The increase of exotic zoonotic helminth infections: The impact of urbanisation, climate change and globalisation

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Keywords: Zoonosis, helminthiasis, globalisation, molecular diagnostics

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## **1. Abstract**

Zoonotic parasitic diseases are impacting increasingly on human populations due to the effects of globalisation, urbanisation and climate change. Here we review the recent literature on the most important helminth zoonoses, including reports of incidence and prevalence. We discuss those helminth diseases which are increasing in endemic areas, and consider their geographical spread into new regions within the framework of globalisation, urbanisation, and climate change to determine the effect these variables are having on disease incidence, transmission, and the associated challenges presented for public health initiatives, including control and elimination.

## 2. Introduction

A zoonosis is a disease whereby a pathogen can be naturally transmitted from animals to humans. This review covers zoonotic helminths, many of which appear to be on the rise. Figure 1 shows a number of zoonotic helminths and their main definitive hosts. Definitive hosts are hosts in which the helminth reaches maturity, while reservoir hosts, another term used in this review, are long-term definitive hosts for a helminth which can be important sources of human infection. Helminth infections are generally responsible for chronic disease and morbidity and are not commonly associated with high mortality levels in humans. In the 2002 global burden of disease (GBD) study it was estimated that helminths (including: schistosomiasis, onchocerciasis, and intestinal worms), accounted for 177,000 deaths, and 20 million disability adjusted life years (DALYs), or 1.3% of the global burden of disease (Mathers et al., 2007). However, many zoonotic helminths were not represented in the GBD study, such as *Clonorchis* or *Opisthorchis* species, which can lead to infection associated morbidity and the more serious cholangiocarcinoma.

Climate change is also playing a role in the spread of helminth zoonoses by changing ranges of animals and habitats of helminth vectors such as mosquitoes as well as increasing survivability of soil transmitted helminths (STH) by providing the right conditions of warm, moist soil resulting from the expansion of tropical and sub-tropical zones due to climate change (Genchi et al., 2011, Montarsi et al., 2015, York et al., 2014). Globalisation increases the risk of food-borne helminths (FBH), particularly in fish and other meat products, but also vegetables and fruits, due to the large amounts of exports and imports of food products occurring globally. Meanwhile, increasing urbanisation has meant that human habitats are intruding ever further into the natural world. This results in closer contact between wildlife and humans, and gives rise to a number of novel parasitic infections in humans. Raccoons and the red fox are important examples of wildlife hosts that exist in urban environments (Kellner et al., 2012, Page et al., 2014, Plumer et al., 2014). Helminths of wildlife crossing to domestic animals, which live in close contact with humans, is another mechanism whereby a zoonosis can spread (Magwedere et al., 2012, Jones et al., 2013, Miller et al., 2013). Many of the helminth species discussed in this review

In this review we will focus on the prominent literature from the last five years (2010-current) and discuss important transmission factors, the impact of climate change, urbanisation, and globalisation, and prevention and control strategies, to minimise the risk of zoonotic helminth infections.

**Figure 1:** Animal families and their associated zoonotic helminths grouped as either helminths of wildlife, wildlife and companion animals, or wildlife and livestock.

## 3. Globalisation

The ease and increasing availability of air travel, and the subsequent movement of a large number of people around the world as tourists or immigrants, will lead to more cases of zoonotic helminthiases occurring in non-endemic countries (Shaw et al., 2003). For some of these species, such as the filarial worms, the presence of the appropriate intermediate hosts may lead to exotic species becoming established in new countries, while changes in climate to warmer temperatures, ideal for soil transmitted helminths (STH), can lead to their establishment in non-endemic areas. Infections occurring in tourists returning from developing countries may not be diagnosed readily due to lack of expertise by medical staff in countries where these helminths are not endemic and are therefore rarely seen. Immigration and, in particular, refugee intakes are also potential sources of new infections. Most developing countries perform health checks of refugees which will identify and treat any infectious diseases found (Redditt et al., 2015, Martin and Mak, 2006, Seybolt et al., 2006, Varkey et al., 2007). For this reason any of the zoonotic helminths can be affected by globalisation and imported cases can be identified worldwide (Figure 2). Under the appropriate conditions some of these parasites could become established in newareas.

Figure 2: Spread of zoonotic helminths grouped by globalisation, climate change, and urbanisation, showing the different influences which lead to increased distribution or cases of zoonotic helminths.

Globalisation is an important aspect in the food-borne transmission of parasites. Fish and other animals produced in areas endemic for FBH are shipped globally, as are fruit and vegetables which may contain helminths such as *Fasciola* spp. Depending on the food regulations in the country these products are imported to, infected fish, meat, or fruit and vegetables may make it to the consumer, leading to infection in non-endemic areas. Imported live animals can also harbor parasites either from their originating country or having been picked up en route. In Israel, bovine cysticercosis (*Cysticercusbovis*) was found in live cattle imported from Australia which may have helped to establish this tapeworm infection in cattle herds in that country (Meiry et al., 2013). Australia is a country with a low incidence of this zoonotic tapeworm, *T. saginata,* although an outbreak occurred there due to a feedlot, traced back to commercially available feed, ‘copra meal’, imported from Papua New Guinea (Jenkins et al., 2013).

An estimated 60 million tons of fish are shipped globally each year, primarily from South East Asia, an area endemic for fish borne FBH. Introduction of rats and exotic species, such the giant African snail, *Achatina fulica,* by ships and in shipping containers with their successful colonization in new countries is a concern in the spread of angiostrongyliasis , as well as providing suitable hosts for a number of zoonotic filariasis species, and predator-prey helminths. Rats are often found in peri-domestic and domestic areas in urban and rural areas where they come into close contact with humans and can carry a number of zoonotic helminths. *A. fulica* is an extremely good colonizer and is a host for *Angiostrongylus cantonensis.* While there are other molluscan hosts of *A. cantonensis,* the giant African snail has spread very quickly, and may help transmit the disease globally? (Stockdale-Walden et al., 2015, Thiengo et al., 2010). In Brazil the giant African snail was thought to have been introduced in the 1980’s and, as of 2013, all bar one of the 25 Brazilian states have reported the presence of *A. fulica*. *A. cantonensis* itself may have been imported to Brazil along with these snails, or much earlier from parasitized rats which would have been introduced on ships (Thiengo et al., 2013, Thiengo et al., 2007).

There have been reports of a number of exotic zoonotic helminths present in non-endemic countries in zoo animals, or in illegally imported animals coming from endemics areas (Davidson et al., 2013, Widmer and Jurczynski, 2012, Luzon et al., 2010). While most zoo animals are kept separately from wild animals in the new country, animals such as rats and birds may interact with these animals. In the case of filarial disease, the spread may occur more quickly if the requisite mosquito host is present. In the USA alone over 37 million amphibians, birds, mammals, and reptiles were illegally imported in the period from 2002-2004 (Wildlife, 2007). In the same period the number of legally imported animals was over 1 billion, including fish, and a number of unidentified species (Wildlife, 2007).

Food-borne helminth (FBH) infections are a common source of zoonotic infection in humans with 40-50 million people thought to be infected worldwide (Chai et al., 2009), particularly in populations that consume raw meat. FBH occur mainly after eating raw or undercooked infected meat, but can also be found contaminating raw vegetables or fruit. Fish and other marine animals account for a large proportion of FBH, with 59 species of FBH from fish known (Hung et al., 2013). Here we focus on the most medically important FBH species, for both common infections and those that are emerging. A comprehensive review of fish-borne zoonoses was published in 2014 by Waikagul and Thaenkham (Waikagul and Thaenkham, 2014).

FBH, more than any other group of helminths, have the most impact in terms of potential geographic spread of cases, and are particularly affected by globalisation – the movement of food, including live exports/imports, and the movement of people around the world (Figure 2). The movement of people for travel and immigration is also a major factor in globalisation, and can result in exotic infections being identified in non-endemic areas, and the risk of new species becoming endemic. This aspect of globalisation can impact on the spread of all helminth diseases.

### Aquatic Food Borne Helminths

For aquatic FBH, globalisation has led to an increased demand for fish and other marine foods worldwide, which requires suppliers to increase production, naturally leading to an increase in farmed fish and other aquaculture. Increased levels of intensive aquaculture give rise to increased infections of fish borne FBH (Nguyen et al., 2012, DPI, 2015, Phan et al., 2010b). Freshwater fish hatcheries and pens in streams can easily be contaminated by human and animal excrement run off (Phan et al., 2010a). This is of particular importance as the majority of zoonotic fish helminths have dogs, cats, and birds as reservoir hosts, complicating control of these parasites. In Vietnam, a study of the prevalence of FBH (*Clonorchis sinensis, Haplorchis pumilio, H. taichui, Centrocestus formosanus*) in artificial hatcheries, was found to be more than 50% in overwintering ponds (Phan et al., 2010b).

From 2000-2006 world fish imports rose 49%, with developed countries accounting for the majority when considering the total cost (FAO, 2008b). China, Vietnam, and Thailand are among the top exporters of fish; these countries are also endemic for a number of zoonotic fish borne helminths (FAO, 2008a). Of the top importers of fish, all are developed countries (FAO, 2008b). These figures for import and export are associated with legal imports of fish only. In the USA in 2011 an estimated $1.3 to $2.1 billion worth of illegal fish was imported (Pramod et al., 2014).

Fish farms are a considerable source of infection for aquatic helminths. Many animal hosts, including dogs and poultry, as well as infected humans, that live near these farms, contribute to disease transmission. Contamination of fish ponds can occur when eggs, defecated by a definitive host, are washed into them, such as by rain (Anh et al., 2010, Nissen et al., 2014). Snail hosts in ponds are also a risk factor for transmission within fish farms (Hedegaard et al., 2012). Interventions to prevent infection include snail control through direct removal of snails and vegetation where snails live, concreting ponds to prevent vegetation growth, and placing filters on water pipes to prevent snail movement between ponds and entry to ponds via pipes (Hedegaard et al., 2012). Snail control measures for aquatic helminths can also be implemented for other helminths species that use snails as an intermediate host. Wild and domestic animals can also act as the definitive host for many fish borne FBH, contributing to the ongoing lifecycle. Felids, canids, pigs, birds, and rodents can act as definitive hosts for *C. sinensis* (Ye et al., 2013, Lin et al., 2011). In Vietnam, poultry have also been found to be an important reservoir host of zoonotic aquatic trematodes in fish farms (Anh et al., 2010).

