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REVIEW

Foodborne Helminthiasis

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Abstract

Purpose of Review This review focuses on key foodborne helminths: providing an overview of their lifecycles and major transmission routes to humans, their geographical distribution, clinical manifestations, human health burden and control aspects.

Recent Findings Many foodborne helminths appear to be increasing in geographical distribution, driven by climatic and demographic changes; predominately increases in global humidity and temperature, favouring environmental survival and changes in human consumption practices, exposing many more people to high-risk foodstuffs. Although current estimates of human health burden indicate the need for us to focus on these diseases it is acknowledged that poor diagnostic performance and inefficient surveillance leads to an underestimate of burden and for some highly neglected helminths no burden estimates have been performed. It is acknowledged that intervention strategies should consider the full value chain and involve multiple stakeholders following a 'One Health' approach.

Summary As well as improving burden estimates, key research needs for foodborne helminths include the need for improved diagnostic tools and better integration of the social sciences to ensure the development of contextually relevant and socially acceptable control strategies.

Keywords Parasites · Helminths · Trematodes · Cestodes · Nematodes foodborne

Introduction

Helminths, incorporating Nematoda (roundworms), Cestoda (tapeworms), Trematoda (flukes) and Acanthocephala (thorny headed worms) are an important global public health threat and a significant route of helminth infections for humans is through the consumption of larvae or eggs in food products, foodborne helminthiasis. Foodborne helminth infections cause a substantial health burden with a particularly high impact in low- and middle-income countries, particularly affecting people living in rural deprived areas [1]. Some foodborne helminthiasis have been traditionally underappreciated and represent a substantial fraction of the neglected tropical diseases [2]. It is important, however, to appreciate that these helminths are a global concern due to their worldwide distribution, globalisation of the food supply, the increase of international travel and highly susceptible populations, changes in eating patterns and improvements in diagnostic techniques and communication [3]. In this article, we provide an overview of the most relevant helminths transmitted to humans by consumption of food-products. We focus on those where the food-product forms an integral aspect of the parasite lifecycle rather than when food products are inadvertently contaminated by parasite eggs. These products predominately include those of animal origin where the animal represents the intermediate host of the parasite, though we also include aquatic vegetation which represents a key vehicle of transmission for metacercariae of *Fasciola* spp. from the intermediate host to a human definitive host. We focused on parasite life cycle, pathogenesis, health burden, clinical symptoms, and

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diagnosis, control aspects and throughout have identified areas of consideration for research. A summary of key helminth species, their geographical distribution, transmission routes, clinical manifestations and human health burden is provided in Table 1.

Trematoda (Flukes)

Foodborne trematodes are considered to infect 75 million people, with 750 million people living at risk of infection [5, 6]. Parasites from this class are also known as flukes and are classified in three groups: liver flukes (Fasciolidae & Opistorchiidae), lung flukes (Paragonimidae) and intestinal flukes (of multiple families) [6]. Figure 1 provides an overview of the lifecycles of these different flukes.

(A) Fasciolidae: (1) Humans and ruminants are the definitive host with the adult fluke developing within the hepatic ducts. Eggs are released into the biliary tree and excreted in faeces. (2) Eggs embryonate in the water and miracidia emerge from the egg. (3) Miracidia penetrate an aquatic snail intermediate host of the family Lymnaeidae where they develop into cercariae (4) Free swimming cercariae emerge from the intermediate host. (5) Cercariae encyst on aquatic vegetation such as watercress as metacercariae (6) Upon ingestion by of vegetation with metacercariae by the definitive host, the newly excysted juveniles penetrate the intestinal wall and burrow into the hepatic ducts before developing into adult worms. **(B) Opistorchiidae:** (1) Humans, carnivores and many birds are the definitive host. Embryonated eggs are excreted in faeces. (2) Eggs are ingested by the aquatic snail first intermediate host of the families Bithyniidae, Hydrobiidae, or Thiaridae where the miracidia hatch, migrate to the intestine where they develop into cercariae (3) Free swimming cercariae emerge from the intermediate host. (4) Cercariae seek the second intermediate host, being fish or crustacean where they develop into metacercariae. (5) Upon ingestion of the second intermediate host containing metacercariae by the definitive host, juvenile flukes migrate to the liver where they mature. **(C) Paragonimidae:** (1) Humans and many domestic and wild animals including pigs, dogs and cats are the definitive host with the adult fluke developing within the respiratory tract. Unembryonated eggs are released into the tracheobronchial tree and coughed out or coughed up and swallowed after which they are excreted in faeces. (2) Eggs embryonate within water and miracidia emerge from the eggs. (3) Miracidia penetrate an aquatic snail first intermediate host of the families Assimineidae, Hydrobiidae, Pomatiopsidae, Pleuroceridae and Thiaridae where they develop into cercariae. (4) Free swimming cercariae emerge from the snail host. (5) Cercariae invade a crab or crayfish second intermediate host and develop into metacercariae. (6) Upon ingestion of raw, undercooked, or picked crabs and crayfish containing metacercariae by the definitive host, juvenile flukes migrate from the intestine, through the diaphragm into the lungs where they develop into adults. **(D) Intestinal Flukes:** (1) Humans and multiple wild and domestic mammals and birds are definitive hosts of intestinal flukes and pass unembryonated eggs in their faeces. (2) Eggs embryonate and miracidia emerge from the eggs in water. (3) Miracidia penetrate the body pf an aquatic snail as first intermediate host in which they develop into cercariae. (4) Free swimming cercariae. (5) Cercariae either encyst on aquatic vegetation or invade a second intermediate host (fish) and encyst into metacercariae. (6) Definitive hosts ingest fish or aquatic vegetation with metacercariae.

