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Review

Seafood-Borne Parasitic Diseases: A "One-Health" Approach Is Needed

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Abstract: Global consumption of seafood is steadily increasing, as is the variety of seafood, including dishes with raw or undercooked fish, leading to an increased risk of seafood-borne parasitic diseases. To address today's challenges to understand the biology and ecology of these parasites in an ever-changing environment and to tackle their pathogenicity, multidisciplinary research is needed. In addition, the gap between research and stakeholders must be bridged to decrease the risk these parasites pose to public health. A "One-Health" approach to research is necessary to ensure that consumers, aquatic animals, and environmental health questions are assessed in an integrated and holistic manner, resulting in a more comprehensive understanding of the issues associated with seafood-borne parasitic diseases and potential solutions. However, when it comes to seafood-borne parasitic diseases, there is limited guidance available for a "One-Health" approach since these diseases can be less known. In this article, the focus is on parasitic diseases caused by seafood, which have been less studied even in some developed countries where seafood is popular. A brief overview of some of the seafood-borne parasitic diseases is provided followed by the significance of the awareness among various stakeholders in a country. In this article, it is argued that researchers and stakeholders are closely connected and a knowledge gap in one can result in a gap in knowledge and awareness in the other, causing an inability to accurately estimate the issues caused by these parasites. It is suggested that raising awareness, supporting research and training of all stakeholders are crucial for the prevention of seafood-borne parasitic diseases and the protection of the health of seafood consumers.

Keywords: Anisakidae; diagnosis; stakeholders; fishes

1. Introduction

Seafood is the primary source of protein for over a billion people and is the source of over a quarter of the world's total animal protein [1]. There is an increasing body of medical research suggesting a positive correlation between red meat consumption and potentially fatal conditions such as cancer and cardiovascular diseases, while showing the health benefits of seafood [2]. Therefore, along with the rise in the world's population, the demand for seafood continues to increase at a higher rate than other foods [3]. Indeed, the global fishery and aquaculture sectors have shown sustained growth in overall production and consumption [4]. Although seafood is part of a healthy diet, as with any other food, seafood consumption is not risk-free [5, 6]. Consumption of seafood contaminated with toxins or infectious agents can cause illnesses ranging from mild gastroenteritis to life-threatening syndromes. Seafood is responsible for a significant portion of food-borne illness worldwide [7]. This article focuses on seafood-borne parasitic diseases with the view that in the light of increased popularity of seafood as well as dramatic environmental changes (both natural and anthropogenic), they are as important in developed countries as they are in developing countries.

There is a view that developed countries usually have stricter environmental and food safety standards which apply to both aquaculture and wild capture products to ensure fish grown in their waters are safe to eat. However, rapid population growth, immigration, widespread international travel and trade, and climate change may adversely affect the current status of food safety in these countries. In addition, there is also a view that parasitic diseases are associated with poverty [8] and they may not be as significant in developed countries. This in turn may have led to a shift of the direction of the research funding away from parasitic diseases in developed countries [9], a decline in relevant expertise [10] and massive reforms in teaching parasitology related topics in their educational sectors [11], providing opportunity for parasitic diseases to emerge.

In this article, it is argued that researchers and stakeholders are connected and that a knowledge gap in one can result in a knowledge gap and lack of awareness in the other, leading to an inability to accurately estimate the issues caused by these parasites. It is suggested that raising awareness, supporting research, and the training of all stakeholders are crucial for prevention of seafood-borne parasitic diseases. The word 'seafood' in this context encompasses fish and shellfish products from marine and freshwater ecosystems that directly or indirectly (as feed) are meant for human consumption (https://www.britannica.com/topic/seafood).