Other control methods relevant for all zoonotic helminths include chemotherapy of humans and animals, such as dogs, in transmission areas (Erfe et al., 2013, Inobaya et al., Ross et al., 2014). In fish aquaculture, fences to keep animals out and walls around ponds to minimalize surface run-off, which may be contaminated with infected faeces, are also used in efforts to reduce transmission (Hedegaard et al., 2012, Pitaksakulrat et al., 2013, Phan et al., 2010a). Similar issues are also relevant for wild fish in polluted waterways. Chemotherapy targeting dogs living around fish farms has been unsuccessful for control due to high re-infection rates (Anh et al., 2010, Nissen et al., 2014).

Climate change also plays a role in fish borne FBH. A study on the effects of temperature, rainfall and humidity on human cases of clonorchiasis, caused by infection with *Clonorchis sinensis* in China, found a positive association between cases and increasing temperature and rainfall, while humidity had an inverse relationship (Li et al., 2014b). With increasing global temperatures due to global warming this may indicate an increase in fish-borne helminths, particularly *C. sinensis* (Figure 2)*.*

Fish-borne trematode families known to infect humans are *Clinostomatidae*, *Echinostomaidae*, *Heterophyidae*, *Opisthorchiidae* and *Troglotrematidae* (Waikagul and Thaenkham, 2014). There are several variations of the trematode life-cycle, but all species are similar in that they require at least two hosts – a definitive and an intermediate molluscan host (Doughty, 1996). Of these, the *Opisthorchiidae* are important in human health due to the association of *Opisthorchis* and *Clonorchis* spp. with the development of liver cancer.

Worldwide, 45 million people are estimated to be currently infected with trematode liver flukes; 35 million are infected with *C. sinensis*, 10 million with *O. viverrini,* and 1.6 million with *O. felineus* (Keiser and Utzinger, 2009, Hung et al., 2015). These parasites are most commonly found in Asia, particularly in developing countries, with the exception of *O. felineus* which is found in humans and animals in Europe. The emergence of clinical *O. felineus* in Europe can be linked both to changes in human diet, due to the popularization of consuming raw fish products, and those fish products smoked or marinated since neither process kills metacercariae contained in the muscle of infected fish, and to cultural practices of eating raw fish that already exist in some European countries, such as Iceland (Pozio et al., 2013).

*Clonorchis sinensis* and *Opisthorchis viverrini* are known to cause cholangiocarcinoma in humans, while *O. felineus* has been implicated as a potential cause of cancer, although this needs to be further investigated (Correia da Costa et al., 2014, de Martel et al., 2012, Watanapa and Watanapa, 2002, Ogorodova et al., 2015). The only other helminth currently linked to the development of cancer in humans is *Schistosoma haematobium*, the cause of urogenital schistosomiasis in Africa, although the underlying mechanism involved is yet to be determined (Honeycutt et al., 2014, Thomas et al., 1990)**.** There is some discussion as to whether *S. japonicum* causes an increased risk of developing colorectal adenocarcinoma (Peterson and Weidner, 2011). The estimated number of cancers caused by *O. viverrini* and *C. sinensis* infection in 2008 was estimated at 2,000, while cancer caused by *S. haematobium* was estimated at 6,000 (de Martel et al., 2012).These helminths cause cancer by indirect releaseof carcinogens or direct physical irritation, both of which lead to chronic inflammation (Sripa et al., 2012). Due to the location of the adult worms and eggs, *C. sinensis* and *O. viverrini* cause hepatic and biliary cancers while *S. haematobium* causes bladder cancer. Cancer in *C. sinensis* and *O. viverrini* occurs due to secretions from adult flukes into the bile, while in *S. haematobium* cancer results from the inflammatory response to eggs lodged in the bladder wall and the induction of chronic inflammation (Oh and Weiderpass, 2014).

Common infections of humans are *Diphyllobothrium* spp.*, Anisakis simplex,* and *Pseudoterranova decipiens*. Up to 20 million people are estimated to be infected worldwide with *Diphyllobothrium* spp., while there are 12,000 confirmed cases of anisakiasis, although more are likely to be infected due to under-reporting (Scholz et al., 2009, Murrell, 2014). Allergic reactions are common with *Anisakis* spp. infection (Audicana and Kennedy, 2008a). There are 14 species of *Diphyllobothrium*  which cause disease in humans; of these *D. latum* and *D. nihonkaiense* are the most common (Table 1). People travelling to endemic countries are also at risk due to the cultural practice of eating raw fish products in many South East Asian (SEA) countries, and some European countries such as Iceland and the Netherlands.

Fish borne infections are likely to become even more prevalent due to the global increases in food imports and exports. Cases can occur in non-endemic countries if the parasites have not been adequately killed (Esteban et al., 2014, Santos and Faro, 2005, Pastor-Valle et al., 2014). This is of particular concern given that for some fish borne and ‘terrestrial’ helminths (see below), freezing for 24 hours is insufficient to kill the infective stages. (Lacour et al., 2013, Pozio et al., 2013). Various sources quote freezing at different temperatures and for different lengths of times to inactivate and kill parasites. The most stringent recommendations recommend freezing at -20°C for 7 days, particularly for products that are eaten raw or ‘cooked’ in a manner that would not inactivate parasites, such as the smoking of food (Audicana and Kennedy, 2008b, FAO, 2001, FAO, 2008b).

###  ‘Terrestrial’ Food Borne Helminths

There are a number of ‘terrestrial’ food borne helminths which can be further classified into two main groups. Those that are present in meat and those that are on vegetables or fruit. In both cases human infection occurs on eating infected or contaminated meat or plant material that has been improperly cooked or washed.

Consumption of raw, unwashed vegetables is common source of infection for FBH and is the main source of infection with *Fasciola* spp., *Fasciolopsis* spp., and for the rarer Dicrocoelium spp., as well as a possible route of infection with A*ngiostrongylus* cantonensis. At least one case of *Angiostrongylus* in Australia was due to the intentional consumption of a raw slug as a dare by a young adult (Blair et al., 2013). In developed countries, access to clean running water allows for easy washing of vegetables and fruits, but in developing countries, particularly in rural areas, clean water for washing food is scarce, and the consumption of plants containing infected ants (*D. dicrocoelium*) or metacercariae (*Fasciola hepatica* and *F. gigantica*, *Fasciolopsis buski*) is a particular concern.

Ingestion of raw water plants such as *Zizania* (wild rice), watercress, scallion, or *Latifolia aquatic*, harbouring metacercariae is a common cause of infection for *Fasciola* spp. and *F. buski* (Mailles et al., 2006, Croese et al., 1982, Kumari et al., 2006, Adamu et al., 2012). Metacercariae of *F. buski* have been found on tomatoes, along with a number of other helminths, including hookworm, in Ghana, while a fatal case of faciolopsiasis in India was traced to consumption of raw caltrops and water chestnuts (Duedu et al., 2014, Kumari et al., 2006, Adamu et al., 2012).

Fascioliasis in humans is caused by *F. gigantica* and *F. hepatica,* with the former more common in tropical areas and the latter more prevalent in temperate zones; however, geographic distribution overlaps occur (Gray et al., 2008b, Chaudhry et al., 2015, Ashrafi et al., 2015, Chen et al., 2013, Gu et al., 2012). *Fasciolopsis buski* is the largest intestinal fluke of humans and is the only recognised species in the genus *Fasciolopsis.* Human infections of *F. buski* in Southeast Asia have decreased from 10 million in 1984 to 1.3 million in 2009, but the parasite may be returning to areas where it has been previously controlled (Beaver et al., 1984, Keiser and Utzinger, 2009, Bhatti et al., 2000).

Adult *Fasciola* worms live in the liver of the definitive host, with the flukes often being found in bovines but also in other animals such as non-human primates (Legesse and Erko, 2004, Gray et al., 2008b). Pigs and cattle are hosts for *F. buski,* and the rearing of either host is considered a risk factor for infection (Muralidhar et al., 2000). Infection with *Fasciola* spp. can result in neurofascioliasis and ophthalmofascioliasis (Mas-Coma et al., 2014b), and a review by Mas-coma *et al.* (Mas-Coma et al., 2014a)provides a comprehensive list of all published reports (80 in number) prior to 2014 of fascioliasis resulting in minor or major neurological and ocular manifestations in Europe.

*D. dendtriticum* isa rare parasite of humans that can also be acquired by ingesting raw fruit and vegetables, as well as through drinking contaminated water (Schweiger and Kuhn, 2008). Human infections of *D. dendriticum* among children in Kyrgyzstan were found to be as high as 8% while other recent cases of human dicroceliasis have also been found in Turkey , Iran , Egypt, Ghana , USA , Italy and Spain (Jeandron et al., 2011, Cengiz et al., 2010, Ashrafi, 2010, El-Shafie et al., 2011, Steinmann et al., 2010). *D. dendriticum* has been identified in ruminants (including bovines, equines, cervines and ovines), cats, dogs, and non-human primates from countries in Europe, Africa, the Middle East, and North America (Arias et al., 2011, Bian et al., 2013, Bolukbas et al., 2012, Borji et al., 2012, Dadak et al., 2013, Katsoulos et al., 2011, Mahmoodi et al., 2010, Ofori et al., 2015, Gualdieri et al., 2011, Khalil et al., 2013, El-Shafie et al., 2011, Cabeza-Barrera et al., 2011, Sammet et al., 2013). Human infections are often asymptomatic and are thus frequently undiagnosed (Schweiger and Kuhn, 2008, Haridy and Morsy, 2003).

Pseudo-infections of dicrocoeliasis in humans are more common than true infections, and occur due to the consumption of raw sheep liver infected with adult flukes of *D. dendriticum* (Cabeza-Barrera et al., 2011, Haridy and Morsy, 2003). Of 208 cases of dicrocoeliasis in Saudi Arabia, only 7 were thought to be true infections (el-Shiekh Mohamed and Mummery, 1990). In Lebanon, Lebanese Halzoun syndrome (LHS) is an allergic reaction in the upper respiratory tract which can occur after the consumption of raw sheep or bovine liver (a traditional Lebanese dish) (Khalil et al., 2013). Of 32 patients presenting with LHS, parasites were recovered from 3 and morphologically identified as *D. dendriticum*, indicating that this helminth may be the cause of LHS(Khalil et al., 2013).