Fasciolidae

Fascioliasis is a re-emerging disease which is clustered in tropical & subtropical regions [7]. *Fasciola hepatica* and *Fasciola gigantica* are the two most important foodborne trematodes of the family Fasciolidae [8]. Ruminants are definitive hosts of *F. hepatica* and *F. gigantica* and fascioliasis often correlates with the presence of livestock, although once established in humans, animal reservoirs become dispensable with infection more likely to be correlated with poor sanitation [8]. Infection with *F. hepatica* is most widely reported, with wild aquatic vegetation such as wild watercress with the encysted metacercariae (see Fig. 1a) most often implicated as the source of infection [8].

Clinical severity, from asymptomatic to severe hepatic and intestinal manifestations, depends on worm burden and host immune response. The acute phase, driven by juvenile fluke migration, manifests as fever, abdominal discomfort, and gastrointestinal disturbances, and is sometimes accompanied by anorexia, flatulence, nausea, diarrhoea, urticaria, and coughing. The chronic phase, appearing months to years after infection, can present with biliary colic, epigastric pain, nausea, and jaundice [8]. Infections are generally diagnosed by coproscopy, and treatment primarily relies on triclabendazole and remains effective [9], although there are resistance concerns in livestock which stem from Its excessive use in animals [8].

Opistorchiidae

The *Opistorchiidae* is a family of liver flukes of which the three most important species are *Clonorchis sinensis*, *Opistorchis felineus*, and *Opistorchis viverrini*. Their intricate life cycles involve a freshwater snail as the first intermediate host, followed by a second intermediate host, frequently a freshwater cyprinid fish [10] as summarised in Fig. 1b.

Table 1 Summary of globally important foodborne helminths

Class, Family, Genus	Geographical distribution	Key foodborne transmission route to humans	Key clinical manifestations in humans	Burden (Disability adjusted life years/yr) [4]
Trematoda				
Fasciolidae				
Fasciola spp.	Worldwide but clusters in tropical & subtropical regions	Ingestion of Metacercariae on aquatic vegetation	Acute: Fever, abdominal discomfort, GI disturbances. Chronic: abdominal disturbances & Jaundice	90,041 (58,050–209,097) DALY/yr
Opistorchiidae				
Opisthorchis spp.	Worldwide *O. viverrini* clusters in South East Asia *O. felineus* in Eastern Europe & Russia	Consumption of raw, dried, or salted fish	Abdominal discomfort, cholangiocarcinoma as a severe sequalae	188,346 (151,906 – 235,431) DALY/yr
Clonorchis sinensis	Predominately South East Asia			522,863 (431,520–635,232) DALY/yr
Paragonimidae				
Paragonimus spp.	Tropical & subtropical Asia, Africa & Americas	Consumption of raw or undercooked crustaceans and water contaminated with metacercariae	Pulmonary form results in allergic response with fever, chest pain, urticaria. Most common sign is a persistent cough. Spinal involvement leads to neurological deficits, cerebral form leads to headaches, seizures and visual disturbance and 10% case fatality	1,048,937 (743,700-1,438,588) DALY/yr
Intestinal flukes (multiple families including: Echinostomatidae, Gymnophalidae, Heterophyidae, Nanophytetidae, Neodiplostomidae, and Plagiorchiidae	Worldwide	Consumption of raw or undercooked fish and aquatic plants contaminated with metacercariae	Mild Infections: headache, abdominal pain constipation or mild diarrhoea Moderate-heavy infections: colic, vomiting, fever, nausea, oedema intestinal ulceration, haemorrhage, erosions, or abscesses.	155,165 (118,920 – 198,147) DALY/yr
Cestoda – Family Taeniidae				
Taenia solium	Worldwide but predominately in South America, Sub-Saharan Africa and South East Asia	Consumption of raw or undercooked pork products. Faecal-oral contamination or autoinfection from taeniasis cases results in aberrant intermediate infection (cysticercosis)	Taeniasis is generally asymptomatic through abdominal discomfort can occur and there are rare gastrointestinal sequalae reported. Neurocysticercosis, symptoms including epilepsy, headaches, and visual disturbances	2,788,426 (2,137,613-3,606,582)
Taenia saginata	Worldwide	Consumption of raw or undercooked beef products	Taeniasis is generally asymptomatic through abdominal discomfort can occur and there are rare gastrointestinal sequalae reported. Cysticercosis not reported	Burden estimate unknown
Taenia saginata asiatica	Asia	Consumption of raw or undercooked pork products		
Nematoda				
Trichinella spiralis	Widely distributed with reports from Africa, America, Asia, Europe and the Pacific	Consumption of raw or undercooked pork, game meat and horse	Fever, headache, vomiting, facial oedema, conjunctivitis, myocarditis, paralysis	550 (285–934) DALYS/Yr

Table 1 (continued)

Class, Family, Genus	Geographical distribution	Key foodborne transmission route to humans	Key clinical manifestations in humans	Burden (Disability adjusted life years/yr) [4]
Anisakidae	Worldwide	Consumption of raw or undercooked seafood	Gastro-intestinal symptoms and those related to parasite migration to other organs and/or allergic issues, anaphylaxis, and death	Burden estimate unknown
Acanthocephala – Family Polymorphidae				
Family Polymorphidae (multiple species)	Worldwide	Consumption of raw or undercooked seafood	Gastro-intestinal symptoms, potential severe sequalae of abdominal perforations	Burden estimate unknown

Humans are infected upon the consumption of raw, partially cooked or fermented fish or crustaceans containing the metacercariae and can be the definitive host of all species [11].