2. Seafood-Borne Parasitic Diseases

Seafood-associated infections are caused by a variety of viruses, bacteria, and parasites resulting in a wide variety of clinical syndromes, with diseases caused by parasites being significantly understudied compared to other infectious agents. To date, over 40 species of parasites associated with seafood, including protozoa, cnidarians, tapeworms, flukes, round worms, and thorny-headed worms, have been reported in humans (Table 1). With steady change in the climate this number is expected to increase. Some parasites listed in Table 1, e.g., *Giardia, Toxoplasma, Clinostomum*, and *Anisakis* have global distribution. While some parasites, such as *Corynosoma*, have rarely been reported in humans, infection with other parasites, such as Anisakids is observed on a regular basis worldwide. As Table 1 shows seafood-borne parasites are highly diverse group of organisms, ranging from protozoa to acanthocephalans, therefore not only is their morphology highly diverse, their life cycle, transmission pattern, migratory pattern in/on the host and clinical signs also show great variation. Dealing with detailed life cycle and host range of these parasites is beyond the scope of this article. A summary of pathogenicity associated with some of the parasites, and novel aspects related to their emergence as a cause of seafood-borne parasitic disease is provided below.

Table 1. List of the genera of seafood-borne parasites reported from humans.

Protozoa	Cnidaria	Cestoda (Tapeworms)	Trematoda (Flukes)	Nematoda (Round Worms)	Acanthocephala (Thorny-Headed Worms)
Cryptospoidium	*Kudoa*	*Adenocephalus*	*Appophalus*	*Angiostrongylus*	*Corynosoma*
Enterocytozoon	*Myxobolus*	*Diphyllobothrium*	*Centrocestus*	*Anisakis*	*Bolbosoma*
Giardia	*Toxoplasma*	*Diplogonoporus*	*Clinostomum*	*Capillaria*	
	Unicapsula	*Ligula*	*Clonorchis*	*Contracaecum*	
		Spirometra	*Cryptocotyle*	*Dioctophyma*	
			Diplostomum	*Echinocephalus*	
			Echinostoma	*Eustrongyloides*	
			Haplorchis	*Filaria*	
			Heterophyes	*Gnathostoma*	
			Heterophyopsis	*Hysterothylaccium*	
			Metorchis	*Philometra*	
			Metagonimus	*Pseudoterranova*	
			Nanophyetus		
			Opisthorchis		
			Phagicola		
			Procerovum		
			Paragonimus		
			Prohemistomum		
			Pygidiopsis		
			Schistosoma		
			Stellantchasmus		

Stictodora

2.1. Protozoa

Of protozoa listed in Table 1 *Giardia* and *Toxoplasma* have been known to cause disease in humans for a long time; however identification of seafood origins for diseases caused by them is recent. *Giardia duodenalis* have been isolated from dolphins, sharks, and farmed and wild fish in Western Australia, implying that fish may act not only as a reservoir for waterborne giardiasis but may also present a source of infection for food-borne giardiasis and a public health risk to fish processing workers or recreational fishermen [12]. There have been several reports of human infection with *Cryptosporidium.* However, there is no report of seafood being directly involved with zoonotic transmission of cryptosporidiosis. Zoonotic strains of *Cryptosporidium* have been isolated from marine fish in Australia [13] which would have to implicate seafood as a potential source of risk of this disease to fisherman, fish processing workers, and consumers.

2.2. Cnidaria

Several species of *Myxobolus*, *Kudoa* and *Unicapsula* have been reported in several fish [14-17] and there are several cases of human infections worldwide, including in Australia, Canada, and Columbia. These parasites cause infection-associated diarrhea due to intestinal invasion. Very little is known about the prevalence, genetic diversity and effect of these parasites in marine environments and the role that marine animals play in transmission of these parasites to humans.

2.3. Cestoda

Some tapeworms or Cestoda such as *Diphyllobothrium* spp. are common parasites in seafood that have been known to infect humans for centuries. They have mainly been recorded in Scandinavia, western Russia, and the Baltics, but are also present in other parts of the world such as North America, especially the Pacific Northwest. Since these tapeworms become adult in humans, human infection becomes important from a different aspect. An adult tapeworm, such as *Diphyllobothrium* can produce up to 1,000,000 eggs per day per worm and therefore an infected human can play an important role in transferring the parasite to new geographical areas. For example in Australia, a country that has been a popular destination for immigrants from around the world for over a century, Diphyllobothriasis and Sparganosis (caused by broad tapeworms belonging to the genera *Diphyllobothrium* and *Spirometra*) have been reported among immigrants from Syria, East Timor, Estonia, Finland and Ireland [18, 19] and then later in locals who never left the country [20]. These tapeworms are involved with freshwater systems and human infection occurs by the ingestion of raw or undercooked flesh of infected freshwater fish, as well as infected snakes and frogs and drinking untreated water containing infected Copepoda. In case of *Spirometra* it has been shown that larvae may infect humans by penetrating intact human skin [20]. These parasites have low host specificity in both adult and larval stages and concerns have previously been raised [18] that they could easily become established in this country.

