; Scala et al., 2001).

Anisakidosis has been labeled an emerging zoonosis (Bao, Pierce, Pascual, et al., 2017) due to recent upticks in reports of the disease from Japan, New Zealand, coastal areas of Europe, the United States, Canada, Brazil, Chile, and Egypt (Audicana et al., 2002; Audicana & Kennedy, 2008; Chai, Murrell, & Lymbery, 2005; Hochberg, Hamer, Hughes, & Wilson, 2010). The rising incidence of anisakidosis could be due to: more accurate detection and diagnosis (Lohi et al., 2007), increased rates of consumption of raw or undercooked fish (Nawa, Hatz, & Blum, 2005), or an increased abundance of the parasites in the commercially fished hosts. We sought to assess whether the risk of anisakidosis to human consumers has increased over time due to increasing abundance of anisakid parasites in wild seafood.

Past efforts to track change in parasite abundance over time have used "vote-counting" meta-analytic approaches (Rudel, 2008). For example, Ward and Lafferty (2004; see also Wood, Lafferty, & Micheli, 2010, appendix S1) used the proportion of total reports of a taxon that addressed infectious disease (i.e., number of papers about disease in a taxon/total number of papers about that taxon) to assess whether rates of disease in marine hosts had changed between 1970 and 2001. Fey et al. (2015) used a similar approach to show that, among animals, the number of mass mortalities caused by infectious disease increased between 1940 and 2000. However, because these approaches depend on counting the number of reports on a particular topic, they are susceptible to literature bias (Fey et al., 2015).

Because we were interested in a single, well-studied parasite clade, we were able to perform a true meta-analysis, in which we extracted data from studies rather than tallying the number of studies showing a particular effect. We sought to assess change in anisakid nematode abundance over the past several decades. Although no study before ours has assessed temporal change in anisakid abundance at a global scale, thousands of studies have empirically quantified the abundance of anisakids in fish and invertebrate hosts at specific times and locations across the world. We assimilated these studies into our meta-analysis, harnessing the statistical power of many studies conducted in many regions across many host species. We specifically focused on studies of fish and invertebrate intermediate and paratenic hosts, as they have been systematically assessed for parasites by many prior studies.

There are several ecological differences between Anisakis spp. and Pseudoterranova spp. that could cause the genera to exhibit divergent responses to global change. First, while Anisakis spp. use cetaceans as definitive hosts, Pseudoterranova spp. use pinnipeds (Measures, 2014). If the trajectories of change in abundance for these two definitive host groups differ, or if the two parasite genera differ in their degree of dependence on the definitive host (e.g., if cetaceans are "life-cycle bottlenecks" for Anisakis spp., but pinnipeds are not "life-cycle bottlenecks" for Pseudoterranova spp., sensu Lafferty, 2012), the two genera might differ in their change in abundance over time. As a cetacean specialist with larvae that swim in the water column, Anisakis spp. are pelagic (Measures, 2014; Smith & Wootten, 1978), whereas Pseudoterranova spp.—pinniped specialists with larvae that sink and stick to benthic habitat—are associated with demersal habitats (McClelland, 2002; Measures, 2014). Anthropogenic pressures affecting shallow, coastal habitats (e.g., chemical pollution, nutrient pollution, coastal development) would therefore be likelier to influence Pseudoterranova spp. than Anisakis spp. Finally, Anisakis spp. can proceed directly from the crustacean intermediate host to a marine mammal definitive host, although they often use fish or cephalopod paratenic (i.e., "transport") hosts (Figure 1b; Hays, Measures, & Huot, 1998; Measures, 2014), whereas Pseudoterranova spp. must infect a fish or cephalopod intermediate host in order to complete its development (Figure 1c; McClelland, 2002; Measures, 2014). We might therefore expect Anisakis spp. to be more resilient to long-term biodiversity loss than Pseudoterranova spp., since parasites with many obligately required hosts are more likely to lose one of those hosts as biodiversity loss...
proceeds than are parasites with few obligately required hosts (Wood et al., 2015; Wood, Sandin, Zgliczynski, Guerra, & Micheli, 2014).

We conducted a meta-analysis of change over time (1967-2017) in the abundance of anisakid nematodes in fish and invertebrate hosts collected in any location around the world, finding that *Anisakis* spp. increased over time while *Pseudoterranova* spp. remained unchanged. These findings have important implications for human anisakidosis risk, as well as implications for marine mammal health and fisheries profitability.