Global infection estimates underscore the widespread impact of these flukes, with *C. sinensis* affecting around 35 million people, *O. viverrini* 10 million in Southeast Asia, and *O. felineus* afflicting 1.2 million in Eastern Europe and Russia [11]. Infection sources differ regionally and is often facilitated through traditional cuisine. Local dishes like goi ca. mai, raw fish salad in Vietnam, yusheng in China, and sushi in Korea and Japan, contribute to *C. sinensis* transmission, while dried or salted fish constitutes the main source of *O. felineus* infection in Eastern Europe and Russia. Considering the consumption of undercooked freshwater cyprinid fish, over 680 million individuals are at risk of infection [11].

Clinical symptoms, like that of fascioliasis are usually non-specific and dependent on the parasite load and host susceptibility [11]. One of the most severe potential consequences of infection is the development of cholangiocarcinoma, with the carcinogenic potential of *O. felineus* being lower than that of *C. sinensis* and *O. viverrine* [12]. Coproscopy remains the key diagnostic method, yet its effectiveness is hindered by the potential resemblance of eggs to those of other trematodes, often necessitating specialized expertise [10]. A suite of serological tests for clonorchiasis and opisthorchiasis are available which exhibit increased sensitivity and specificity compared to faecal examination techniques. Praziquantel is the drug of choice having high efficacy and no indication of resistance to date, although reinfection rates following treatment are high [11].

Paragonimidae

The genus *Paragonimus* of the family Paragonimidae, has a very broad geographical distribution which includes tropical and subtropical Asia, Africa, and the Americas. An estimated 20.7 to 22 million individuals are infested by *Paragonimus* species, while 195 to 292.8 million live in areas of risk [13]. At least 15 species of the lung fluke have been reported in humans, with *P. westermani* responsible for most human cases [14]. This trematode usually resides in the respiratory tract of its wide array of mammalian definitive hosts, including humans, dogs, pigs, and domestic and wild cats [14]. Extrapulmonary infections do occur, particularly in the brain and spinal cord, but also in the subcutaneous tissues, hepatobiliary system, and colon [13, 15].

Paragonimiasis is contracted through the ingestion of raw, undercooked or pickled crustaceans, and as such, cultures with a strong tradition of consuming raw fish dishes exhibit a higher prevalence of paragonimiasis [14]. Metacercaria

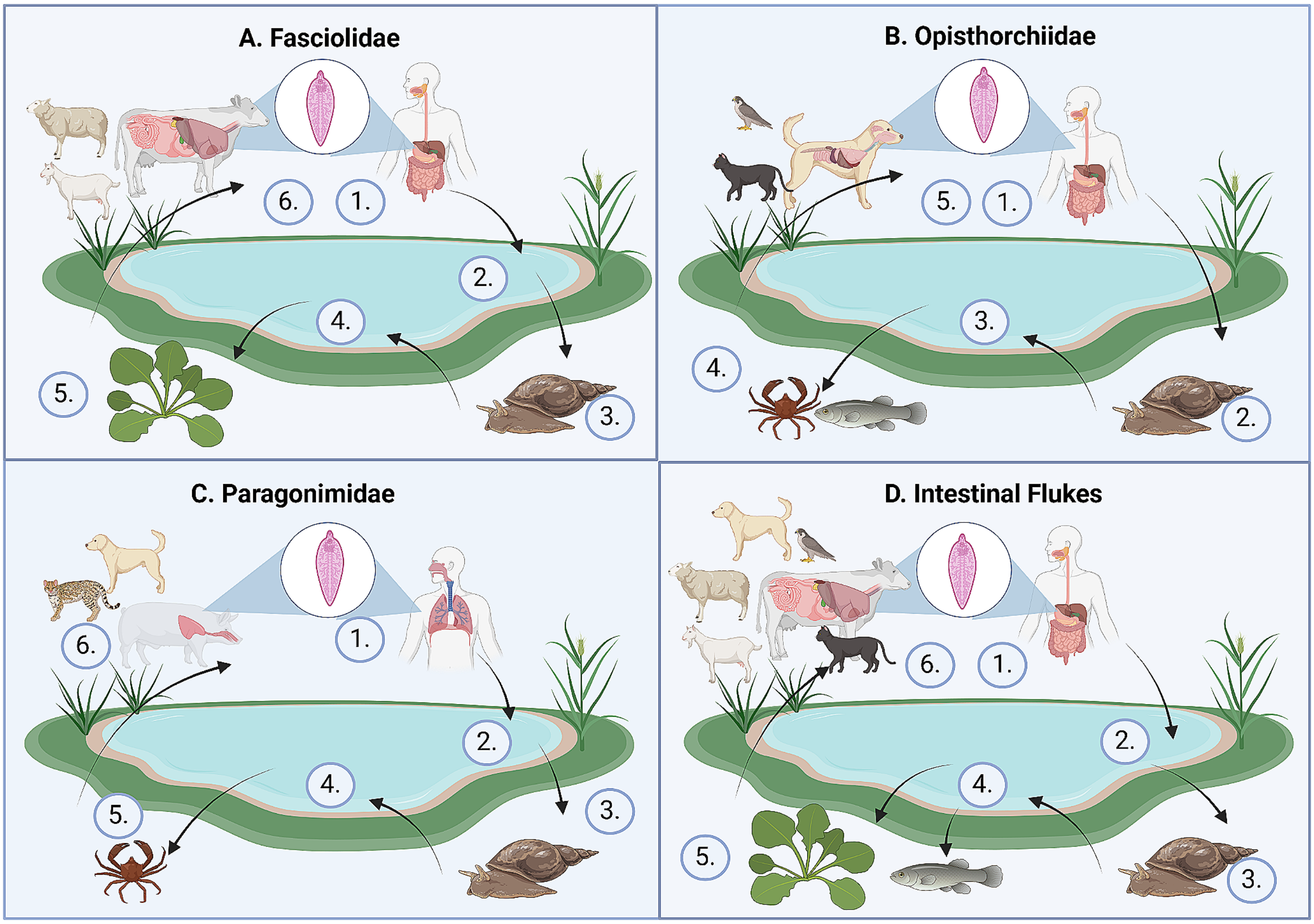

Fig. 1 Life cycle of key foodborne fluke families. Figure created with biorender.com

can also enter a non-definitive paratenic host, such as wild boar, and encyst as a juvenile parasite, leading to the infection of definitive hosts with no history of crustacean ingestion [15].