*Trichinella spiralis* and *Taenia* spp. also cause disease in humans due to consumption of infected or contaminated and improperly cooked meat. In the case of *T. spiralis* there have been 337 clinical cases, including an outbreak in Argentina, infections identified during community surveys in the People’s Democratic Republic of Lao (Lao PDR), and two cases in the USA, since 2010 (Conlan et al., 2014, Calcagno et al., 2014, Holzbauer et al., 2014). All cases were traced to eating raw or undercooked pork. In the USA the two cases were a father and son who had hunted and eaten inadequately cooked wild boar (Holzbauer et al., 2014). The outbreak in Argentina was from undercooked commercially available pork (Calcagno et al., 2014), while in Lao PDR there have been a number of outbreaks over the years due to consumption of raw pork, a local delicacy (Conlan et al., 2014).

There are three main *Taenia* spp. which cause zoonotic taeniasis or cysticercosis, namely *Taenia solium, T. saginata* and *T. asiatica.* Known as the beef tapeworm, *T. saginata* is found in bovines, while *T. solium* the pork tapeworm and *T. asiatica* infect pigs (Ale et al., 2014). Despite having different definitive hosts, *T. asiatica* is very similar genetically to *T. saginata*, much closer than it is to *T. solium* with whom it shares a common host (Bowles and McManus, 1994, Jeon et al., 2007, Gordon et al., 2015). To date, there have been no reports of *T. asiatica* infection occurring outside Asia (Figure 3, Supplementary Table 1).

*T. solium* causes cysticercosis in humans, where ingestion of eggs or gravid proglottids of *T. solium* causes cysticerci to develop in body tissues, similar to the process in a porcine host. In contrast, *T. saginata* and *T. asiatica*  cysticerci do not develop in humans and only cause intestinal taeniasis (adult worms in the gastrointestinal system (GIT)). Ingestion of raw or undercooked meat containing cysticerci of *Taenia* spp.results in adult worms in the intestine. Poor hygiene is a key part of transmitting cysticercosis, with individuals harbouring adult *T. solium* worms able to autoinfect themselves by ingesting expelled eggs, or infecting others by contaminating the environment and food products. Neurocystercercosis (NCC) occurs when cysticerci of *T. solium* form in the brain of the host, causing severe neurological complications including behavioural changes (psychosis and depression) and death in some individuals (Almeida and Gurjao, 2010, de Almeida and Gurjao, 2011, Verma and Kumar, 2013, Sarangi et al., 2013) (Table 2). Depression is associated with NCC, as has been observed in 84% of NCC patients in Brazil (de Almeida and Gurjao, 2011). However, cysticerci can develop in any tissue and can cause a range of symptoms (Figure 3, Table 2). Since 2010 there have been 81 published case reports of NCC (n=81) (Figure 3, Table 2). Seizures are the most common symptom of NCC, together with headache and numbness (Table 2). Largely, NCC has been reported in developing countries, particularly India, with cases in Europe and the USA generally attributed to immigrants and returning travellers (Bouteille, 2014).

*T. asiatica* has never been reported as causing cysticercosis in humans (Galan-Puchades and Fuentes, 2013b) and this is supported by the genetic similarity of *T. asiatica* with *T. saginata,* which likewise does not cause human cysticercosis (Jeon et al., 2009, Jeon et al., 2007). Molecular diagnosis of cysticerci in humans, rather than immunodiagnosis, which does not distinguish between *T. solium* and *T. asiatica*, is a method whereby species identity can be confirmed. However, the morphology of the scolecesof *T. solium* and *T. asiatica* are sufficiently distinct that species diagnosis can be made (Galan-Puchades and Fuentes, 2013a). In contrast, *T. asiatica* and *T. saginata* are morphologically quite similar and cases of taeniasis may thus have been misdiagnosed (Galan-Puchades and Fuentes, 2013b, Parija and Ponnambath, 2013). Differentiating between those two species is important in an epidemiological context to determine whether *T. asiatica* has spread beyond Asia.

**Figure 3:** World map showing the geographic locations of human and animal infections with *Taenia asiatica, Taenia solium,* and *Taenia saginata* based on the 2010-2015 published literature. Pie graphs show the relative proportions of each species for humans and animals based on the number of cases identified (Suppl. Table 1) from the 2010-2015 published reports..

Other zoonotic *Taenia* spp.include *T. multiceps, T. serialis* and *T. brauni*, which cause coenurosis, while *T. crassiceps, T. ovis, T. taeniaeformis* and *T*. *hydatigena* cause taeniasis (<http://www.cdc.gov/dpdx/coenurosis/index.html>) (Webman and Gilman, 2013)*.* These are rare infections, however, with only small numbers of *T. multiceps* (n=3), and *T. crassiceps* (n=4) infections reported in humans since 2010 (Ambekar et al., 2013, Mahadevan et al., 2011, Goesseringer et al., 2011, Flammer Anikpeh et al., 2014, Ntoukas et al., 2013, Roesel et al., 2014). These tapeworms can be found in a variety of animals including domestic and wild canids and felids as well as ruminant animals worldwide (Image 1);humans act only as intermediate hosts for these *Taenia* species*.*

*Taenia crassiceps* may in future be an emerging zoonotic helminth, with its emergence likely linked to immune deficiency, such as that associated with HIV AIDs, as it is more common in individuals who are HIV-positive (Goesseringer et al., 2011, Giordani et al., 2014, Tian et al., 2012, Flammer Anikpeh et al., 2014).

## 4. Urbanisation

Cats and dogs are responsible for a number of zoonotic helminths with *Echinococcus*, hookworm, and *Toxocara* among the most well-known. These animals have considerable contact with humans, being popular pets worldwide. In addition to the presence of these companion animals, stray cats, wild dogs and other canids such as foxes, are often found around human dwelling sites having adapted well to urban and semi-urban environments. Rodents are another group of animals that have adapted well to urban environments. The black rat, *Rattus rattus,* has an almost global distribution due to human movement around the world and it may be responsible for the introduction of new species of zoonotic helminth to previously non-endemic areas (Figure 2). Helminth infections in wild animals, which may normally have limited human contact, can be introduced to domestic animals which do have contact with humans (Figure 4). This leads to the increased potential of human helminth infections which were once generally considered diseases of wildlife only (Figure 1, 2, 4). Hunting and consumption of wild animals, such as boar, are another mode of FBH infection in humans (see section on ‘Terrestrial’ Food Borne Helminthiasis) (Figure 4).

Environmental modification is the main driver of wildlife spill-over into human environments, and includes deforestation, city development, mining and dams. Deforestation is a major factor in the spill-over of wildlife zoonoses. In the last 10 years, 13 million hectares of forests were annually? cleared globally, compared with 16 million hectares per year in the 1990’s (FAO, 2010) (Figure 4). While deforestation has slowed it still occurs at a high rate, reducing the natural habitat available for native animals. Much of this land is converted into farmland or city development. By reducing natural habitats, native animals are forced into closer contact with domestic animals and humans which has led to disease spill-over from wildlife to humans and domestic animals, but also from domestic animals to wildlife. In the case of echinococcosis there are both sylvatic and domestic lifecycles whereby the tapeworm infection can be transmitted between the two groups of animals. There are species of *Echinococcus* that are primarily parasites of wildlife but which can also be found in domesticated animals (Addy et al., 2012, de la Rue et al., 2011). Foxes, which frequent rural and semi-urban areas, are important definitive hosts of *E. granulosus*.

**Figure 4:** Venn diagram showing transmission pathways of zoonotic helminths between wild animals, domestic animals and humans.

Figure 1 shows different host groups, the parasite species covered in this review that they carry, and indicates whether these groups involve wildlife, livestock or domestic infections. The majority of these parasite species overlap these three categories being either wildlife/livestock or wildlife/domestic, with the remainder considered wildlife only. *Baylisascaris procyonis* is an important wildlife parasite of raccoons which, due to the mammal’s rapid adaptation to urban environments, is now occasionally found in domestic dogs, and is a clear zoonotic infection risk for humans.

### Echinococcosis

Arguably the most important of these helminths are the *Echinococcus* species. Echinococcosis is a clinically important disease and among the most prevalent of the zoonotic helminthiases with 2-3 million individuals worldwide estimated to be infected with *E. granulosus* and 0.3-0.5 million with *E. multilocularis* (McManus, 2010, Craig et al., 2007)*.*

*E. granulosus* occurs globally while *E. multilocularis* infections mainly occur in the Northern hemisphere (Figure 5, Suppl. Table 2) (McManus et al., 2012). *E. multilocularis* causes alveolar echinococcosis (AE), while *E. granulosus* causes cystic echinococcosis (CE).

Definitive hosts for *E. granulosus* and *E. multilocularis* are typically dogs or other canids including foxes, coyotes, and wolves, as well as cats (McManus et al., 2003). Feeding raw offal to dogs is an important mode of transmission and a risk factor for human CE infection(Van Kesteren et al., 2013, Li et al., 2014a). Intermediate hosts for *E. granulosus* tend to be livestock such as sheep, goats, pigs, cattle, horses and camels (Cardona and Carmena, 2013, McManus et al., 2003); while the intermediate hosts of *E. multilocularis* are typically small rodents (McManus et al., 2003). *E. vogeli* and *E. oligarthrus* have rodents as intermediate hosts and bush dogs and wild felids as definitive hosts, respectively.

The fox is an important definitive host of *E. multilocularis* and *E. granulosus* , and one that has increasing contact with humans in both urban and rural environments. Most cases of echinococcosis occur in developing countries where rapid urbanisation is occurring in combination with poor hygiene and food safety practices (Figure 5, Suppl. Table 2). In this case, increases of *Echinococcus* spp.in the wild animal population may be indicative of potential human infections. *E. vogeli* cases, resulting in polycystic echinococcosis (PE), are rare in humans and are primarily limited to rural areas of South and Central America (Figure 5). However, with the population expansion and deforestation that is occurring in South America, the interface between humans and the animals carrying *E. vogeli* will only increase. Since 2010 there have been 7 cases reported in the literature of *E. vogeli* infection including one imported case in the Netherlands (Figure 5, Suppl. Table 2) (Stijnis et al., 2013).

Figure 5 and Suppl. Table 2 outline details of reported human echinococcosis cases occurring world-wide since 2010. The majority of these cases are assumed to be *E. granulosus,* although immunological or molecular diagnostics are rarely performed on the cysts once identified as a hydatid.