In addition to the above cases caused by known species of tapeworms, there are emerging cases of human infection by new species. For example, in 2015, a young boy with a history of raw fish consumption from the Eyre Peninsula in South Australia was diagnosed being infected with the pacific broad tapeworm, *Adenocephalus pacificus* [21], a new species of tape worm.

2.4. Trematoda

Similar to tapeworms, human infection with Trematodes or flukes also usually occurs after consuming raw or undercooked infected freshwater fish or shellfish. As can be seen in Table 1 flukes are the most diverse group of seafood-borne parasites, and can be grouped into lung, liver, and intestinal flukes.

Paragonimiasis is caused by adult lung flukes of the genus *Paragonimus*. The disease occurs after ingestion of raw, pickled, or undercooked infected freshwater crabs and crayfish. Symptoms include chronic cough with intermittent rusty brown or blood-stained sputum production which may mimic pulmonary tuberculosis. The parasite may migrate to central nervous system causing symptoms such as visual impairment and meningitis. Although it is known to be an endemic disease in Asian countries, it has now been reported elsewhere for example in Australia where the disease has been reported in immigrants from Laos [22, 23].

Aquatic liver flukes belonging to genera *Clonorchis*, *Opisthorchis* and *Metorchis* are also the most prevalent human Trematodes endemic in south-eastern Asian countries that have been spread to new countries. They are considered to be a serious public health issue in several countries (e.g., China, Spain, Italy, Canada and USA) with 200 million people at constant risk and an estimated 17 million people infected worldwide [7]. These parasites are classified as biological carcinogen, causing cancer in the liver and bile duct. Human infection with these parasites (*Clonorchis* and *Opisthorchis*) has been reported in Australia [24-26]. In the United State of America, over the past 15 years, 845 out of about 1.4 million Vietnam-era veterans have been diagnosed with hepatic duct or biliary duct cancer or cholangiocarcinoma. Although some argue that this is not indicative of Vietnam veterans to being greater risk, a large-scale epidemiologic study in progress to investigate any link between liver fluke exposure and cholangiocarcinoma risk (http://www.usmedicine.com/clinical-topics/oncology/va-launches-study-to-address-liver-fluke-bile-duct-cancer-concerns/).

Intestinal flukes can also be a major seafood safety issue. Pathogenicity of aquatic intestinal flukes (mostly belonging to the family Heterophyidae) is associated with the heart, brain, and spinal cord of humans and can be fatal [7]. Among the aquatic intestinal flukes, *Metagonimus* and *Heterophyes* are the most important in terms of the abundance of human cases worldwide. One of the new areas for the parasite is Australia where members of Heterophyidae flukes have been reported in fish, turtle [27, 28] and ornamental fish imported to the country [29]. Although many of these parasites are not endemic to Australia, disease caused by them may occur in any region through imported products. Another risk occurs when infected people travel or migrate to other countries. These parasites become adult in humans and can produce many eggs daily which can enter the environment through faeces. Several of the abovementioned countries are among major suppliers of Australian imported seafood. Australia is also both a popular tourist destination and a country of residence for people from these countries.