2 | METHODS

2.1 | Literature search and data extraction

To identify papers estimating anisakid abundance, we conducted a search in ISI Web of Science. We used the search string: TS = (anisak* or “herring worm” or “herringworm” or *Pseudoterranova* or *whale worm* or “whale worm” or *phocanema* or “whale-worm”), on October 10, 2017, which yielded 2,284 papers. We then used a systematic screening process to eliminate nonrelevant papers (Figure 2a). The screening process was performed by EAF, CAW, and KAD. We first screened titles for suitability, excluding papers that quantified anisakids in humans, birds, or marine mammals and titles that clearly indicated that the paper concerned a different suite of parasite species. After title screening, we retained 1,336 papers for the next stages of the screening process. We then screened abstracts to further focus the dataset, excluding publications that examined anisakids in humans, birds, or marine mammals, that performed experimental manipulation of parasites or hosts, or that were reviews. This process resulted in the retention of 576 papers, which were read in full to determine their eligibility for inclusion in the study. To qualify for final inclusion, papers were required to contain information on host species identity, parasite genus identity, location of host collection (either as a named place or latitude and longitude), collection year or year range, size of the host, how the hosts were examined for anisakids, and either prevalence and intensity of infection with an error estimate or abundance with an estimate of error. Ultimately, we extracted data from 123 papers, resulting in 755 data points (i.e., unique estimates of parasite abundance for a host species in a particular location at a particular time). Of these 755 data points, 69.7% described *Anisakis* spp. (Figure 2b) and 30.3% described *Pseudoterranova* spp. (Figure 2c). For each data point, we extracted information on host species identity, collection location, year of collection, portion of the host examined (i.e., all, viscera, fillet, alimentary tract), host examination method (i.e., standard visual assessment/
candling, microscopy, UV light, acid digestion), parasite genus (i.e., Anisakis or Pseudoterranova), parasite prevalence (i.e., proportion of hosts infected), parasite intensity (i.e., average number of parasites per infected host), error associated with parasite intensity (i.e., standard deviation, range, standard error, or confidence intervals), parasite abundance (i.e., average number of parasites per host for all hosts), and error associated with abundance (i.e., standard deviation, range, standard error, or confidence intervals).

2.2 | Data standardization

We standardized data prior to analysis. For example, to standardize host length, which was reported in different ways (i.e., standard length, total length, fork length) across studies, we used the standard linear conversion equation,

\[
\text{Length}_{\text{standard}} = a + b \times \text{Length}_{\text{reported}}
\]

We obtained the \(a\) and \(b\) parameters for each fish species from FishBase (Froese & Pauly, 2000), using the average \(a\) and \(b\) if multiple values were provided by FishBase.

Parasite abundance was quantified as the number of parasites per host, including uninfected hosts (Bush, Lafferty, Lotz, & Shostak, 1997). When parasite abundance was not reported, but parasite intensity and prevalence were, we calculated parasite abundance by multiplying intensity and prevalence and propagating the error through in quadrature (the square root of the sum of squares). If the range of intensity or abundance was provided but the standard deviation was not, we estimated standard deviation by optimizing the negative binomial distribution for the dispersion parameter. We assumed that the maximum abundance or intensity was the 95th quantile of the negative binomial distribution, since parasites often follow a negative binomial distribution (Shaw, Grenfell, & Dobson, 1998). With this assumption, we used the supplied mean intensity or abundance as the mean of the negative binomial distribution with the dispersion parameter unknown. We then used an optimization algorithm to estimate the dispersion parameter that best fit the supplied mean and 95th percentile. With the given mean and estimated dispersion parameter, we were able to calculate the error of the mean given that the variance of a negative binomial distribution is the sum of the mean and the squared mean divided by the dispersion parameter. We also converted other forms of error reported in the studies (i.e., standard error, confidence intervals) back to standard deviation. To convert from standard error to standard deviation, we multiplied the standard error by the square root of the sample size. To convert from a confidence interval, we took the difference between the upper bound of the confidence interval and the mean and then divided that difference by the appropriate \(z\)-score and multiplied by the square root of the sample size. For location information, we grouped data points based on major FAO fishing region (FAO, 2008) using ESRI ArcGIS (ESRI, 2011), to match our data to FAO major fishing region.

2.3 | Data analysis

To assess change over time in anisakid abundance, we developed two parallel meta-analytic regression models for the two genera of anisakid nematodes contained in our dataset (i.e., Anisakis and Pseudoterranova). For each model, we fourth-root transformed the abundance and standard deviation of the abundance to meet normality assumptions of the model. In our data, we had observations of anisakid abundance with associated error equal to zero. This arose if only a single host was examined, if reported anisakid abundance was zero, or if anisakid abundance was greater than zero, but all the fish that were sampled had the same anisakid burden. Since meta-regression uses the inverse of variance to weight each observation, we corrected the variance to account for observed zero error. We chose to add 1 to every variance to prevent overweighting (i.e., adding a small value like 0.000001 to every zero-error observation will overweight these observations). Adding a very small variance correction would give many orders of magnitude more weight to observations with zero variance compared to any observation that had greater than 1 variance. By adding 1 to the variance, we prevent this issue and observations with zero error get full weight while all other observations receive progressively less weight. We included year of collection and host length as moderators in the meta-regression model. We also included host species, portion of the host examined nested in host species, FAO major fishing area (to account for geographic clustering of points), method for detecting parasites, and paper ID as random effects using the \texttt{rma.mv()} function in the package \texttt{metafor} (Viechtbauer, 2010) in R. The final models took the form:

\[
(\text{Anisakis}_{\text{abundance}_{ijkl}})^{1/4} \text{ or } (\text{Pseudoterranova}_{\text{abundance}_{ijkl}})^{1/4} \\
\sim \text{host_length}_{ijkl} + \text{year}_{ijkl} + (1|\text{host_species}_{ijkl} + \text{portion_of_fish}_{ijkl}) \\
+ (1|\text{FAO_region}_{ijkl}) + (1|\text{method_of_detection}_{ijkl}) \\
+ (1|\text{manuscript_ID}_{ijkl}).
\]

where the response variable \(x_{ijkl}\) represents a measurement of parasite abundance from the \(i\)th study in the \(j\)th location at the \(k\)th time in the \(l\)th host species.

We were also interested in testing which fish species, geographic regions, detection techniques, and portions of host examined drove the patterns observed in the above meta-regression, so we performed four subanalyses. First, we sequentially excluded each host species and reran the model. We extracted an updated estimate of change over time and compared the estimate for the effect of time to that of the full model, which included all host species. This allowed us to determine whether a single host species was driving the patterns we observed. We then performed the same analysis, but instead sequentially excluded each geographic region to determine whether a single geographic region was driving the patterns we observed. To test the influence of detection technique, we excluded studies that used techniques that came into common usage over the study period: digestion of fish tissues with acids and use of UV light.
for parasite detection. We sequentially excluded (a) all studies that used digestion, including digestion combined with other techniques, like microscopy and (b) all studies that used UV, including UV combined with other techniques. We then extracted an updated estimate of change over time and compared the estimate for the effect of time to the full model that included all detection techniques.

Finally, to test the influence of the portion of host examined, we sequentially excluded all studies that quantified anisakid burden in the (a) alimentary tract, (b) fillet, (c) viscera, and (d) whole body. We then extracted an updated estimate of change over time and compared the estimate for the effect of time to the full model that included all categories of portion of host examined.

3 | RESULTS

We obtained 755 unique host–parasite–location–year combinations (i.e., data points; *Anisakis* spp. *n* = 526, *Pseudoterranova* spp. *n* = 229) across 123 papers, 215 host species, 53 years, and four oceans. A total of 56,778 fish were examined across all studies, resulting in enumeration of 446,615 anisakid nematodes. For *Anisakis* spp., data were obtained across 15 FAO regions and 182 host species (Figure 2a); 31 data points were obtained by standard visual assessment/candling, 25 by standard visual assessment/candling plus microscopy, 69 by digestion, 13 by digestion plus microscopy, eight by digestion plus UV, 363 by microscopy, 10 by microscopy plus UV, and seven by UV. For *Pseudoterranova* spp., data were obtained across nine FAO regions and 92 host species (Figure 2b); seven data points were obtained by standard visual assessment/candling, nine by standard visual assessment/candling plus microscopy, four by digestion plus microscopy, 206 by microscopy, and three by microscopy plus UV.

In our meta-regression models, we detected an increase through time (all estimates = regression coefficients for the effect of time on fourth-root transformed anisakid abundance, from a model that controls for host length; estimate = +0.0206, *SE* = 0.0069, *z* = +2.9922, *n* = 526, *p* = 0.0028) in abundance of *Anisakis* spp. (Table 1a; Figure 3a) and no change (estimate = −0.0019, *SE* = 0.0093, *z* = −0.2063, *n* = 229, *p* = .8366) in abundance of *Pseudoterranova* spp. (Table 1b; Figure 3b). For *Anisakis* spp., we detected a 283-fold increase in abundance across the standardized time period of 1978–2015. Change in abundance over this time frame is measurable for both anisakid genera; thus, constraining our effect estimates to this period allows for fair comparison of results between anisakid genera.

In terms of fish length-corrected modeled abundance, we observed an increase from an average of less than 1 anisakid per 100 hosts examined (mean = 0.0037, 95% CI = 0.0017–0.0062) to more than 1 anisakid in every host examined (mean = 1.0356, 95% CI = 0.1273–4.0681) over the time period for which we have data from both parasite genera (1978–2015).