 In Australia, *E. granulosus* is of veterinary importance with the life cycle maintained in rabbits, kangaroos, wallabies, wombats, feral pigs, foxes, dingoes and dog/dingo hybrids in the wild, and the domestic life cycle involving livestock and domestic dogs.. The prevalence of *E. granulosus* is of concern for potential human infection through public use of rural areas for picnicking, hiking and camping. Dingoes, foxes and wild dogs are also increasingly encroaching into urban areas bringing the parasite closer to the human population (Jenkins, 2006, Jenkins et al., 2014a, Jenkins et al., 2014b, Beveridge and Spratt).

**Figure 5:** World map showing the geographic location of human and animal infections with *Echinococcus* spp. based on the 2010-2015 published literature.. Pie graphs show the relative proportion of each species infecting? humans and animals based on the number of cases recorded for the period 2010-2015 (Suppl. Table 2)..

However, all countries with rising rates of urban expansion will lead to in increased human contact with new and novel parasitic diseases of animals. Developed countries are thus hardly immune to the impact of parasitic zoonoses due to increasing population size, urbanisation and extension into new areas and habitats, an example being tree clearing in the Amazonian rainforest for new urban developments and farming.

### Emerging wildlife zoonoses

Increasing habitat destruction and human encroachment on natural areas has led to an increase in the contact of wild animals with humans, and also with companion animals (Figure 4). Spillover of zoonotic helminths occurs between wildlife and domestic animals; spillover can go both ways, wildlife to domestic and vice versa. Animals such as raccoons and skunks are known pests in the Northern hemisphere, and are often found in cities living off household rubbish. As indicated above, raccoons carry *Baylisascaris procyonis*, a nematode which can cause severe neurological disease in humans (Cottrell et al., 2014). In Africa and Asia, primates are often found in cities and villages, and are hunted for food, allowing for possible human infection with zoonotic agents including *Oesophagostomiasis bifurcum* and *Schistosoma mansoni* (Ghai et al., 2014, Erko et al., 2001). It is inevitable that as wild habitats are destroyed and global warming impacts on food sources that transmission of wildlife zoonosis to humans will increase. Due to urbanisation, wildlife zoonoses are currently emerging as medically important diseases of humans, *O. bifurcum* (Africa), *B. procyonis* (North America)*, Angiostrongylus cantonensis* (worldwide) and *A. mackerras* (Australia)*,* and *Haycocknema perplexum* (Australia)*,* among them.

*Oesophagostomum bifurcum* is primarily a parasite of monkeys, but is also the most common cause of oesophagostomiasisin humans. Similar to most other nematode species, the lifecycle of *O. bifurcum* is direct, with humans becoming infected by ingesting infective larvae (<http://www.cdc.gov/dpdx/oesophagostomiasis/index.html>). All human and animal cases reported in the literature since 2010 have occurred in Africa (Ghai et al., 2014) (Table 3). Around 250,000 individuals in Ghana and Togo are thought to be infected with *O. bifurcum*, while human cases were identified in Asia and South America prior to 2010 (Bogers et al., 2001). Random amplified polymorphic DNA (RAPD) comparison of *O. bifurcum* from humans and primates showed distinct clustering with the human isolates genetically distinct to those from different primate species (de Gruijter et al., 2004, de Gruijter et al., 2006). This would suggest that zoonotic transmission does not occur.. Similarly, while a high prevalence of *O. bifurcum* was found in primates from an area of Northern Ghana, no human cases were reported despite the fact that activities considered to promote zoonotic transmission occurred in this location (van Lieshout et al., 2005). Cryptic species of *O. bifurcum* have been described in Uganda with at least one found in humans and five other species of primates (Ghai et al., 2014). Experimental infection of primates with *O. bifurcum* cultured from human stools resulted in infection in primates, indicating that while zoonotic transmission may not be apparent, the biological potential is there (Eberhard et al., 2001).

*Alaria* is similar to *Oesophagostoma* in that it has the biological potential for zoonotic transmission.. Alariosis is due to infection with a larval trematode and can be categorised as a FBH as human infection occurs following the consumption of raw or undercooked intermediate hosts (Gonzalez-Fuentes et al., 2014), much in the same way as gnathostomiasis, which is caused by *Gnathostoma* spp., parasites of amphibians, reptiles, and birds. Alariosis is rare, with only one reported human case in North America, and caused by infection with *A. americana* (Fernandes et al., 1976, Freeman et al., 1976, McDonald et al., 1994). However there are concerns in Europe regarding the zoonotic potential of *A. alata,* since it has been found in animals across the continent , particularly wild boars and foxes (Table 3). Wild boars are a common paratenic host in Europe and may be the cause of future zoonotic infections of *A. alata* in humans.

Baylisascariasis and Angiostrongyliasis are infections caused by the nematodes *Baylisascaris procyonis* and *Angiostrongylus* spp., respectively. A survey of birds and mammals in the USA found *B. procyonis* in 87 birds (18 species) and 64 mammals (8 species), including raccoons (Evans, 2002a). Raccoons pose the most threat to humans due to the close association between human habitats and these animals (Evans, 2002a). *A. cantonensis* is known colloquially as the rat lung worm, the rat being the main definitive host of this parasite, and it is found worldwide (Aghazadeh et al., 2015). Rats, much like raccoons, are commoninhabitants of urban environments.

*B. procyonis* has been found in animals from USA, Germany, Canada, China and Japan (Jardine et al., 2014, Evans, 2002a, Kuchle et al., 1993, Popiolek et al., 2011, Xie et al., 2014), although reported human cases are restricted to Germany, Canada and the USA, with the most occurring in the USA (Table 3). There have been four human cases of *B. procyonis* since 2010 and 23 reported since 1975, with 21 recorded since 1993, showing that this disease is likely on the increase (Table 3).

Humans are accidental hosts of infection with both *A. cantonensis* and *B. procyonis.* Infection with *A. cantonensis* occurs when an infected molluscan host is consumed, while *B. procyonis* infection results from ingestion of embryonated eggs (<http://www.cdc.gov/parasites/baylisascaris/biology.html> ; <http://www.cdc.gov/parasites/angiostrongylus/biology.html>). In both species the larval stage of the parasite migrates to various tissues causing visceral larva migrans (VLM), ocular larva migrains (OLM) and neural larva migrans (NLM) (Boschetti and Kasznica, 1995, Chun et al., 2009, Gavin et al., 2002, Kazacos et al., 2013, Aghazadeh et al., 2015). Human infections with both species are rare and often occur in children who accidentally ingest contaminated soil (*B. procyonis*) or infected snails/slugs (*A. cantonensis*).

Twenty species of *Angiostrongylus* have been described but only *A. cantonensis,* and *A. malaysiensis* have been found to cause meningitis in humans (Aghazadeh et al., 2015). *A. vasorum* is commonly found in dogs but no human cases have been identified. While diagnosis of angiostrongyliasisin a clinical setting is based on morphology, there are several serological tests available although none have been certified for clinical use. Clinical indicators such as eosinophilic meningitis and neurological signs are common symptoms associated with *Angiostrongylus* infection (Mackie et al., 2013). Molecular diagnostics have not yet been used in the clinical setting for angiostrongyliasis although LAMP and PCR assays have been developed for the detection of *A. cantonensis* in snails and for retrospective PCR on the cerebral spinal fluid of previously identified human cases of *Angiostrongylus* spp. (Chen et al., 2011, Constantino-Santos et al., 2014, Eamsobhana et al., 2013). Morphological identification can only occur when fully mature adult worms are available as the other life-cycle stages are virtually identical (Bhaibulaya, 1968, Aghazadeh et al., 2015)*.* It is therefore possible that some of the worms removed from humans and animals may have been *A. mackerrasae*, an *Angiostrongylus* spp. native to Australia(Aghazadeh et al., 2015)*. A. mackerrase* has recently been found in a flying fox in Queensland, Australia. This is the first report of *A. mackerrase* in an accidental host and demonstrates biological potential for human infections with this species (Mackie et al., 2013). Birds (tawny frogmouths) and possums from Sydney, Australia, have both been shown to be infected with *A. cantonensis* causing neurological symptoms in these animal hosts. Infections in tawny frogmouths follow a seasonal pattern which indicates that they could be an important sentinel species for *A. cantonensis* (Ma et al., 2013). Two human infections from Sydney Australia, occurred in autumn and winter, further indicating a seasonal pattern for this helminth in Australia (Aghazadeh et al., 2015).

*A. (Parastrongylus) costaricensis* is an intestinal parasite of rats and has also been shown to cause intestinal or abdominal angiostrongyliasis in humans. However, this parasite has been poorly studied with only limited reports of human infection in the literature over the past ten years, although there are likely to be many unreported cases (Palominos et al., 2008, Incani et al., 2007, Quiros et al., 2011, Rodriguez et al., 2008, Waisberg et al., 1999, Pena et al., 1995, Graeff-Teixeira et al., 1991).

The worldwide distribution of *A. cantonensis*  was likely due to the introduction of infected rats or snails in ships and shipping containers. Thiengo *et al* (Thiengo et al., 2013) present a distribution map of the imported African snail, *A. fulica*, in Brazil, showing an almost universal spread throughout the country. While other snail species in Brazil, including native snail species, act as intermediate host, the explosive geographical distribution of *A. fulica* is a concern (Thiengo et al., 2010, Thiengo et al., 2013). In China, *A. fulica* and the large freshwater snail, *Pomacea canaliculata,* are both introduced species which have similarly spread throughout the country. Recent outbreaks of *A. cantonensis* in China can be traced back to consumption of *P. canaliculata* (Thiengo et al., 2013, Lv et al., 2009, Lv et al., 2008)*.*

Infected slugs and/or snails may be ingested either by consumption of raw or undercooked molluscs on purpose, or accidentally. Snails are regularly consumed in China as a delicacy. A study on washing vegetables focusing specifically on removal of snails from lettuce found that even after rinsing each lettuce leaf individually, some snails remained, providing a simple mechanism for accidental infection (Yeung et al., 2013, Ewers and Anisowicz, 2014).

*H. perplexum* is an emerging nematode parasite of humans in Australia. Similar to *Trichinella,* itoccurs in the muscle fibres of the host. Six cases have been reported since 1994 with the most recent case identified in 2011 (Table 3) (Basuroy et al., 2008, McKelvie et al., 2013, Spratt et al., 1999). Progressive muscle weakness and wasting are the common signs of infection and all cases were formally identified after muscle biopsy detected nematode worms in the muscle fibres. Three cases each occurred in the Tasmania and in North Queensland.