2.5. Nematoda

Several genera of aquatic nematoda from a diverse taxonomic group can cause disease in humans. One is anisakidosis, a disease caused by the larvae of several genera and species of Anisakid nematodes, including *Anisakis* spp, *Pseudoterranova* spp, and *Contracaecum* spp. Although *Hysterothylacium* spp are no longer classified under the family Anisakidae, in the literature the disease caused by them is still referred to as anisakidosis. Unlike tapeworms and flukes mentioned above, in anisakidosis, the human is usually infected with larval stages of the parasite and therefore infected humans are a dead-end for these parasites that do not play any role in geographical transportation of the parasites. Apart from anecdotal reports, the only published report of a female gravid adult anisakidosis is due to *Hysterothylacium* in Japan [30]. The disease is usually associated with consumption of raw or undercooked fish such as sushi, sashimi, and pickled, salted, marinated, or smoked fish as these processes do not kill Anisakid larvae. Infection of seafood with these parasites is very significant because even in properly cooked fish where all the larvae are dead, allergic reaction can occur due to heat-resistant molecules in parasites' body [31]. Although reports of the parasite in animal hosts date back centuries, the first human case was reported in 1960 [32] and since then the number of human cases has risen sharply, making it a significant emerging zoonotic disease of humans globally. With low specificity of the parasite for its fish hosts, along with increased popularity and demand for seafood, worldwide the disease has been reported from many countries with prospects of being increasingly reported more in the future. It is also estimated that the number of human cases are significantly higher than reported due to high levels of misdiagnosis since the symptoms are vague (e.g., diarrhea, vomiting, abdominal pain), and mimic food poisoning or other gastrointestinal diseases [9, 33, 34].

Gnathostomiasis is another disease caused by several species of the nematode belonging to the genus *Gnathostoma*. Currently diagnosis is based on a serological test developed in Thailand which has not been tested for cross reactivity with a closely related genus of Gnathostomatid nematodes, *Echinocephalus*. The latter occurs in fish and shellfish, therefore, diagnosis of some human cases of Gnathostomiasis have been questioned [9]. Gnathostomatid nematodes cause symptoms due to movement of parasites in the body of infected people starting with fever, lack of appetite, nausea, vomiting, diarrhea, or abdominal pain, followed by a later phase with symptoms such as swellings under the skin that may be painful, red, or itchy due to the parasite reaching the skin after being ingested. The swelling can occur 10 to 30 days after ingestion of the parasite and may last several weeks at a time. Occasionally parasite may enter other parts of the body, including the lungs, bladder, eyes, ears, and nervous system, including the brain causing more severe symptoms.

Capillariasis is another disease caused by aquatic nematoda, mainly *C. philippinensis*. When humans are infected, eggs produced by female *Capillaria* nematodes can embryonate in the intestine and release larvae than can cause autoinfection and result in large numbers of worms or hyperinfection. Human fecal contamination of water is also a source of infection of freshwater fish [35]. Capillariasis is characterized by disturbances in gastrointestinal function which increases in severity as worm population increases with autoinfection. Initial diarrhea and vomiting can progress to a chronic malabsorption syndrome, characterized by weight loss, cachexia, and signs of hypoproteinemia such as lower limb edema, ascites, and pleural effusion. The disease can be fatal due to severe electrolyte imbalance and secondary bacterial infection [36].

Capillariasis can be diagnosed through examination of faeces for presence of eggs but it has been found that due to intermittent egg shedding by female adult worms, several examinations over time were required for a definitive diagnosis. The development of molecular methods for identification will assist in more definitive and rapid diagnosis of capillariasis reducing the duration of illness suffered by affected individuals [37].

2.6. Acanthocephala

Species of acanthocephalans including species of *Bolbosoma* and *Corynosoma* which may have zoonotic potential have been found as juveniles (i.e., infective stage) in several edible fish in Australia [38] and other parts of the world, e.g, [39]. There is no reported case of human infection with these parasites reported in Australia but it has been reported in other countries for example in Japan [40].

3. Local-Global Interconnectedness

Due to significant increases in international seafood trade, human movements, and varieties of exotic raw or undercooked seafood, seafood safety is a global concern that cannot be seen in isolation and as a matter of importance for one country only. Unlike many other sources of parasitic diseases which are known to be associated with poverty and low income and are an issue in developing countries, seafood-borne parasites are a problem of both developing and developed countries, requiring efforts from all nations and many sectors.