We evaluated the influence of high-leverage data points, as well as the influence of host species, geographic region, and detection technique on these trends. For the *Anisakis* spp. analysis, the record from 1962 was a temporal outlier, but did not qualitatively alter our results (with the 1962 record, the effect of time is +0.0206 with a standard error of 0.0069, *p* = .0028; when the record from 1962 is excluded, the effect of time is +0.0222 with a standard error of 0.0070, *p* = .0017). Sequentially removing single host species from our model did not change our results either, as the effect of time was always significantly positive for *Anisakis* spp. (Figure S1). Despite not changing the overall temporal patterns, the host species that leveraged the largest absolute change to the temporal effect size for *Anisakis* spp. was the black scabbardfish, *Aphanopus carbo*; the exclusion of this species nonsignificantly decreased the effect of time (without *A. carbo*, the effect of time is +0.0169 with a standard error of 0.0068, *p* = .0132). Sequentially removing individual geographic regions from our model also did not substantially change our conclusions. The effect of time for *Anisakis* spp. was always significantly positive, except when we excluded FAO region 27 (northeastern Atlantic), which resulted in the effect becoming marginally significant (without region 27, the effect

| Table 1 | Regression coefficients from meta-regression of fourth-root transformed parasite abundance for (a) *Anisakis* spp. and (b) *Pseudoterranova* spp. Year of collection and host length are included as moderators in the meta-regression model. We also included host species, portion of the host examined nested in host species, FAO major fishing area (to account for geographic clustering of points), method for detecting parasites, and paper ID as random effects. Models were run using the *rma.mv()* function of the package metafor (Viechtbauer, 2010). We calculated pseudo-$R^2$ for each model as the amount of variability captured by the full model (including moderators year of collection and host length + random effects) that was not captured by the null model (including only random effects). Pseudo-$R^2$ = .14 for the *Anisakis* spp. model and .00 for the *Pseudoterranova* spp. model |
|-------------------------------|------------------------------|-------------------------------|-------------------|------------------|------------------|------------------|
| (a) *Anisakis* spp.           | Estimate                     | SE                            | *z*-value         | *p*-value        | CI lower         | CI upper         |
| Intercept                     | −40.5379                     | 13.7751                       | −2.9428           | .0033            | −67.5366         | −13.5392         |
| Year                          | 0.0206                       | 0.0069                        | 2.9922            | .0028            | 0.0071           | 0.0341           |
| Host_length                   | 0.0127                       | 0.0021                        | 6.1656            | <.0001           | 0.0087           | 0.0168           |
| (b) *Pseudoterranova* spp.   | Estimate                     | SE                            | *z*-value         | *p*-value        | CI lower         | CI upper         |
| Intercept                     | 4.4327                       | 18.5596                       | 0.2388            | .8112            | −31.9435         | 40.8089          |
| Year                          | −0.0019                      | 0.0093                        | −0.2063           | .8366            | −0.0202          | 0.0163           |
| Host_length                   | 0.0048                       | 0.0048                        | 0.9926            | .3209            | −0.0047          | 0.0142           |
of time is +0.0140 with a standard error of 0.0072 and $p = .0503$; Figure S2). FAO region 27 encompassed a substantial proportion of the data in our Anisakis spp. dataset (123 data points of 526), but was only the second most data-rich FAO region in our dataset (Figure S2). For Pseudoterranova spp., we detected no change in abundance between 1978 and 2015, and sequential exclusion of individual species (Figure S3) and geographic regions (Figure S2) did not alter this finding. Finally, we also explored the potential influence of changing detection techniques on the change in anisakid burden over time. Neither the exclusion of studies using digestion as a technique for anisakid detection (without digestion, the effect of time is +0.0202 with a standard error of 0.0078, $p = .0097$) nor the exclusion of studies using UV light (without UV, the effect of time is +0.0175 with a standard error of 0.0068, $p = .0107$) eliminated the significant, positive trend over time for Anisakis spp. Similarly, neither the exclusion of studies using digestion (without digestion, the effect of time is –0.0045 with a standard error of 0.0090, $p = .6164$) nor the exclusion of studies using UV light (without UV, the effect of time is –0.0015 with a standard error of 0.0097, $p = .8800$) shifted the trend over time for Pseudoterranova spp. from nonsignificant to significant.

4 | DISCUSSION

From our analysis of 123 manuscripts and 755 data points summarizing 56,778 fish and 446,615 anisakid nematodes over almost four decades, we found a long-term increase in the abundance of Anisakis spp. and no long-term change in the abundance of Pseudoterranova spp. This finding implies a rising risk of anisakidosis for humans and cetaceans, and an unchanging risk of anisakidosis for pinnipeds; it also suggests that the profitability and sustainability of fisheries could be compromised by the rising rates of Anisakis spp. infection.