The lifecycle of *H. perplexum*  is unknown and the parasite may originate from a vertebrate, invertebrate or plant host, or from the soil. The history of the known human infections with *H. perplexum* suggest that it is a zoonosis occurring in native Australian animals such as wombats, Tasmanian devils, wallabies and kangaroos, and potentially in domestic animals such as dogs, chickens and rabbits (Basuroy et al., 2008, McKelvie et al., 2013, Spratt et al., 1999). Native animals in Australia are increasingly found in urban and semi-urban areas and these include tawny frogmouths and possums which are known hosts of *A. cantonensis* (Gelis et al., 2011, Ma et al., 2013).

## 5. Climate change

### Zoonotic filariasis

Filarial nematodes require an insect vector, often a mosquito, although blackflies (*Simulium* species) transmit *Onchocerca* spp. The larvae of filarial nematodes mature in the insect vector before being injected into the definitive host. Of all the zoonotic helminths, filarial nematodes are the most likely to increase their areas of future transmission due to climate change and weather changes which will result in the expansion of the relevant insect vectors into new regions.

#### Onchocerca spp.

The most prevalent filarial nematodes of humans are *Onchocerca* and *Dirofilaria* spp. *Onchocerca* spp. could also be included under urbanisation as a number of species causing human disease are found primarily in wild animals, or have experienced spill over from wild animal populations into domestic. *Onchocerca* spp*.* which cause disease in humans and originate from wildlife are *O. lupis*, originally identified in wolves but now found in domestic dogs, *O. dewittei japonica* in wild boars, and *O. jakutensis* in wild deer (Sréter-Lancz et al., 2007, Egyed et al., 2001, Otranto et al., 2013c, Koehsler et al., 2007, Burr et al., 1998, Labelle et al., 2013, Eberhard et al., 2013). Domestic herds of deer are at risk of infection with *O. jakutensis* thereby establishing a domestic lifecycle. *O. gutterosa* and *O. cervicalis* are parasitic in bovines and horses and mules, respectively.

There have been 14 cases of zoonotic onchocerciasis reported in the literature since 2000, nine identified as *O. lupi* and three as *O. dewittei japonica* and three where a species was not determined (Figure 6, Suppl. Table 3). Onchocerciasis caused by *O. lupi* in dogs and wolveshas been reported worldwide (Egyed et al., 2001, Labelle et al., 2013, Otranto et al., 2013a, Otranto et al., 2013b). The first reported case of *O. lupi* in a human originated from Turkey and was identified both morphologically and by molecular analysis using the *12S* ribosomal and *cox1* mitochondrial genes (Otranto et al., 2011). Further human cases have been identified in the USA, Turkey, Tunisia and Iran (Mowlavi et al., 2014, Eberhard et al., 2013, Otranto et al., 2012) (Figure 6, Suppl. Table 3).

Being primarily a canine helminth, monitoring of canine populations for *O. lupis* will help inform the potential risk for human infection. Originally identified in wolves, *O. lupis* is a good example of a wildlife helminth which has transitioned from a sylvatic to a domestic lifecycle.

#### Dirofilaria spp.

*Dirofilaria* spp. are more prevalent in humans than *Onchocerca* spp. and are increasing both in incidence and geographical range. *Dirofilaria* spp.have a similar lifecycle to *Onchocerca* spp., with *D. immitis* differing in that the adults are found in the pulmonary arteries, rather than in the skin and subcutaneous tissues (<http://www.cdc.gov/dpdx/dirofilariasis/index.html>). Other *Dirofilaria* spp., such as *D. repens*, are commonly found as nodules, often migratory, in subcutaneous tissue. Vectors for *Dirofilaria* spp. (*D. immitis, D. repens, D. tenuis,* and *D. ursi*)are mosquitoes, including *Culex pipiens, Anopheles maculipennis,* and *Ades albopictus,* while *D. ursi* utilizes a black fly. *D. immitis* causes pulmonary disease in humans while other *Dirofilaria* spp.produce subcutaneous nodules which can be painful and sometimes migratory; these nodules can occur all over the body (Figure 6, Suppl. Table 3). *Dirofilaria* spp. are found worldwide; *D. tenuis* isfound in North America and is primarily a helminth of raccoons. Only two cases of human infection with *D. tenuis* have been reported since 2010, both in the USA (Figure 6, Suppl. Table 3). The most recent human case of *D. ursi* was reported in 1996 but it still occurs in bear populations of North America (Michalski et al., 2010, Haldane et al., 1996).

*D. immitis* and *D. repens* are the most common causes of dirofilariasisin humans with the majority of *D. repens* human cases reported post-2010 occurring in Europe (proportion of reports in the literature 73.8%), and the majority of *D. immitis* human cases from the same period occurring in Africa (proportion of reports in the literature 54.5%) (Figure 6, Suppl. Table 3).

In Hong Kong there is some evidence of a novel zoonotic *Dirofilaria* species.The sequences of filarial helminths, taken from a small number (3) of humans, were identical to each other but did not share 100% homology with the sequences from *D. repens* or *D. immitis* (To et al., 2012). In the same study, worms were also taken from dogs (n=200) and cats (n=100) and the majority were identified as *D. immitis* and *D. repens,* although 3% of the worms from dogs were identical in sequence to those of human origin (To et al., 2012). This demonstrated a potential zoonotic transfer from dogs to humans for this new species, which the authors suggested the taxonomic name of *Candidatus dirofilaria hongkongensis* [synom. *Dirofilaria honkongensis*] (Figure 2)*.*

Mosquito monitoring is an important measure to determine the potential for clinical impact of zoonotic filariasis, by specifically determining which species are circulating within a region. Such studies on mosquitoes have documented the spread of vectors and filarial nematodes throughout Europe. *D. immitis* and *D. repens* have been found in North and South America. In Europe there are many studies identifying these species in mosquitoes and dogs, as well as in humans (Carleton and Tolbert, 2004, Cuervo et al., 2013a, Eberhard, 2013, Ermakova et al., 2014, Kronefeld et al., 2014, Salamatin et al., 2013, Cuervo et al., 2013b, Bockova et al., 2013, McKay et al., 2013, Sassnau et al., 2013, Joseph et al., 2011, Cielecka et al., 2012) (Figure 6, Suppl. Table 3). A 2014 study of mosquitoes in Germany identified the presence of *D. immitis, D. repens* and *S. tundra* (Kronefeld et al., 2014). This reflects the introduction of exotic mosquito species capable of carrying dirofilarial helminths emerging in new areas within Europe since 2010 (Bockova et al., 2013, Capelli et al., 2011, Ferreira et al., 2015, Kronefeld et al., 2014, Montarsi et al., 2015, Yildirim et al., 2011). The prevalence of *Dirofilaria* spp*.* in mosquito vectors and dogs in the same area indicates that human infections are autochthonous in Europe, rather than originating from abroad. Due to climate change, allowing the spread of the mosquito vectors to new regions, as well as the movement or spread of infected hosts (i.e. dogs, both wild and domestic, transmitting *D. repens*), dirofilariasis is an emerging disease in Europe with potential for human transmission. *D. repens* causes 90.7% of human cases in Europe, while *D. immitis* has been reported in 5.9% of cases (Figure 6, Suppl. Table 3). Human dirofilariasis cases are becoming more common in Europe, as reflected in the recent literature (Figure 6, Suppl. Table 3). Whereas there had been only 30 prior cases of dirofilariasis in Serbia, serology of 297 individuals in 2014 was *Dirofilaria* spp.-positive in 18.3% of the study population with both *D. repens* and *D. immitis* reported as being present (Tasic-Otasevic et al., 2014). Similarly, seroprevalence of *Dirofilaria* spp.in blood donors from Russia was 10.4% (n=317) in 2011 (Kartashev et al., 2011).

Based on the results of one very large antigen-based study on *Dirofilaria* spp. in dogs (1.3% positive; 142,426/10,734,132) in the USA, *D. immitis* is considered the most common zoonotic infection of dogs over the last 5 years (Figure 6, Suppl. Table 3) (Little et al., 2014). In Europe, both *D. repens* and *D. immitis* are responsible for a high proportion of reported cases in the literature in animals (36.78% and 42.68%, respectively) (Figure 6, Suppl. Table 3).

Other rare *Dirofilaria* spp.causing human infection are *D. striata*, which is a filarial nematode of bobcats, although it has also been found in dogs (Orihel and Ash, 1964, Orihel and Isbey, 1990, Pacheco and Tulloch, 1970), and *D. subdermata*, a filarial nematode of porcupines. There are no recent reported human cases due to these species.

#### ***Thelazia spp.***

Thelaziasis is a rare nematode infection in humans caused by *Thelazia callipaeda* and *T. californiensis* (<http://www.cdc.gov/dpdx/thelaziasis/index.html>). Despite its current relative rareness , it has the potential for increased human prevalence as the geographical distribution of *Thelazia* spp. in animals is showing an upward trend (Figure 6, Suppl. Table 3). A range of animals can act as definitive hosts with canids the most common. In all hosts the worms reside in the conjunctival sac, leading to eye irritation, watering and sometimes pain. For humans, the presence of a “foreign body” sensation has been described in many case reports since 2010 (Table 4) (Magnis et al., 2010, Maia et al., 2014). Originally known as the oriental eye worm, it has been increasingly reported in animals from European countries including a recent report of canine ocular thelaziariasis caused by *T. callipaeda* in Greece, the first report of this parasite in an animal from that country (Diakou et al., 2015). Based on the high prevalence of *T. callipaeda* in animals and its increasing geographical distribution, human cases from other countries are inevitable (Figure 6, Suppl. Table 3). Human infections with *T. californiensis* are rare with no reports in the literature since 1996, and only three case reports since 1975, all from the USA (Doezie et al., 1996, Knierim and Jack, 1975, Kirschner et al., 1990).

**Figure 6:** World map showing geographic locations of human and animal infections with zoonotic filarial nematodes based on the published literature from 2010-2015. Pie graphs showing the relative proportions of each species infecting humans and animals based on the number of cases identified (Suppl. Table 3) from reports published in 2010-2015.

### ***Schistosoma* species**

Clinical schistosomiasis occurs worldwide in the tropics and sub-tropics, and is caused by four main species of schistosome, *S. haematobium* (Africa), *S. mansoni* (Africa, South America, the Middle East) and *S. japonicum* and *S. mekongi* (SEA).Of these, only *S. japonicum* and *S. mekongi* are traditionally considered zoonotic. However hybridization occurring in Africa between *S. haematobium* and other species, particularly *S. bovis* and *S. curassoni,* may give rise to a third zoonotic schistosome (Webster et al., 2013) while natural infections of *S. mansoni* have also been found in nonhuman hosts (Muller-Graf et al., 1997, Legesse and Erko, 2004). Autochthonous infections of *S. haematobium* have recently been found in Europe marking a new expansion of this species (Boissier et al., 2015).