3.1. Role of Stakeholders and Researchers in Seafood Safety

As reviewed in Section 2, there is a wide range of parasites found not only in seafood but also in consumers of seafood and transferred daily between continents as a result of advanced transport technologies for both food and humans. As a result, new and emerging seafood-borne diseases are on the rise. To keep the green and safe image for seafood and for the public to enjoy the full benefit of this healthy source of protein, effective communication and engagement of various stakeholders is crucial (Figure 1). The main factors that can adversely affect key elements of the seafood supply chain and seafood safety are reviewed below:

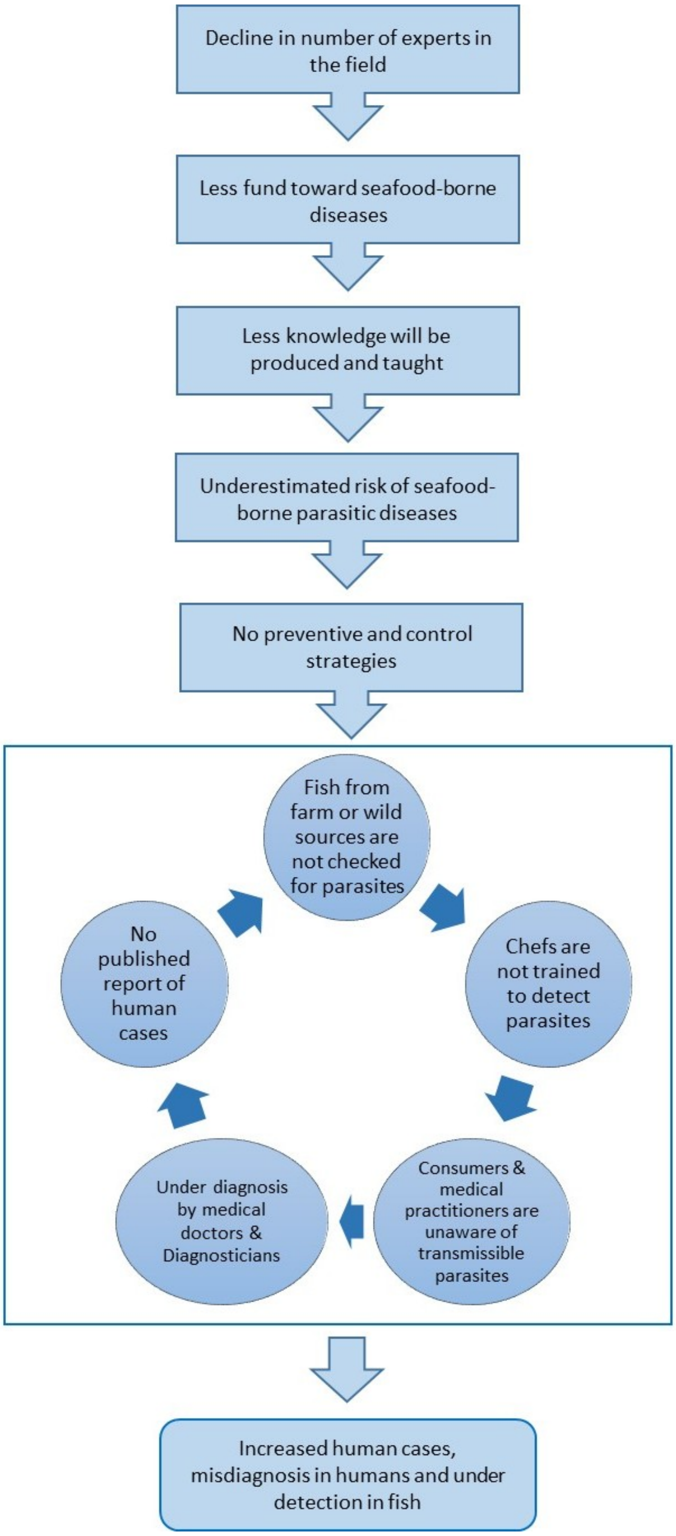

Figure 1. Diagrammatic view of the significance of the communications between various stakeholders in terms of being aware of seafood safety issues.