On average, we estimated that Anisakis spp. abundance increased from less than 1 anisakid per 100 hosts in 1978 to more than 1 anisakid in every host examined in 2015. This pattern was not driven by any single host species. The host that had the largest influence on the temporal increase in Anisakis abundance was the black scabbardfish (A. carbo), but the influence of this one species did not drive the temporal pattern observed across all hosts (Figure S1). One FAO region did appear to influence the outcome of our results; exclusion of data points from FAO Region 27 (northeastern Atlantic) caused the change over time in Anisakis spp. abundance to become marginally nonsignificant ($p = .0503$). In short, the increase in Anisakis spp. abundance across the time frame of our study appears to be robust across host species, but the positive temporal trend we reveal here was strongly driven by the northeastern Atlantic.

The northeastern Atlantic FAO region encompasses the Barents, Norwegian, Baltic, North, and Irish Seas and represents a major source of the data points on Anisakis spp. included in this study ($n = 123$ out of 526, the second most well-represented region in the study, after FAO region 37, the Mediterranean, and Black Seas). It is possible that temporal increases in anisakid burden are likelier
to be detected where data are ample. It is also possible that recent increases in cetacean populations have been especially influential in the northeastern Atlantic. This region is dominated by *Anisakis* simplex sensu stricto, whose definitive hosts include minke whales (*Balaenoptera acutorostrata*), common dolphins (*Delphinus delphis*), long-finned pilot whales (*Globicephala melas*), white-beaked dolphins (*Lagenorhynchus albirostris*), killer whales (*Orcinus orca*), and striped dolphins (*Stenella coeruleoalba*; Bilksa-Zajac et al., 2015; Mattiucci et al., 2014, 2018; Pierce et al., 2018). Some of these cetacean species have increased in abundance since International Whaling Commission regulations came into effect in the mid-1980s (e.g., Hammond et al., 2013; Murphy, Pinn, & Jepson, 2013; Skaug, Oien, & Bothun, 2004). Other world regions have probably also experienced increases in marine mammal abundance due to legislative or regulatory protections enacted within the timeframe of our study, but the northeastern Atlantic has a particularly long history of intense exploitation of marine mammals (Clapham & Link, 2006). Relaxation of this pressure might therefore have produced an especially robust increase over time in *Anisakis* spp. Although the increase over time that we detected was strongly influenced by this region, the positive relationship between time and *Anisakis* burden remained marginally significant (\(p = .0503\)) when data points from the northeastern Atlantic region were excluded, suggesting that this temporal increase is not a phenomenon unique to that region.

In contrast, we did not detect a similar increase over time in the abundance of *Pseudoterranova* spp. Because it is ecologically similar to *Anisakis* spp. and subject to many of the same long-term environmental changes (e.g., climate change), we expected to observe similar patterns between the two genera. Finding no significant change in *Pseudoterranova* spp. could indicate either that this genus is unaffected by the changes experienced by ocean ecosystems over the past few decades, or that the factors determining its abundance are responding to global ocean change antagonistically, such that any gain in abundance (e.g., from increases in pinniped populations), is counteracted by a negative effect on abundance (e.g., decreases in larval parasite survival with increasing temperatures). Excluding individual host species, geographic regions, and detection techniques did not alter the estimate of the change over time for the abundance of *Pseudoterranova* spp.

The fact that we observed different temporal patterns between the *Anisakis* and *Pseudoterranova* genera gives us some confidence that these patterns are not driven exclusively by literature bias. All meta-analyses are susceptible to literature bias (Borenstein, Hedges, Higgins, & Rothstein, 2009), and we envisioned that improvements in anisakid detection capacity, increasing interest in anisakids as a research subject, or an increase in "file-drawer" bias over time could generate artifactual temporal increases in anisakids. However, any of these sources of literature bias should apply roughly equally to both *Anisakis* spp. and *Pseudoterranova* spp. To observe a dramatic increase in one genus and no change in the other suggests that literature bias is not entirely responsible for the temporal change observed, and that the increase in *Anisakis* spp. is therefore likely to reflect an actual temporal change in nature. There are some differences between *Anisakis* spp. and *Pseudoterranova* spp. that might make data on one genus more susceptible to literature bias than data on the other. For example, the two genera are morphologically similar (Hurst, 1984), but *Anisakis* spp. might be slightly more challenging to detect than *Pseudoterranova* spp., given that *Anisakis* spp. larvae tend to be small and translucent while *Pseudoterranova* spp. larvae are large and dark in color (Measures, 2014; Smith & Wootten, 1978). If detection techniques have improved over time, this could lead to an apparent increase in abundance for *Anisakis* spp. and little change for *Pseudoterranova* spp. However, we explored the influence of detection technique on our results, and our findings show that no one detection technique drove the change over time in *Anisakis* spp. burden. Additionally, we anticipated that, because both *Anisakis* spp. and *Pseudoterranova* spp. pose threats to human health, there would be roughly equal incentives for scientific study of the two genera (Buchmann & Mehrdana, 2016). However, because *Anisakis* spp. tends to be more pathogenic in human host than is *Pseudoterranova* spp., it might be the case that there is more incentive for the study of *Anisakis* spp., and this could drive an increasing number of reports over time of high *Anisakis* spp. burdens. We are unable to test this hypothesis with our current dataset, but we encourage others to ground-truth the patterns we document here using, for example, estimates of parasite burden in fluid-preserved fishes held in natural history collections (Harmon, Littlewood, & Wood, 2019; Howard, Davis, Lippert, Quinn, & Wood, 2019) or long-term monitoring of *Anisakis* spp. burdens at individual sites.