Clinical signs of paragonimiasis vary depending on the stage and location of the parasite. Migration of worms from the intestine into the abdomen may result in symptoms such as diarrhoea and abdominal pain. Migration into the lungs often elicits an allergic response, characterized by fever, chills, coughing, chest pain, urticaria, and eosinophilia and can often be misdiagnosed as tuberculosis or pulmonary neoplasia. Spinal involvement can lead to paraplegia, monoplegia, limb weakness, and sensory deficiencies, whilst cerebral paragonimiasis can lead to headache, fever, vomiting, seizures, and visual disturbances. An estimated one out of ten cases of cerebral paragonimiasis results in death [14].

The gold standard for diagnosing the disease is the microscopic examination and identification of eggs in either the sputum or stool. However, the intermittent discharge of eggs in the sputum and its similarity to other trematode eggs can decrease its sensitivity [15]. The drug of choice for treatment of paragonimiasis is praziquantel, although bithionol and triclabendazole has also successfully treated the disease [14].

Intestinal Flukes

The intestinal flukes are a group of approximately 74 species of trematode worldwide distributed which can colonise the human intestinal tracts including those from the families: Echinostomatidae, Gymnophalidae, Heterophyidae, Nanophytetidae, Neodiplostomidae, and Plagiorchiidae [16]. Humans become infected by *Fasciolopsis buski*'s on consumption of aquatic vegetation with encysted metacercariae whilst other intestinal flukes such as *Metagonimus yokogawai* or *Metagonimus miyatai* from the family Heterophyidae, have a freshwater fish (sweetfish, dace, chub, or minnow) as second intermediate host, infecting humans after the consumption of raw or undercooked fish [10].

Infected patient clinical symptoms are strongly associated with the parasite load. In mild infections, symptoms such as headache, abdominal pain constipation or mild diarrhoea are observed. Whilst moderate to heavy infections can cause colic, vomiting, fever, nausea, oedema in patients, being sometimes fatal if the parasites cause intestinal ulceration, haemorrhage, erosions, or abscesses [6]. Intestinal flukes in humans are generally diagnosed by coprological examinations to recover eggs and posterior microscopic observation. For human echinostomiasis, the identification of adult flukes is also highly recommended [17] although sometimes can be difficult due to the lack of molecular data and understanding of the taxonomy of this parasite [18]. For *Fasciolopsis buski* diagnosis, serological tests are available to detect antibodies that might help for the diagnosis [19]. Praziquantel and Niclosamide have both proven effective in treating intestinal flukes [10].

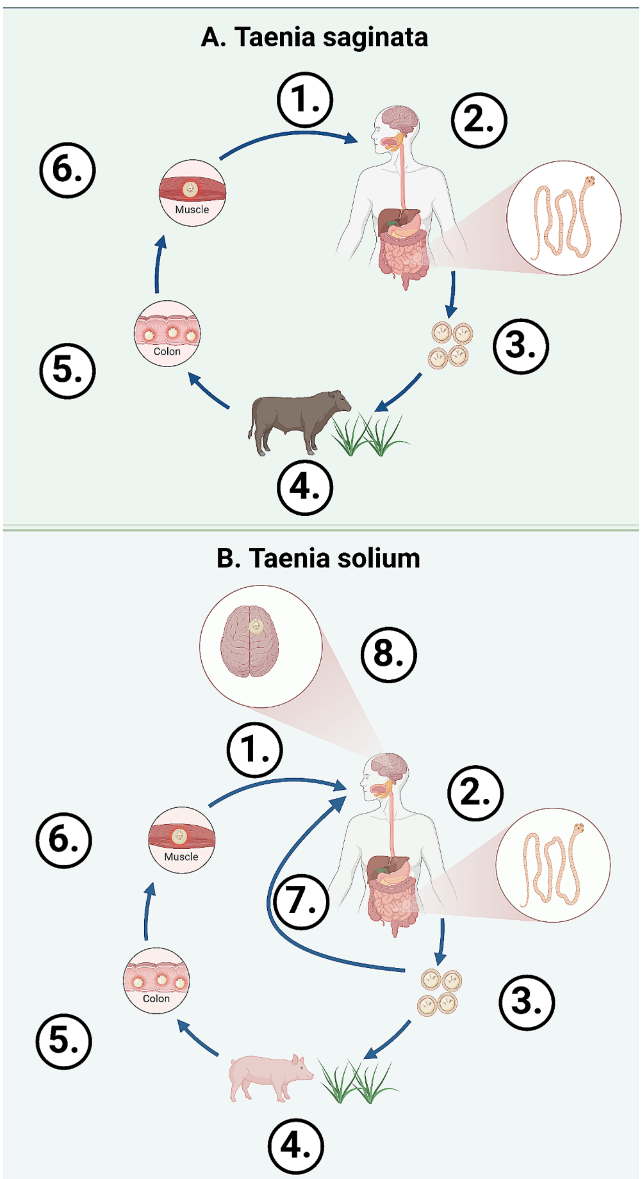

Fig. 2 Life cycle of *Taenia* spp. of foodborne importance. created with BioRender.com