3.2. Fish Producers and Chefs and Cooks

Capture fisheries and aquaculture are the two main direct sources of seafood in most countries. Seafood in the market or restaurants may be locally produced or imported from other countries. A review of the literature shows that in some countries, some wild caught fish can be heavily infected with parasites while there are no such reports for many other countries [41–43]. Published reports of infection of farmed fish with zoonotic parasites are much fewer [44] which may be due to social concerns regarding the negative perception of these parasites by consumers which can result in rejection of fishery products and adversely influence consumers' confidence and business profit. Therefore the absence of published data on seafood-borne parasites does not preclude the possibility of the presence of these parasites in seafood in any country. Published literature on the awareness of fish producers of the presence of parasites both in wild catch fisheries and aquaculture is limited. Some countries such as Japan and the Netherlands have recommended policies to prevent transfer of these parasites. For example, the Netherlands recommend that the viscera of fish be discarded immediately after fish is caught. However in some other countries, including Australia, no such guidelines are considered necessary [45, 46]. After fish are caught or cropped, one of the next key elements in the supply chain are chefs and cooks whose knowledge is extremely important. Considering the increase in seafood consumption and popularity of eating raw or undercooked seafood globally, it is important for chefs to have a thorough knowledge of how to prepare seafood to minimize the risk of seafood-borne parasitic disease to consumers.

3.3. Consumers

In some developed countries, there is a considerable difference between the perceptions of the public and the authorities and their response to seafood-borne parasites compared to other food-borne parasites such as infection with taenid tapeworms in red meat. Published literature in some developed countries suggest that public's assumption is that fish is free from parasites. For example, the case where a new tapeworm, *Adenocephalus pacificus,* was found in a 3-year-old child who regularly ate raw marine fish, caught by his father during recreational fishing. Despite several publications recommending raising awareness about seafood-borne parasites and risk associated with it [6, 9, 21, 47] there has been no educational campaign to raise such awareness in Australia.

When it comes to red meat, poultry or vegetarian meals, there are protocols in place that all members of the society are aware of and practice. For example, children are taught from an early age that they should wash their hands to prevent the spread of germs and parasites. Abattoirs have proper meat inspection in place and parasite infected meat is condemned to prevent spread of parasitic diseases from meat to humans. This is very different to the case of seafood in some countries and despite increase annual consumption there is no effective guideline in place to protect consumers.

3.4. Medical Doctors, Diagnosticians, and Publishing Relevant Cases

Medical doctors are usually the first point of contact when people feel unwell. Therefore, a differential diagnosis for seafood-borne parasites by medical doctors in patients with a history of seafood consumption is essential. However, this may not be the case in some circumstances. Firstly, some seafood-borne parasitic diseases cause symptoms that can easily be confused with other diseases. For example, anisakidosis can present similarly to appendicitis, Crohn's Disease, food poisoning, or even stomach cancer. Subsequently, even in a country such as Japan, where the disease is common, it has been estimated that more than 50% of cases are misdiagnosed [34]. Another issue is in countries where the disease has not yet been reported. This usually leads to the belief that among many other agents of disease these parasites are less important and therefore they are not included in the curriculum in medical schools which may result in lack of awareness among medical doctors and diagnosticians at a national level. For example in Australia, there has been several reports of infection with seafood-borne parasites, mainly among immigrants in early 20th century. Shamsi and Shorey [9] believed that was due to the availability of expertise, teaching a deeper and broader parasitology topics and availability of research fund on that period. Later, after those researchers retired, there has been a period of several decades without any report of seafood-borne parasites in the country, lasting until early in the 21st century. Lack of publication resulted in lack of awareness and underestimation of the risk these parasites may pose to Australians' health, with no proper coverage of diseases caused by these parasites in the country. As a result, there have been several cases of misdiagnosis [33]. For example, when in the early 21st century a woman was hospitalized after consuming raw fish and for weeks was severely unwell with no proper response to the medications, it was no surprise that no one in the medical team considered infection with seafood-borne parasite. It was an extremely lucky as well as an extremely unusual occasion that in a bowel motion parasite was released alive and was collected but it was identified as being *Trichostrongylus* or *Ascaris.* It was serendipitous that authors of the case, one a PhD student at the time working on fish parasites in the University of Melbourne and the other one a senior laboratory pathologist in Queen Elizabeth Hospital in Adelaide, had a conversation about the disease caused by seafood-borne parasites which led to further examination of the larva collected in 2004 and its identification as Anisakid larva (*Contracaecum* sp.) however it was several years before the case was published [48] which then prompted a risk assessment being carried out by the South Australian Government on seafood-borne parasites [46]. If this case, as with some other anecdotal cases mentioned by Shamsi and Shorey [9] had remained unpublished the assumption that the country is free from anisakidosis would still persist. Despite case reports being a valuable resource of unusual information and a great resource for final education of true experts [49] they are not published as much as they should be, resulting in a lack of awareness among the public and experts.