Our study is correlational and precludes conclusions regarding causation, but we have developed two hypotheses that could simultaneously explain the dramatic increase in *Anisakis* spp. and the lack of change in *Pseudoterranova* spp. First, as complex life-cycle parasites, anisakids can respond to changes in the abundance of any intermediate host (copepod, krill, fish), paratenic host (fish, cephalopod), or definitive host (marine mammal; Arneberg et al., 1998). We do not know which host is the most important determinant of anisakid abundance (i.e., which host serves as the life-cycle bottleneck; sensu Lafferty, 2012), but we do know that several anisakid hosts have changed in abundance over the past half-century. Since 1972, all marine mammals have been protected in the United States under the Marine Mammal Protection Act and many countries adhere to the moratorium on commercial whaling imposed by the International Whaling Commission in 1982. This protection has allowed for the recovery of many cetacean and pinniped populations (Magera, Fleming, Kachner, Christensen, & Lotze, 2013). Marine mammal-driven increases in anisakids have been observed at small spatial scales; for example, fish collected near seal haul-out sites have been found to harbor a greater number of *Pseudoterranova* spp. than fish collected near non-haul-out sites (Jensen & Idas, 1992; Marcogliese & McClelland, 1991). As many marine mammal populations recover their former abundance, the increased number of definitive hosts could support larger parasite populations. One of the biggest differences between *Anisakis* spp. and *Pseudoterranova* spp. concerns their use of cetaceans and pinnipeds as definitive hosts, respectively (Figure 1b,c). Perhaps it is the case that definitive mammalian hosts are an important life-cycle bottleneck for *Anisakis* spp.
only, and that increases in cetacean populations have alleviated a bottleneck for Anisakis spp., whereas increases in pinniped populations have not done the same for Pseudoterranova spp. While this may be perceived as a recent increase in anisakid abundance, our data cover only the period of time since the enforcement of the Marine Mammal Protection Act in 1972, and thus the increase we observe in Anisakis spp. abundance could be a return to the historical anisakid abundance levels present before exploitation-driven declines in marine mammal abundance. Second, it is possible that, because Anisakis spp. marine mammal hosts (i.e., cetaceans) tend to be vagile and migratory and Pseudoterranova spp. marine mammal hosts (i.e., pinnipeds) tend to remain within a limited home range, it may be easier to detect broad-scale change in the abundance of Anisakis spp. than in Pseudoterranova spp. Our meta-analysis was not geographically finely resolved (Figure 2b,c), and could have missed areas where Pseudoterranova spp. abundances are changing. Long-term monitoring of individual sites is the most direct way to detect temporal change in Pseudoterranova spp., if these changes are only detectable in the geographic areas where pinnipeds congregate (i.e., Jensen & Idas, 1992; Marcogliese & McClelland, 1991).