*S. japonicum* is endemic in China, the Philippines and parts of Indonesia and has been shown to parasitise 46 mammalian species as definitive hosts (He et al., 2001). *S. mekongi* occurs in the People’s Democratic Republic of Lao (Lao PDR) and Cambodia, and is currently only thought to infect dogs, in addition to humans. In China an estimated 600 million people are at risk of infection and approximately 0.3 million people are currently infected, while in the Philippines 6.7 million people live in endemic areas; of these, 1.8 million people are considered to be directly exposed to infection through water contact activities (McManus et al., 2009, Carabin et al., 2005, Riley et al., 2005).

A number of drug-based intervention trials have indicated that bovines are major reservoir hosts for schistosomiasis japonicain China (Gray et al., 2009a, Gray et al., 2007, Gray et al., 2008a, Gray et al., 2009b, Guo et al., 2006). The results of these intervention trials, combined with mathematical modelling, found bovines are responsible for approximately 75% of human transmission (Gray et al., 2009a, Gray et al., 2007). These animals are used as work animals, primarily on the marshlands (China) or rice paddy fields (Philippines), where the *Oncomelania* snail intermediate hosts live. As a result it is principally farmers and fishermen who are at most risk of infection with *S. japonicum*, although domestic (washing) and social (swimming) activities are also important risk factors (McManus et al., 2010, Li et al., 2000).

In China the prevalence of *S. japonicum* in humans has fallen, due to extensive control efforts undertaken by the Chinese government, from 12 million in 1949 to 1 million in 2004 to about 300,000 in 2011 (Zhou et al., 2004, McManus et al., 2010). Thousands of livestock remain infected so this number of potential reservoirs of infection means that simply treating humans with praziquantel (PZQ) will not prevent transmission. An individual living in an endemic area can readily become reinfected after treatment. After the implementation of the World Bank Loan Project (WBLP) in 1992-2001 relaxation of control efforts saw an increase in infection in previously controlled areas (Xianyi et al., 2005). Re-emerging schistosomiasis in areas of Sichuan province (China) was studied with 24 counties found to be endemic for the disease with 8 re-emerging (Liang et al., 2006). The average ‘return time’, or time it took for disease to be considered endemic again after cessation of treatment, was 8.1 years with the shortest time 2 years and the longest 15 years (Liang et al., 2006). Other reasons for re-occurrence are unusual flooding events, environmental modification, such as the building of dams, and relaxation in control efforts following the termination of the WBLP (Zhou et al., 2004, Zhu et al., 2008, Zhou et al., 2005, Wu et al., 2008). The Three Gorges Dam (TGD) upstream of the Dongting Lake area in Hunan province, a region highly endemic for schistosomiasis, has raised concerns about the potential redistribution of *O. hupensis hupensis,* in China, and the potential for the spread of schistosomiasis into new areas. An initial 5-year assessment of transmission of schistosomiasis following construction of the TGD found no immediate impact (Gray et al., 2012). A more recent study considered the density of oncomelanid snails in low, medium, and high elevation areas which showed a decrease generally in snail populations during the period 2003-2014, with the exception of the low elevation areas where the snail density began to increase in 2014 (Wu et al., 2015). While the TGD in China seems to have had a limited effect on schistosomiasis transmission to date, this is not true for other areas where dam building projects have been undertaken. In several African countries, the construction of dams, such as the Gezira-Managil Dam in Sudan, the Aswan Dam in Egypt and the Melkasadi Dam in Ethiopia, has led to increased schistosomiasis transmission (Gryseels et al., 2006).

Rodents have previously been thought to be important in schistosomiasis japonica transmission but this is now considered unlikely since they are semi-permissive hosts (Hu et al., 2012). Population numbers are also impossible to determine, limiting how much can be concluded from prevalence studies of these animals, as generally, only a few are trapped during surveillance. Laboratory infections of Chinese field rats, *R. norvegicus* and *R. norvegicus albus,* with *S. japonicum,* showed that 95% and 70-90%, respectively, of worms did not reach the liver and, of those that did, the females had reduced sized ovaries which would further impact their ability to produce viable eggs (Ho and He, 1963). A later study indicated that the transmission potential for rats in the Philippines was low, due to the majority of worms becoming trapped in the lungs with only few maturing to produce eggs (Mitchell et al., 1990, Oshima et al., 1978). Additionally, their small size and the relatively limited amount of faeces they produce would minimise the level of environmental contamination with schistosome eggs.

Horses, donkeys, mules, pigs and dogs – which until recently were uncommon in rural areas – are susceptible to infection but are not considered important in transmission due to their relative lack of water contact. Nevertheless, an increase in infection of humans in mountainous areas of Yunnan Province in China has been linked to an increase in the numbers of domestic animals in the area (Jiang et al., 1997b). In mountainous areas with low bovine numbers, transmission appears to involve a human-snail cycle, particularly as human faeces are used fertiliser (Jiang et al., 1997a). The use of human faeces as fertiliser will likely vary from village to village and its use has reportedly been decreasing in China (Wang et al., 2005). From these studies it can be concluded that humans probably act as the main hosts for schistosomiasis transmission in areas where there are low numbers of domestic animals, even though wild rodents are present.

As indicated earlier*, S. mekongi* is found inLao PDR and Cambodiaand was endemic in Thailand, although this schistosome has not been reported there since the 1980’s, although the requisite snail intermediate host, *Neotricula aperta,* can still be found in some areas (Limpanont et al., 2015, Bunnag et al., 1986). To date only humans, dogs and pigs in Cambodia have been found infected with *S. mekongi* (Khieu et al., 2013, Matsumoto et al., 2002). Recent reports of *S. mekongi* in humansfrom Lao PDR infection indicated a prevalence of 0.1% in 2012, 8.6% co-infection with *Opisthorchis viverrini* from 2006-2007, and 24.3% in 2006 (Sayasone et al., 2012, Laymanivong et al., 2014, Sayasone et al., 2015).

*S. haematobium*, the cause of urinogenital schistosomiasis,is considered to be a parasite only of humans with no animal reservoirs involved in its life cycle. However, recent multi-loci molecular analysis of parasite samples has shown that hybridization events have occurred between *S. haematobium* and ruminant schistosome species resulting in *S. haematobium/S. bovis* and *S. haematobium/S. curassoni* hybrid worms (Webster et al., 2013). These hybrid schistosomes were found in children, but not in ruminants, in Senegal (Webster et al., 2013). In another worrying trend for the emergence of new foci of schistosomiasis, *S. haematoboium* has recently been reported in Europe where a number of human cases in France, Italy and Germany were linked to a popular tourist spot in France (Boissier et al., 2015). While no snails infected with *S. haematobium* have been identified in this area, laboratory infections with locally occurring *Bulinus* spp. snails were successful in producing cercariae. The emergence of schistosomiasis in Europe may be linked to climate change and globalisation. Globalisation, through the movement of people from endemic areas to new areas, may have played a role in introducing *S. haematobium* to the waterways while climate change may allow the snail hosts to better survive and migrate to new areas for longer periods of time.

### Soil transmitted helminths: Hookworm/*Toxocara/Ascaris/Trichuris*

The term soil transmitted helminth (STH) refers to intestinal worms which are transmitted through soil contaminated with infectious eggs or larvae and generally used for the human only helminths - hookworm (*Ancylostoma duodenale* and *Necator americanus*), *Ascaris lumbricoides*, and *Trichuris trichiura*. However these helminths have zoonotic counterparts – hookworm (*A. ceylanicum, A. caninum, A. braziliense*, and *Uncinaria stenocephala*), *Ascaris suum,* and *Trichuris suis*. *Toxocara* species (*T. cati* and *T. canis*) which can also be transmitted via contaminated soil. Climate change will be an important factor in worm development in a range of helminths including *Ascaris* spp. Temperature is an important factor for the embryonation of eggs in the external environment;whereas the embryonation of *Ascaris suum* eggs can occur at 25°C, the speed of embryonation is increased at the higher temperature of 35°C (Kim et al., 2012). Increasing global temperatures will likely speed up development of newmatode larvae in eggs, potentially increasing the level of transmission.

#### Hookworm

*Ancylostoma* spp.from cats and dogs present a range of different disease states in humans; from dermatitis caused by *A. braziliense*, patent infections caused by *A. ceylanicum* and eosinophilic enteritis due to *A. caninum* (Loukas et al., 1992, Prociv and Croese, 1996). The eggs of different *Ancylostoma* spp. are morphologically identical so that definitive microscopic diagnosis impossible. Precise diagnosis is important for monitoring hookworm prevalence in cats and dogs – both domestic and wild. *A. ceylanicum* and *A. braziliense* are hookworms of both cats and dogs, while *A. caninum* is the dog hookworm (<http://www.cdc.gov/parasites/hookworm/biology.html>). *A. braziliense* is a common cause of nematode-induced cutaneous larval migrans (CLM) in humans, although other helminths, particularly trematode species such as *Schistosoma* spp.*, Trichobilharzias* spp., and *Uncinaria stenocephala*, can also cause this condition (Le Joncour et al., 2012). The morbidity most commonly associated with an accidental infection with *A. caninum* is eosinophilic enteritis, and potentially unilateral subacute neuroretinitis.

It has been posited that many human hookworm cases caused by *Ancylostoma* spp. may have been incorrectly diagnosed as *A. duodenale* when they were actually due to *A. ceylanicum* (Traub, 2013, Schär et al., 2014, Ngui et al., 2012b). As indicated above, the eggs of *Ancylostoma* spp. are indistinguishable microscopically and larval culture is required for precise morphological identification of the later developmental larval? stage. Whereas molecular diagnosis can be specific and sensitive there is also high molecular similarity between *A. duodenale* and *A. ceylanicum* and PCR primers need to be carefully designed for species-specificity. High resolution melting (HRM) after PCR amplification has previously been used to distinguish between hookworm species (Ngui et al., 2012a). Differentiation between the species in animals is an important factor in planning public health measures due to the differences in the pathology in humans ranging from CLM to eosinophilic enteritis. Historically, *A. ceylanicum* had been thought to be a rare or abnormal infection in humans.