Cestoda (Tapeworms)

Family Taeniidae

The Taeniidae is a family of tapeworms of the order Cyclophyllidea with four genera, *Echinococcus*, *Hydategera*, *Taenia* and *Versteria* [20]. *Taenia solium* and *Taenia saginata* are classical foodborne parasites, with humans being the definitive host after ingestion of raw or undercooked meat from infected livestock species, being pigs and cattle respectively. The Asian tapeworm *T. asiatica* which utilises swine as the intermediate host was originally assumed to be a separate species, is now considered most likely a local variant of *T. saginata*, due to only minor genetic differences [20]. The adult *Taenia* spp. worm reside in the small intestine, taeniasis, and eggs or whole proglottids containing eggs, are excreted with faeces of the definitive host which are then ingested by the intermediate host as illustrated in Fig. 2a&b. Humans can also act an aberrant intermediate host of *T. solium* due to faecal-oral contamination (see Fig. 2a) developing encysted metacestode larvae in the brain, known as neurocysticercosis (NCC), but also in skeletal muscle, eye, heart, skin, and subcutaneous tissue.

Taeniasis is generally asymptomatic thought episodes of diarrhoea, nausea, epigastric pain, weight loss or increased hunger might be caused by the tapeworm and some rare severe sequalae such as gall bladder perforation have been reported. The diagnosis of taeniasis is difficult due to poor sensitivity of microscopy due to intermittent shedding of gravid proglottids and free eggs. Microscopy is poor at speciation of Taeniid eggs, molecular or immunological methods are available for speciation, but rarely used in a clinical capacity. Taeniasis of all species can be effectively treated with Nicolsamide, Praziquantel and triple dose of Albendazole [21]. *T. solium* has the highest health burden of all foodborne parasites [22], making it the most important of the Taeniidae family due to the severe consequences of NCC, including the development of seizures and epilepsy [23]. Neurocysticercosis is believed to be one of the most common causes of acquired epilepsy in endemic countries, responsible for approximated 1/3 of cases [24]. No reports of humans as aberrant intermediate hosts have been made for either *T. saginata* or *T. saginata asiatica.* They are therefore of relatively low public health importance, though bovine cysticercosis has a high economic burden due to the processing, downgrading, or condemnation of infected beef [25].

While *T. saginata* has a worldwide distribution [26–31], *T. solium* is distributed predominately in rural areas of India, Africa, South America, and Southeast Asia where risk factors, such as the presence of free-ranging pigs, low sanitation provision and poor access to health care are prevalent

[32]. Reports of *T. solium* are however, reported in high income countries due to human mobility [25, 33, 34].

Cases of NCC are likely highly under-reported due to the paucity of diagnostic capacity in endemic countries with advanced neuroimaging (CT & MRI) being the gold standard. Serological tests are also available, including a highly sensitive and specific enzyme-linked immunoelectrotransfer blot assay, but these are also rarely applied in a clinical setting in endemic areas. The treatment of neurocysticercosis requires an individual case by case approach depending on viability, cyst location and host clinical signs, which vary from the symptomatic treatment of seizures with antiepileptic drugs to surgical intervention [35].

(A) ***T. saginata***: (1) Humans eat raw or undercooked cysticerci infected meat. (2) Parasites grow to its adult form in the small intestine (taeniasis). (3) Eggs are deposited in the large intestine and released to the environment. (4) Cattle (or pigs in the case of *T. saginata asiatica*) become infected by ingesting infective eggs in the environment. (5) Oncospheres penetrate the intestine wall and travel to the musculature. (6) Oncospheres develop into cysticerci in muscle of the intermediate host (cysticercosis). **(B)** ***T. solium***: (1) Humans eat raw or undercooked cysticerci infected meat. (2) Parasites grow to its adult form in the small intestine (taeniasis). (3) Eggs are deposited in the large intestine and released to the environment. (4) Pigs become infected by ingesting infective eggs in the environment. (5) Oncospheres penetrate the intestine wall and travel to the musculature. (6) Oncospheres develop into cysticerci in muscle (porcine cysticercosis). (7) Faecal-oral contamination or auto-infection leads to ingestion of eggs by humans. (8) Oncospheres penetrate the intestinal wall and travel to the musculature, ocular and nervous tissues, humans become an aberrant intermediate host.

Nematoda

Nematodes, also known as roundworms, account a range of 100,000–1 million species, of which several are transmitted to humans through consumption of raw or undercooked meat, fish or slugs [36]. Key foodborne nematode species include: *Trichenella spiralis*, *Anisakis* spp., *Gnathostoma* spp., *Angiostrongylus* spp., (*cantonensis & costaricensis*) and their lifecycles are summarised in Fig. 3.