Other factors might also have driven the temporal increase in Anisakis spp., but it is not as clear how they would simultaneously leave the abundance of Pseudoterranova spp. unaffected. For example, as fisheries exploitation has increased over the past several decades, intermediate fish host density may be on the decline (Christensen et al., 2014). If fish hosts are not a transmission bottleneck (sensu Lafferty, 2012), and reduced fish density leads to a relaxation in competition for krill and an increase in the number of krill intermediate hosts consumed per fish, a reduction in fish density could actually result in an increase in the per-fish burden of anisakid parasites, as worms become more concentrated in the few remaining fish hosts. However, given that both Anisakis spp. and Pseudoterranova spp. are host generalists for their fish intermediate/paratenic hosts (Buchmann & Mehrdana, 2016), this would not explain the dramatic increase in one genus and the lack of temporal change in the other. Similarly, long-term climate change could also influence the abundance of anisakid nematodes, as increases in temperature can increase host susceptibility to infection by compromising the ability of fish hosts to immunologically or behaviorally resist infection (Burge et al., 2014; Harvell et al., 2002). Increasing temperatures can also facilitate faster growth and shorter generation times in aquatic parasites (Marcogliese, 2001a, 2001b). This could lead to increases in Anisakis spp. and not Pseudoterranova spp. if Anisakis spp. are able to capitalize on their hosts’ compromised immunity, while Pseudoterranova spp. are not, or if increasing temperature shortens the generation times of Anisakis spp. while leaving those of Pseudoterranova spp. unaffected. Finally, as agriculture and logging intensify, nutrients are released into coastal ecosystems (e.g., Cuo, Lettenmaier, Alberti, & Richey, 2009), which can fuel phytoplankton blooms (e.g., Beman, Arrigo, & Matson, 2005) that in turn increase the abundance of copepods and other zooplanktonic crustaceans (e.g., Siokou-Frangou & Papanastassiou, 1991; Uriarte & Villate, 2004). If crustacean first intermediate hosts are a life-cycle bottleneck for Anisakis spp. and not for Pseudoterranova spp., or if only the crustacean hosts to which Anisakis spp. is specific respond to nutrient pollution with increases in abundance, then this could lead to temporal increases in the abundance of Anisakis spp. and stasis for Pseudoterranova spp. However, if nutrient pollution is influential, one might expect it to drive a pattern opposite to the one actually observed: nutrient-driven increases in crustacean first intermediate hosts should benefit coastal anisakids (i.e., Pseudoterranova spp., which uses pinniped hosts and is associated with the host’s coastal habitat), rather than pelagic anisakids (i.e., Anisakis spp., which uses cetacean hosts and is associated with their pelagic habitat).

Whatever the drivers of the increase in anisakid abundance, such an increase could have substantial economic, ecological, and human health impacts on a global scale. First, increases in anisakid abundance could increase the risk of anisakidosis in people (Bao, Pierce, Pascual, et al., 2017). The more anisakid worms that are present in commercially exploited fish and invertebrates, the greater the likelihood that the resulting seafood meal contains a worm. While the symptoms of anisakidosis are rarely life-threatening, increased incidence of anisakidosis could increase hospitalizations, representing a burden on public health (Bourée et al., 1995). Occasionally, people exposed to anisakid worms will develop hypersensitivity to worm antigens, leading to severe anaphylactic reactions upon further anisakid exposures (Alonso, Daschner, & Moreno-Ancillo, 1997; Audicana et al., 2002; Audicana & Kennedy, 2008; Daschner et al., 2000; del Pozo et al., 1996). These allergic reactions can be initiated by both live and dead worms (Alonso et al., 1997; Audicana et al., 2002; Audicana & Kennedy, 2008; Daschner et al., 2000) and even through nonconsumptive exposure, as in fishermen and fish-processing workers (Armentia et al., 1998; Nieuwenhuizen et al., 2006; Purello-D’Ambrosio et al., 2000; Scala et al., 2001). Allergies to anisakids are regularly misdiagnosed as allergies to fish or shellfish (Acha & Szyfres, 2003; del Pozo et al., 1996) and, in some regions, anisakid allergy may be more common than true seafood allergy (Kimura, 2001). Such severe anaphylactic reactions are a grave and growing concern, given the increasing abundance of Anisakis spp. worms in commercially exploited marine fish species that we reveal here.

In addition to the threat they present to public health, anisakids can also cause disease in their definitive marine mammal hosts. Anisakids are commonly found in necropsied marine mammals, including species that are endangered (Dailey & Stroud, 1978; Gibson et al., 1998). The presence of anisakids in marine mammals can cause gastric obstruction, ulceration, and, in some cases, death (Geraci & St. Aubin, 1987; Spraker, Lyons, Tolliver, & Bair, 2003; Young & Lowe, 1969). These worms also divert energy that would otherwise be used for host survival, growth, and reproduction (Dailey & Stroud, 1978); for example, intestinal parasites (including anisakids) may be hampering the recovery of endangered populations of killer whales (Krahm et al., 2002). Anisakid infections have also been empirically linked to a mass mortality of sea otters in Cordova, Alaska (Ballachey, Gorbics, & Doroff, 2002). Although our study suggests that pinnipeds are not at risk of increasing rates of anisakidosis (because the abundance of Pseudoterranova spp. remained unchanged throughout the time period
of our study), cetaceans now face a 283-fold greater risk of contracting Anisakis spp. from consuming the fishes assessed in our meta-analysis, and this risk could be an important threat to the population viability of these vulnerable and—in some cases—endangered species.