A recent study in Cambodia found a high prevalence of hookworm in both human and dog populations. Of the infected dogs, 90% harboured *A. ceylanicum* while51.6% of humans with hookworm were infected with *A. ceylanicum* (Inpankaew et al., 2014, Schär et al., 2014)*.* The remaining 48% of hookworm-positive individuals harboured *A. duodenale* (3.2%) and the human-only hookworm spp. *Necator americanus* (44.8%) (Inpankaew et al., 2014). Hookworm is prevalent in tropical regions such as SEA due to the prevailing environmental conditions which result in damp soil conditions, a factor conducive for the survival of hookworm larvae (Bethony et al., 2006).

Indded, climate change may play a major role in changing the distribution of hookworm spp. by modifying the environment through the production of warm moist soil, thereby increasing the survival rates of hookworm larvae, or conversely by causing soil to become too dry to support larval development.

#### ***Toxocariasis***

Toxocara canis and T. cati are nematodes parasitic in dogs and cats, respectively, but are also zoonotic. Toxocara infections in companion animals are a source of human transmission in developing countries due to stray dogs and cats and in developed countries attributable to domestic pets.

Toxocariasis is caused by the migration of Toxocara larvae through tissues, known as visceral larva migrans. Liver abscesses are normally thought to be a rare complication of human infection with Toxocara spp.; however, there have been 13 reported cases of toxocariasis resulting in this pathology since 2010, and it is therefore of medical importance, likely representing an emerging syndrome. There has been a total of 150 cases of human infection with Toxocara spp. reported since 2010 with various pathologies (Table 5) (Zibaei et al., 2014).

Studies from developed countries have shown worrying trends in the prevalence of Toxocara eggs on the fur of pets and the poor hand washing practices of their owners. A study in the Netherlands found high prevalence of Toxocara spp. eggs on the fur of 12.2% (n=152) of dogs and 3.4% (n=60) of cats (Overgaauw et al., 2009). The same study looked at the behaviour of dog and cat owners with 50% reporting that they allowed their animal to lick their face. Only 15% of dog owners and 8% of cat owners always washed their hands after touching the animal. This is a potential risk as simply patting an infected animal and not washing hands afterwards can lead to infection and toxocariasis. Similar studies have been performed in Italy, where two studies found 6.6% - 9.7% of stray and pet dogs harboured T. canis infection (Simonato et al., 2015, Paoletti et al., 2015).

#### ***Ascaris suum* and *Trichuris suis***

*A. suum* and *T. suis* are nematodes of pigs which can infect humans.Humans and pigs become infected with *A. suum* by ingesting eggs or food contaminated with eggs (<http://www.cdc.gov/parasites/ascariasis/biology.html>;<http://www.cdc.gov/parasites/whipworm/biology.html>). *A. suum* is found worldwide while *A. lumbricoides*, a human only *Ascaris* species,is restricted to the tropics, particularly in developing countries. *A. suum* has been linked to visceral larval migrans and eosinophilic pneumonia in humans (Izumikawa et al., 2011, Pinelli et al., 2011).

*A. lumbricoides* and *A. suum*, are very similar morphologically and genetically. There has been considerable discussion as to whether they are in fact the same species, which may mean that *ascariasis* occurring in developed countries may be due to pig *Ascaris* (Arizono et al., 2010, Shao et al., 2014, Leles et al., 2012, Dutto and Petrosillo, 2013, Betson et al., 2014). Hybridization between *A. suum/A. lumbrioides* has resulted in at least one human case (Dutto and Petrosillo, 2013). Meanwhile, human cases of *Trichuris suis* and hybrids of *T. suis* and *T. trichiura* have been identified in Uganda (Nissen et al., 2012, Cutillas et al., 2009). Such hybridization events will impact on the zoonotic potential of *T. suis,* potentially increasing its infectivity to humans*.*

## 6. Points for discussion

### **Health education**

In 2000, unsafe water, inadequate sanitation and poor hygiene were attributed to 3.7% of the global disease burden and disability (as measured by DALYs), leading to 1.7 million deaths (Mathers et al., 2007). With many parasitic helminths the same features are major risk factors for infection. Health education packages have been developed for a number of helminth infections. In China an education package for the prevention of human STH infections ( *A. duodenale, A. lumbricoides*, and *T. trichiura*) which targets school children has been successful in increasing hand washing, awareness of STH and significantly reducing the incidence of STH (McManus et al., 2014, Bieri et al., 2013). The worms have zoonotic counterparts in - *A. caninum* and *A. ceylanicum*, *A. suum*, and *T. suis,* which could also be targeted for control using this developed and tested education package.

A health education program for control of taeniasis has also been trialled in Tanzania. The program consisted of a trained teacher presentation, video, and pamphlet which increased knowledge of cysticercosis in the school children (Mwidunda et al., 2015). One of the interesting outcomes of this trial was an increase in the willingness of children to condemn infected pork, although there was a reluctance to report cysticercosis in their own pigs, partly due to lack of effective treatment available in the study area (Mwidunda et al., 2015). Introduction and use of latrines in endemic areas helps prevent infection by increasing hygiene practices and preventing pigs from eating human faeces. However, in some areas cultural taboos prevail, particularly among men, relating to sharing a latrine, who were therefore more likely to defecate in the open than in a latrine (Thys et al., 2015).

A further helpful education resource is an online program, ‘the vicious worm’, targeting *T. solium* and cysticercosis (Johansen et al., 2014). In addition to good hygiene practices, reducing the overall environmental contamination with helminth eggs and larvae by animal hosts is also necessary. This involves regular deworming of animals, although wild-life populations, such as raccoons, which are infected with *Baylisascaris procyonis,* will be difficult to target in a chemotherapy-based control campaign. Limiting contact with potentially egg-contaminated locations through avoiding communal raccoon defecation areas covering sand boxes and enclosing areas where children play to prevent animals from entering, can also be effective preventative measures.

### Targeting definitive hosts and vectors

Control programs for fascioliasis and Asian schistosomiasis often target animal hosts, thereby reducing the number of eggs entering the environment and limiting human exposure to infection. In the Philippines, methods of control targeting bovines with *Fasciola* specieshave included keeping animals penned, rather than tethered on rice paddies, in rivers, or close to water holes - which are habitats of lymnaeid snail hosts. Other fascioliasis control measures include drying out bovine stool for a number of weeks before utilising it as fertiliser, bovine chemotherapy, and snail control (Gray et al., 2008b). Similar methods would apply for schistosomiasis control although bovine chemotherapy, bovine vaccination, snail control, replacement of bovines with tractors, and barrier farming for bovines have been trialled in China (Gray et al., 2012, Gray et al., 2009a, Gray et al., 2007, Gray et al., 2008a, Gray et al., 2009b, Guo et al., 2006, Hou et al., 2008). In the Philippines, human chemotherapy has often been the only method of schistosomiasis control, although mollusciciding and/or environmental modifications (such as removing vegetation from along waterways) to remove snail habitats have also been employed.

Climate change is also a potential player with regards to expansion of certain parasites to new areas, particularly those helminths whose lifecyles involve mosquito or snail vectors, which often have specific climatic requirements (Genchi et al., 2011, Lv et al., 2006, Caminade et al., 2015, Pedersen et al., 2014). Climate change may also inhibit spread of some disease vectors due to reductions in suitable environments, ana example being *A. cantonensis*, for which mathematical models predict will decrease in prevalence as a result (Lv et al., 2006).

The control of zoonotic filariasis can involve targeting the insect vectors, animal reservoirs and prophylaxis or treatment of humans by chemotherapy. There are currently no human vaccines against any of the filarial worms; however potential vaccine targets have been identified and “veterinary only” vaccines are being trialled (Verma and Jaiswal, 2013, Godel et al., 2012).

### Molecular tools

Molecular techniques can be invaluable for investigating zoonotic helminths including their environmental monitoring, diagnosis and species identification, and the assessment of control interventions, life-cycle elucidation and identification of hosts.

#### Environmental monitoring/surveillance

Monitoring the environment and animal hosts for zoonotic diseases is an important tool in control. Due to the morphological similarity of many helminths, molecular methods are ideal to correctly identify species. Speciation in this case is important for differentiating between animal only parasites and those that are zoonotic. Environmental monitoring is already employed for a number of parasite species such as *B. proyonis* in the USA since raccoons use communal areas for defecation, or racoon latrines, where these areas are examined for eggs (Evans, 2002b, Page et al., 2011, Page et al., 2014). Raccoon latrines pose a risk for transmission of *B. procyonis* to children and animals that may encroach on the latrines. Infections of *B. procyonis* have also been found in dogs, another crossover of a wildlife infection to a domestic animal, and kinkajous (honey badger) (Windsor et al., 2009, CDC, 2011, Rudmann et al., 1996). Sentinel pigs have previously been employed for monitoring the transmission of *T. solium* in Africa with some success (Devleesschauwer et al., 2013, Gonzalez et al., 1994).

Monitoring vectors, such as snails and slugs, and mosquitoes in addition to definitive hosts is an important way of measuring potential exposure to infection and implementing control procedures, or for issuing health warnings. The presence of vectors outside of a recognised parasite-endemic area can be an important indicator of the potential for zoonotic spread into new transmission zones.

#### Species identification

Unambiguous and accurate identification of a parasite species is important when considering potential hosts, control interventions and treatment. As mentioned above, eggs and larvae of many helminths are morphological similar and it is often difficult to identify a particular species. There have been several cases where the original parasite diagnosis has been retrospectively corrected after molecular analysis, including the identification of the novel species *Dirofilaria honkongensis*. Mitochondrial genes, particularly the *cox1* and *nad* genes, and nuclear ribosomal genes, particularly the *ITS1* and *ITS2* genes, have been utilised in molecular identification of helminth parasites infecting humans. Mitochondrial and/or ribosomal genes for most species are available through NCBI GenBank (<http://www.ncbi.nlm.nih.gov/genbank/>).

High resolution melting (HRM) qPCR can be used to distinguish between closely related parasites (Rojas et al., 2015, Li et al., 2015, Ngui et al., 2012a). Identification of zoonotic filariasis is most commonly done after excision of subcutaneous nodules containing the parasite (*Dirofilaria* spp.), or removal of parasites from eyes (*Onchocerca* spp.) and other tissues (*Meningonema peruzzii*) for morphological examination, histopathological characteristics and/or DNA sequencing. There are also a number of commercially available serological tests, particularly for diagnosis of canine filariasis (SNAP 4Dx, Uranotest Dirofilaria, Witness Heartworm, RIM). The pronounced morphological similarity of many worms, which are not always amenable for removal without tissue damage, means that morphological identification to species is difficult and species identification based solely on morphology is almost always not relable or conclusive. Therefore the use of molecular amplification and/or sequencing and immunological techniques have proved invaluable.