(A)***Trichinella spiralis***: Has a single host lifecycle with one animal functioning as both the definitive and intermediate hosts (1) A Human (dead-end host) or non-human animal host consumes raw or undercooked meat from an animal with encysted larva (e.g., pig, horse, rodent, or wildlife). (2) Larvae encysted in the meat are released in the digestive tract and migrate to the small intestinal mucosa (3) Larvae mature to adult worms and undergo sexual reproduction (4) The larvae released by the female parasite migrate through the lymphatic vessels to the striated muscle (5) Within 2 weeks larvae encyst in started muscle, where they can survive and remain infective for many years until ingestion of the infected meat by a new host. (6) The life cycle can be propagated within domestic or sylvatic cycles. **(B) Anisakis spp.** (1) The definitive host acquires infection through the ingestion of raw or undercooked paratenic hosts (fish or cephalopods) and larvae develop into adults in gastric mucosa (2) Unembryonated eggs are excreted in faeces, eggs embryonate in water and free-living larvae hatch from eggs (3) Crustaceans ingest free-living larvae (4) Fish or cephalopod paratenic hosts ingest infected crustaceans and larvae migrate to musculature (5) Marine mammals or humans ingest infected fish or cephalopods. **(C) Gnathostoma spp.** (1) The definitive host (suids, canids, felids) excrete unembryonated eggs from the adult worms which live within in tumour-like masses within the gastric wall. (2) Eggs embryonate in the water and hatch releasing the first stage larvae. (3) The first intermediate host, Cyclops crustaceans, ingest the larvae which develop into the second stage larvae. (4) The second intermediate host, fish or amphibians, ingest the first intermediate host with stage-two larvae which develop into third-stage larvae. (5) Definitive or dead-end (human) hosts acquire infection through the consumption of the second intermediate host or paratenic host (birds or snakes) infected with third-stage larvae. **(D) Angiostrongylus spp.** (1) The adult worm lives in the right ventricle and pulmonary artery of the rat definitive host. The eggs travel through the blood stream to the lungs where they hatch into first-stage larvae which penetrate the alveoli and move up to the trachea. Here they are coughed up, swallowed and excreted with the faeces. (2) Faeces with first-stage larvae are eaten by a slug or snail intermediate host where they develop through to third-stage larvae. (3) Freshwater shrimps, crayfish, land crabs, frogs, toads or monitor lizards may ingest the intermediate hosts becoming paratenic hosts (4) The rat definitive host, or human dead-end host becomes infected through ingestion of the infected intermediate or paratenic hosts. The larvae penetrate the intestinal wall and migrate to the CNS where they develop to the sub-adult stage which in the rat then move to the bloodstream to continue the life cycle.

Trichinella spiralis is a widely distributed parasite for which a wide number of different domestic and wild animal species including reptiles, birds and mammals and be both definitive and intermediate host [37, 38]. *Trichinella spiralis* cause trichinellosis in humans, historically transmitted through the consumption of undercooked meat from pigs, wild game or horses containing encysted *Trichinella spiralis* larvae [39]. Clinical signs of trichinellosis are dependent of