4. Seafood-Borne Parasites as Indicators of Environmental Change

Many seafood-borne parasites, almost all helminths and some protozoa have indirect life cycles, which means that at each developmental stage of their life they live in a different host type. Host species whose bodies serve as home to larval or immature stage of the parasites are known as intermediate hosts and there are often at least two intermediate hosts, first and second, involved in a parasite's life. First intermediate hosts are usually invertebrates such as zooplanktons, crustaceans, or larger invertebrates, such as Cephalopoda. Second intermediate hosts are usually fish or other vertebrates. Those hosts that provide home and food in their body for adult stage of parasites to feed from and breed in are called final or definitive hosts. Parasites reach the definitive hosts when infected fish are consumed by larger fish such as marlin or other fish predators such as shark, fish-eating birds, and marine mammals.

Since a parasite's life is directly associated with its host's life, an increase or decrease in host population has a direct impact on population of these parasites [50]. On the other hand, parasites themselves play a significant role in controlling host populations. However, in almost all conservation or environmental management plans, parasites and their role and impacts are overlooked even though there are more parasitic species in the environment than non-parasitic. A recent example would be the ecological consequences due to significant increase in the population of the Baltic grey seal from a critically low level during the latter part of the 20th century to more than 40,000 individuals at present. This has resulted in a fish catch decline not only due to increased predation by seals but also due to elevated parasitism [51]. *Contracaecum osculatum,* a nematode parasite that infect seals in adult stage and fish in larval stage (also of zoonotic significance), has been shown to preferentially infect the liver of Baltic cod, and adversely affect its population in the region. On the contrast, population of *Anisakis* larvae seem to be declining in Australian waters [52]. It has been hypothesized that climatic variables may have influenced the free-living larval stages of *Anisakis* spp. as well as their predominantly invertebrate hosts.

A "One-Health" Approach Is Needed

The seafood supply chain, both wild seafood or aquaculture products, begins with a producer (the fish farmer or the fisher) and terminates with an end buyer, including local fish markets, restaurants, or consumers. For an effective seafood safety plan extensive engagement between producers (fishermen and fish farmers), chefs, aquatic veterinarians, public health experts, clinicians, diagnostic laboratory staff, general and at-risk communities, and jurisdictional and federal agencies is crucial. More importantly, the dynamic nature of the environment, demands a constant two-sided engagement between researchers and all the abovementioned stakeholders to ensure genuine stakeholder participation and engagement to keep a country's position as a leader in providing safe seafood. Closing the gap between research production and research use is a key challenge for the seafood safety and to achieve an impact, stakeholder engagement should increase across the board.

5. Conclusions

To keep their international reputation as the provider of healthy seafood, being proactive in assessing risk associated with local and imported products and establishing effective control and preventive strategies is important more than ever. Therefore a "One-Health" approach involving various stakeholders and engaged with research is crucial. To enable the continued provision of safe seafood many professionals with a range of expertise working in different sectors should keep updated on the latest trends on parasites infecting seafood, diseases caused by them and join forces to support "One-Health" approaches. Since the public health significance of parasites has largely been underestimated, compared to other food sectors, there is a huge need for the development of seafood safety policies and guidelines in many countries. There remain significant gaps in our knowledge of fundamental aspects of the biology and ecology of many new and emerging seafood-borne parasites which may hinder our ability to establish a more complete understanding of the parasites and the diseases they cause, their relative public health significance and how best to prevent and control parasites' transmission, infection, and disease. Publishing clinical cases caused by seafood-borne parasites is important in the advancement of clinical knowledge. In an era of increased human migration, it is fundamental for clinicians to be able to identify such diseases.

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