Finally, anisakids present a threat to the health of their fish intermediate hosts and associated fisheries. In Atlantic salmon (Salmo salar), red vent syndrome—which causes fish vents to become red, swollen, hemorrhaging, and prolapsed—is attributed to *A. simplex* infection (Beck et al., 2008; Noguera et al., 2009), and can in some cases lead to fatal opportunistic secondary infection by pathogenic bacteria (Beck et al., 2008). Stomach crater syndrome in Atlantic cod (Gadus morhua)—which causes damage to the stomach wall and mucosa—is also attributed to *A. simplex* (Levens & Berland, 2012). Anisakids reduce swimming efficiency of fish when encysted in the musculature (Sprengal & Luchtenberg, 1991), reducing survival by increasing the likelihood that the fish will be consumed a predator (Persson, 1991). Anisakids also have the potential to alter public perceptions of seafood safety (Karl, 2008), reducing the market value of a vast number of commercially fished species (Bao, Pierce, Strachan, et al., 2017). For example, in 1987 German news broadcasters displayed a video of living anisakids nematodes emerging from a filet of fish, driving an immediate 80% drop in seafood sales and loss of fishery-based jobs in Germany (Karl, 2008). In Atlantic Canada, anisakid-related downgrading and discard has been estimated to cost processors US$26.6–50 million annually (McClelland, 2002). For Pacific cod (*Gadus macrocephalus*), it is estimated that monitoring and detection of anisakids constitutes up to 50% of production costs (Choudhury & Bublitz, 1994). In Spain, a majority of consumers are willing to pay more for fish that is guaranteed to be free of anisakids (Bao, Pierce, Strachan, et al., 2017). Rising abundances of *Anisakis* spp. therefore threaten the viability of fish populations and the profitability of the fisheries that depend upon them.

Like all meta-analyses, our study is limited in its temporal scope by the available literature. We used the database ISI Web of Science to survey peer-reviewed publications, and found that the available literature is heavily weighted to the past 50 years (Figure S4). This constrains meta-analyses to near history (~1960s to present), by which time the oceans had already been drastically altered by human activity (Lotze et al., 2006). This limitation prevents meta-analyses from characterizing ocean ecosystems as they were before they were impacted by fishing, pollution, and climate change (Jackson, 2001; Jackson et al., 2001). This lack of an appropriate “baseline” should be acknowledged alongside the results presented here. While we did detect an increase in Anisakis spp. over the past several decades, does this increase represent a rise in infection, or a recovery of anisakids to some pre-impact baseline? In other words, are anisakid abundances increasing in response to human impacts on the environment (e.g., fishing, pollution, climate change), or are they recovering alongside their exploited marine mammal hosts? Our data cannot discriminate among these possibilities, but parasitological analysis of natural history collections (Harmon et al., 2019; Howard et al., 2019) could reveal trajectories of anisakid changes over the past century or more, illuminating patterns across a broader span of time. Finally, another weakness of meta-analytic studies of relatively short temporal duration is their inability to capture short-term or small spatial-scale fluctuations in the response variable of interest. For example, empirical studies in the Gulf of St. Lawrence, Canada document an increase in *Pseudoterranova decipiens* from 1981 to 1990, followed by a precipitous decline from 1990 to 1992; abundances of *A. simplex* remained stable during this time period (Boily & Marcogliese, 1995; Marcogliese, 2001a, 2001b; McClelland & Martell, 2001). While the long-term increase was attributed to increases in gray seal (*Halichoerus grypus*) populations, the short-term decline was attributed to declining water temperatures between 1986 and 1994, which might have inhibited the development and hatching of *P. decipiens* eggs (Boily & Marcogliese, 1995; Marcogliese, 2001a, 2001b; McClelland & Martell, 2001). This vignette highlights that the temporal window selected for a meta-analytic study can strongly influence the perception of whether anisakid burdens are increasing or decreasing, and suggests that the long-term increase in anisakid burden documented here could be reversed if conditions change.

Although disease ecologists suspect a long-term increase in the frequency and severity of infectious disease outbreaks due to ongoing global change, few sources of data exist to test this hypothesis. The meta-analysis we conducted yielded temporally resolved, long-term data on the abundance of two ecologically and economically important parasites, and revealed a long-term increase in the abundance of *Anisakis* spp. and long-term stasis in the abundance of *Pseudoterranova* spp. However, this is the story of only two parasite species among millions that are extant, and we encourage others to use historical ecology approaches (e.g., meta-analysis, parasitological dissection of museum specimens) to track change across a diversity of marine parasite species. Only then will we have the data to indicate whether contemporary oceans are facing a “rising tide” of marine disease.

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**DATA AVAILABILITY STATEMENT**

The data that support the findings of this study are openly available in the Dryad Digital Repository at https://doi.org/10.5061/dryad.kwh70rz0z. The code used to produce the statistical results reported herein is openly available via GitHub at www.github.com/wood-lab/Fiorenza_et_al_2020_GCB.

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**REFERENCES**


**SUPPORTING INFORMATION**

Additional supporting information may be found online in the Supporting Information section.

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