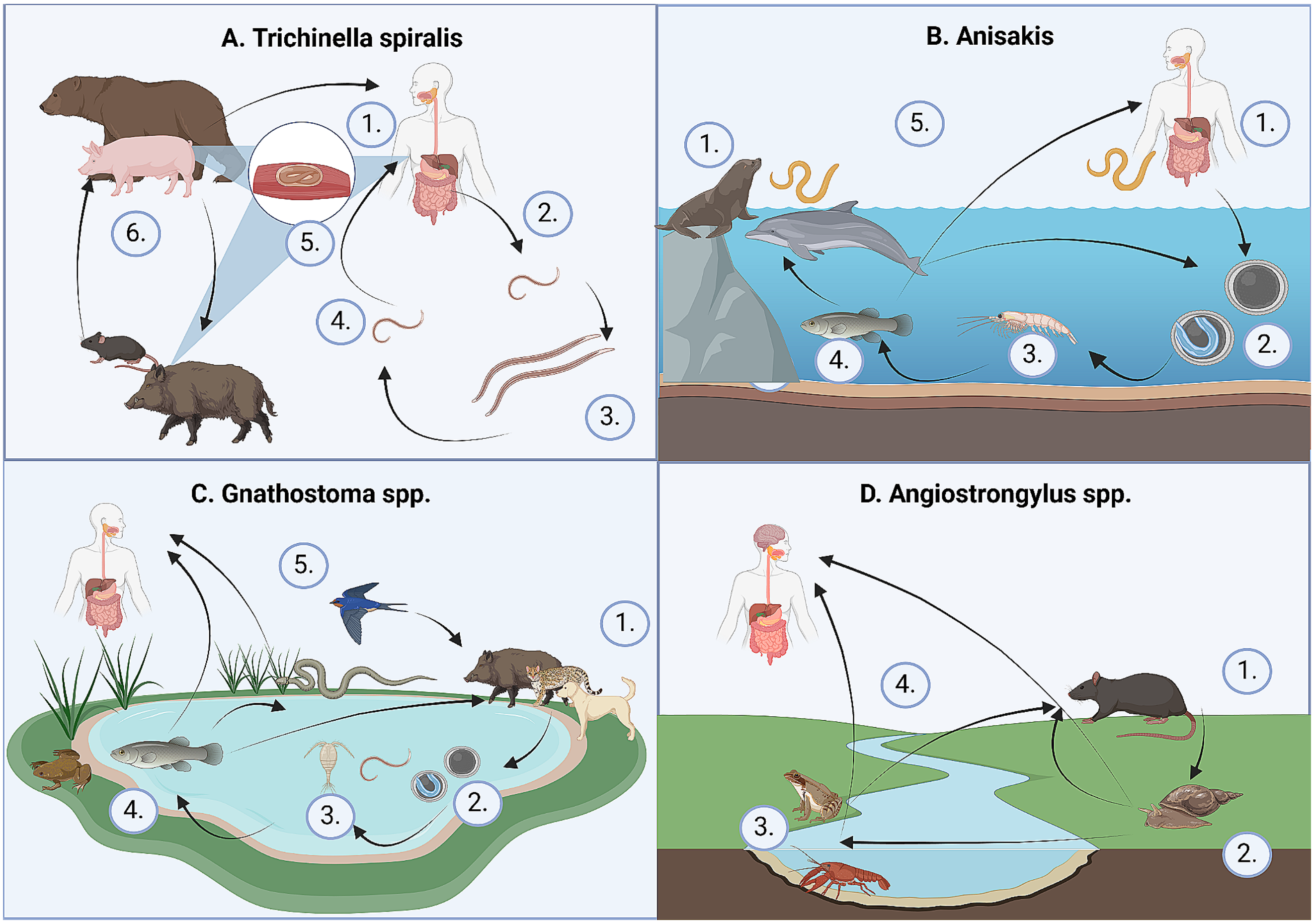

Fig. 3 Lifecycle of key foodborne nematodes. Figure created with BioRender.com

the life cycle phase. During the enteral phase vomiting, mild transient diarrhoea, nausea, and low-grade fever caused by the invasion of the parasite of the intestinal mucosa might be observed. Larval migration and encystment (parenteral phase) can result in periorbital and/or facial oedema, paralysis, conjunctivitis, headache, fever, and myocarditis. Serological tests including ELISA and Western Blot are available for the diagnosis of trichinellosis in humans. Muscle biopsy can be also collected for confirmation of inspection and identification of the species [40] though is not usually used in practice because it as an invasive, painful, and expensive method [36]. Mebendazole, albendazole and pyrantel are the principal drugs to treat trichinellosis. These drugs applied at the enteral phase eliminate the worms from the intestinal tract as well as prevent the skeletal muscle tissue invasion. Together with anthelmintics, glucocorticoids, such as prednisolone, and immunomodulating drugs support the therapy in the acute and severe stages of the disease [41].

Anisakiasis is an emerging nematode infection caused by the aquatic-derived third-stage larvae of the genus *Anisakis* [42]. This worldwide distributed nematode [43], particularly affects populations from countries where raw or undercooked fish is consumed. While Japan, Spain and South Korea have the highest number of published cases 'hot-spots' of allergic anisakiasis appear to be Portugal & Norway [44, 45]. Anisakiasis can cause gastro-intestinal symptoms as well as symptoms related to parasite migration to other organs [44, 45]. A high public health issue is allergic anisakiasis, characterised by allergic reactions within 1-2hrs of ingestion of the fish from mild urticaria to severe anaphylaxis [42]. This disease is both underdiagnosed and underreported due to the lack of diagnostic tests and specific clinical symptoms in affected patients [46]. The assessment of clinical signs, serological anti-Anisakis IgG/A antibody test and the use of endoscopy for gastric anisakiasis and Computed Tomography scan for intestinal anisakiasis are useful for the diagnosis of the parasite [47]. Endoscopic extraction of the *Anisakis* larvae is the elected treatment for gastric anisakiasis whilst conservative treatment is the chosen for intestinal anisakiasis evolving into surgical intervention in severe scenarios [48].

Gnathostomiasis is another emerging foodborne nematode of worldwide distribution, clustering in southeast Asia, caused by the third-stage larvae of *Gnathostoma* spp.

due to the consumption of raw, marinated or undercooked freshwater fish as well as fish, frogs, snake or poultry [49]. Humans are an aberrant host of *Gnathostoma* spp., and the third-stage larvae migrate through the body causing damage, inflammation and allergy and, without proper treatment, death. Clinical signs depend upon the parasitic load and the organs involved in the infection, with cutaneous gnathostomiasis being the most common presentation causing nodular migratory panniculitis with pain and swelling intermittently over time [49]. Morphological identification is required to diagnose the parasite as serological tests might cross react between *Gnathostoma* spp. and the *Echinocephalus* genus [50–52]. Albendazole for 21 days appears to be an effective treatment for human gnathostomiasis and cutaneous gnathostomiasis may be treated by surgical removal of larvae [53].

Foodborne infection with *Angiostrongylus* spp., (*A. costaricensis* and *A. cantonensis*), previously distributed predominately across Asia and Australia, have more recently been recorded throughout the Americas and Caribbean as well Europe [54]. Larval infections of the central nervous system are associated with eosinophilic meningitis or encephalitis due to the strong inflammatory response to the migrating third-stage larvae and result in neurological deficits, paralysis, seizures and sometimes death [55]. Humans acquire infection through ingestion of raw or undercooked gastropod intermediate hosts (slugs or snails) or paratenic hosts including freshwater shrimps, land crabs, frogs, toads or monitor lizards [55]. Diagnoses relies on the detection of eosinophilia in the cerebrospinal fluid, alongside a relevant exposure history and confirmatory serological testing (ELISA or immunoblot) and treatment options are predominately a combination of anthelmintic and corticosteroid therapy, with success dependent upon the location and degree of infection [56].

Acanthocephala

Acanthocephala, commonly known as thorny- or spiny-headed worms, include multiple parasite families spanning approximately 1300 species which can parasitise multiple arthropod and vertebrate hosts [57]. Many species are aquatic and although rarely considered as an important foodborne helminth, the ingestion of undercooked fish or shellfish can lead to gastro-intestinal complications as reported in Japan and Alaska due to infection with *Corynosoma* spp. [58, 59]. *Corynosoma* spp. utilise marine amphipods as an intermediate host, fish as paratenic hosts and marine mammals, including walrus and seals, and birds as definitive hosts [58]. Yet Acanthocephala is considered a minor zoonoses, though species of this phylum have been identified in many edible fish species, indicating the need to ensure appropriate freezing or cooking of seafood products and to consider infection with these parasites in patients presenting with compatible histories [60].

Global Trends in Foodborne Helminth Transmission

Various factors have a strong influence on the trends in global foodborne helminthiasis infections [61]. Climate change has an impact not only in the ability of the foodborne parasite stages to survive in the environment, but also in the biology of the host [61]. An increase in humidity and temperature triggers respectively a longer survival and a faster development of parasite stages in the environment and in the host, favouring the settlement of parasites from tropical regions in temperate ones. Additionally, intense rainfalls favour the spread of eggs and cysts whilst droughts, despite of reducing egg and cyst survival, favour parasite concentration in water [61]. An increase in travel, tourism and migration due to socio-economic circumstances contribute to the globalisation of foodborne helminth transmission and extension of endemic areas [62–64]. New behavioural and cooking habits of eating raw, undercooked, pickled, or smoked foods increase the likelihood of foodborne parasite infection. Popular examples are sushi and marinated anchovies which contain raw fish being responsible of anisakiasis [65, 66]. Rapid expansion of the aquaculture industry and shifts towards outdoor and organic farming practices may also increase the risk of foodborne parasite infection. This can be observed in free-range pig production which increases the risk of *Trichinella spiralis* exposure [65, 66]. Monitoring the prevalence and distribution of foodborne parasites is an important step towards quantifying health burden and stimulating investment in control, additional surveillance activities and data sharing is urgently required.

Controlling Food Borne Helminths

While anthelmintic treatments are available for individuals infected by the foodborne helminths covered in this review, sustainable control of foodborne parasites must focus on breaking the cycle of transmission between humans and the relevant intermediate hosts [67]. Control of food borne helminths, as per other food safety challenges require a farm (sea or pond) to fork approach, with interventions targeting both human and animal hosts likely to improve sustainability of control strategies [67]. Control of these parasites therefore will require a focus on appropriate animal husbandry, effective inspection and processing of food products, improved water, sanitation and hygiene provision and supporting human behaviour change to reduce exposure.

Preventing the transmission of helminths to the intermediate or paratenic hosts which may then be consumed by humans requires strong biosecurity measures, which may include raising animals under highly controlled systems [68], ensuring pasture land cannot be contaminated by sewerage effluent from contaminated stream or surface water [69] and improving human sanitation provision, from building of basic latrines to installation of tertiary treatment plants to prevent contamination of the environment with faeces containing infective eggs [70]. The prudent use of anthelmintics in livestock production is advised in high-risk areas though the risk of resistance must always be considered. The development of effective anthelminthic vaccines, such as that against *Taenia solium* is an exciting development, though the production and distribution of such vaccines requires scaling up for maximal effectiveness [8, 71, 72].

Official veterinary inspectors play an important role in controlling food borne helminths in food processing facilities [73] and therefore, it is crucial that they are adequately trained in recognising life cycles and morphological features of relevant veterinary and human parasites [74]. Currently visual inspection, palpation and incision practices are utilised to detect, and then process or condemn, food products infected with macroscopic parasites such as *Taenia* spp., *Fasciola hepatica* and *Anisakis* spp. Whilst specificity of such techniques may be good, the sensitivity is often poor, particularly in light infections. Classical meat inspection is estimated to have only a 27% sensitivity for light infections of *Taenia* spp., increasing to 78% when more than 20 cysts are present on the carcase [73], the palpation and incision of the gastric surface and the base of the caudate lobe of the liver for *Fasciola hepatica* is estimated to have only 68% sensitivity while visual inspection of fish for Anisakis is limited in its ability to identify the parasite when embedded in the muscle of the fish [75].

Handling and incising food products can also introduce microbial cross-contamination to the meat from authorised officer's hands and equipment and hence a European Union (EU) move towards visual-only meat inspection within risk-based meat assurance systems [76]. These risk-based systems have four components: harmonised epidemiological indicators, food chain information, risk-based meat inspection and reactive interventions and can support a move towards visual-only inspection [77].

Risk-based inspection for *Trichinella spiralis* is already in place in the EU [78]. Additional research is required to support the continued scale-up of risk-based assurance systems in relation to other foodborne helminths, including additional modelling studies to refine risk indicators and determine the most cost-effective inspection processes [79] and the continued improvement in rapid, cost-effective, and sensitive diagnostic procedures. For example, progress has been made in other real-time, non-destructive inspection technologies such as hyperspectral imagining which can be used as a parasite detector to assess the quality and safety of foods [80]. This technique has been applied to accurately detect *Anisakis* on sashimi [81] and in cod fillets [82].

The application of heat, cold or chemical preservation plays an important role in controlling many foodborne helminths. Cooking temperatures (core) 60 –70 °C for 15–30 min or freezing at -5 °C (for 2 weeks) to -18 °C (for 1–3 days) inactivates parasite larvae in most food of animal origin [83]. The application of some other food processing techniques can be also used to inactivate these hazards in meat and fish and may be most applicable when cultural norms relating to cooking restrict the ability to encourage cooking as a control measure [84]. These techniques include marination, fermentation, drying, addition of organic acids and salt, which lower the pH of the product being effective NaCl contents of 2–5% to inactivate food borne parasites, as proved marinating fish in 2.6% acetic acid and 5–6% salt for 12 weeks which inactivates *Anisakis* larvae [83].

To implement sustainable control of foodborne helminths along the whole value chain it is important that the interventions proposed are acceptable to the community and appropriate to the context in which they are being undertaken [85, 86], considering society, culture and gender norms [87, 88]. The social science disciplines play an important role in understanding the contextual aspects of foodborne helminth control and in creating optimal strategies to encourage human behaviour change for the adoption of risk-mitigation strategies and is an area where much research is still needed [89].

Conclusion

Foodborne helminthiasis are a substantial cause of human health burden globally and their distribution is likely to increase due to climate change, global travel and alterations in eating patterns without substantial investment in appropriate integrated control strategies along the food supply chains. Robust surveillance is required to monitor the epidemiological situation and to improve the burden estimates for these pathogens to stimulate investment in control. Further research is required on low-cost, non-invasive, and sensitive diagnostic tools, vaccines for use in food-producing livestock and on the development of contextually appropriate, sustainable control strategies with a particular focus on the social sciences.

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Declarations

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Informed Consent All studies reviewed here with human or animal subjects are published and followed ethical standards.

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