A Russian study investigated human cases (n=8) of echinococcosis using sequencing of the *cox1* gene to differentiate the species, identified *E. canadensis* (genotype G6)as the cause of CE in two of the cases while *E. granulosus* *sensu stricto* (genotype G1) was identified as the cause of CE in the other six cases; all of the AE cases for which sequence information was obtained were shown caused by Asian type *E. multilocularis* (Konyaev et al., 2012). The authors noted that camels, the usual host for *E. canadensis*, were not common in the area from which the patients originated (Konyaev et al., 2012). Other potential hosts of *E. canadensis* include moose (*Alces alces*), Siberian roe deer (*Capreolus pygargus*) and reindeer (*Rangider tarandus*), emphasising that *E. canadensis* is a potentialconcern for human CE infection in areas where camels are absent. Similarly, *E. vogeli* was diagnosed in a hunter from French Guiana using mitochondrial DNA sequencing for species differentiation as serology showed patterns for both AE and CE (Knapp et al., 2009). Further *E. canadensis* cases have been identified in Mongolia and China using molecular techniques (Ito et al., 2014, Ma et al., 2015). In Mongolia, of 43 CE cases examined, 31 were due to *E. canadensis*, while in China a single case of *E. canadensis* infection was identified. Molecular diagnosis is an important approach for *Echinococcus* species identification. Due to the different intermediate and definitive hosts used by the different species (Nakao et al., 2013), correct identification of human cases will help with control efforts and in the monitoring of human disease risk.

Diphyllobothrium latum (the fish or broad tapeworm) is the largest tapeworm infecting humans, reaching up to 10 meters in length (<http://www.cdc.gov/parasites/diphyllobothrium/>). Several other Diphyllobothrium species have been reported to infect humans; they include D. pacificum, D. cordatum, D. ursi, D. dendriticum, D. lanceolatum, D. dalliae, D. nihonkaiense, and D. yonagoensis. Although these species are considered to occur less frequently in humans than *D. latum*, it is possible that misdiagnosis has resulted due to the high level of morphological similarity and/or the poor quality of proglottids obtained for microscopy. In Korea a retrospective study utilising the *cox1* gene found 62 cases originally identified as *D. latum* were actually *D.* nihonkaiense (Jeon et al., 2009). Retrospective molecular analysis in China has also found incorrect identification of D. nihonkaiense as D. latum, although D. latum infection was also confirmed in some cases (Chen et al., 2014). When looking at case reports of Diphyllobothrium species infections since 2010, D. nihonkaiense has been identified more frequently than D. latum (Table 1). The majority of Diphyllobothrium spp. infections do not cause any adverse events and infected individuals only became aware of the infection after passing worm segments.

#### Diagnosis and Assessment of Control Programs

Assessing the effectiveness of control interventions relies on the diagnostics used. In the case of schistosomiasis, diagnosis using the thick faecal smear Kato-Katz (KK) method is the ‘gold standard’ for egg detection in humans. However, it is recognised as having a low level of sensitivity, particularly in low intensity infections (McGarvey et al., 2006, Yu et al., 2007). Similarly, the KK has been shown to underestimate the prevalence of hookworm infection by as much as 80% (Easton et al., 2015). Nevertheless, due to the low cost of implementing the KK (US<4 cents per slide), it remains a popular choice (Speich et al., 2010) but it must be emphasised that evaluating control interventions based on KK data may drastically underestimate the amount of parasite infection present.. The intervention may have reduced intensity, but it may not necessarily have reduced prevalence. In villages in China where mass drug (praziquantel) administration (MDA) for *S. japonicum* was terminated, there was a rebound of infection to the original levels2-15 years later despite the low prevalence and intensity of infections achieved while the MDA was ongoing (Liang et al., 2006). Nebertheless, considerable government effort in China over many years has led to a large reduction in both *S. japonicum* prevalence and intensity of infection, so that the elimination of schistosomiasis there is now conceivable. However, the poor sensitivity of the KK for detecting low intensity infections, will continue to be a problem in China as the control program continues towards the goal of elimination and the authorities will need in future to ensure that rebound infection does not appear. 1. The true endemic picture and impact of schistosomiasis control in the P.R. China can only be measured accurately by implementing more sensitive diagnostic techniques than are used currently. Accordingly, molecular diagnostics can provide an essential adjunct for assessing the true picture in areas where *S. japonicum* prevalence and intensity are low or where elimination is suspected.

### Success stories

#### Schistosomiasis and Dracunculiasis

Although discussed earlier, it is worth re-emphasising here that the control of schistosomiasis in China has been a major success story with the estimated numbers of infection falling from 12 million in 1949 to about 300,000 in 2011 (Zhou et al., 2004, McManus et al., 2010, Yang et al., 2014). Continued surveillance using better diagnostics will be required to maintain the schistosomiasis control efforts into the future so that the goal of elimination can be achieved.

A similar, perhaps even a greater story of success, is dracunculiasis, now slated for global elimination***.*** *Dracunculus medinensis*, or guinea worm, is a parasite of humans in Africa, the Middle East and parts of Asia, primarily India. Guinea worm disease is contracted when people consume water from stagnant sources contaminated with Guinea worm larvae. There have been reports of *Dracunculus* spp.infecting animals such as dogs and donkeys (Bimi et al., 2005). It is unclear if the species infecting these animals is *D. medinensis,* or instead has been misidentifieddue to the considerable morphological similarity of female worms, as diagnosis is primarily based on microscopy. Male worms of different *Dracunculus* speciesdo differ morphologically but they are rarely available for study as they die after copulation. *D. insignis* is known to occur in a range of canids (foxes, coyotes) and felids (bob cat, opossum) in North America (Langlais, 2003, Lucio-Forster et al., 2014). Sequencing of the *18S*-rRNA gene of *D. insignis* and *D. medinensis* isolates from raccoons in North America, canids from Africa and humans in Africa, showed that each species was distinct at the genomic level, although sequence similarity was high (Bimi et al., 2005). Furthermore, sequences from *Dracunculus* spp. removed from canids and humans in Ghana were identical, suggesting that despite being primarily a helminth of humans, there may be instances where *D. medinensis* doesinfect other animals (Bimi et al., 2005). Indeed, recent studies on the state of guinea worm in Chad reported *D. medinensis* in dogs (Al-Awadi et al., 2014, Eberhard et al., 2014). All dog and human specimens collected in the Chad study were subject to sequencing using both the *18S* rRNA and *cox1* genes (Eberhard et al., 2014). All isolates were identical and positively identified as *D. medinensis*. It is therefore possible that dogs can act as reservoir host for *D. medinensis*, leading to increased transmission to humans. Patients in the area were asked a series of dietary questions in order to access the potential of paratenic hosts in the area which might serveas reservoirs of transmission. Generally, humans admitted to eating cooked monitor lizards, snake skin and frogs at certain times of the year (Eberhard et al., 2014). Dogs had been noted to scavenge and eat raw reptiles and amphibians and, particularly to consume fish entrails (Eberhard et al., 2014). *D. insignis* has been shown to require a paratenic host (Eberhard and Brandt, 1995) and it is thought that the infection reported in dogs from Chad, and some of those human infections reported outside the endemic areas, may have been due to consumption of paratenic hosts (Eberhard et al., 2014).

It is unclear whether *Dracunculus* spp. from animals can infect humans. Humans and other animals become infected with *Dracunculus* spp.by drinking water contaminated with copeopods infected with L3 larvae (<http://www.cdc.gov/dpdx/dracunculiasis/index.html>). The initiation of the Guinea Worm Eradication Program (GWEP) has led to a decrease in the number of *Dracunculus* infections from 3.5 million in 1986 to 148 reported cases in 2013 (WHO, 2013) to 126 in 2014 (<http://www.cartercenter.org/health/guinea_worm/index.html>), and as such is a great success. Indeed, Guinea worm disease is set to become the second human disease in history, after smallpox, to be eradicated. It will be the first parasitic disease to be eliminated and the first disease to be eradicated without the use of a vaccine or drug, relying instead on health education and political will to stop the spread of this devastating disease.

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## 7. Conclusions

Underreporting or misdiagnosis of zoonotic helminths leads to an underestimation of their importance for human health. Many of the helminth diseases considered in this review are chronic in nature, and it may be many years before a positive diagnosis is sought and obtained by an afflicted individual. For many zoonotic helminths of public health importance, appropriate and accurate surveillance of animal hosts and vectors is essential to determine the risk for human infections and for mapping the geographical distribution of the diseases they cause. Climate change, urbanisation, and globalisation are increasing and/or changing the distribution of zoonotic helminths. Climate change modifies the environment, creating optimum temperatures and levels of humidity for survival of STH eggs and larvae in soil, and for the movement of vectors including certain mosquito species, and molluscan hosts into new areas, leading to an increased geographical distribution. However, climate change will not always result in increased survivability or the spread of zoonotic infectionsas some areas will become drier, thereby reducing the survivability of STH and limiting the spread of mosquitoes and molluscs.. As an example, , climate change is predicted to have a detrimental effect on the spread of the molluscan hostsfor *Angiostrongylus* spp. Based on climate change predictions a model found that suitable habitats for *A. cantonensis* would decrease (York et al., 2014).

FBH can be readily controlled by implementing food standards and treatment for imported and locally grown foods, as well as education regarding the preparation of food. Simply cooking food adequately kills all zoonotic helminths that may be present in meat or on vegetables and fruit. Similarly, washing vegetables and fruit before consumption will remove up 80% of zoonotic helminths present as eggs, larvae, or within vectors such as slugs or snails (Adenusi et al., 2015, Duedu et al., 2014, Yeung et al., 2013), while freezing fish will help the control of fish-borne helminths at the consumer end.

Environmental monitoring of soil, vectors, and definitive hosts are crucial for measuring the potential impact of zoonotic helminthiases on human populations. Education programs should be undertaken or public warnings given in endemic areas when monitoring shows high infection prevalence in surveyed animals, or during known seasonal transmission times. Mosquito control is already undertaken in some areas for control of viral diseases and the same measures can be implemented for control of filarial nematodes. In the case of *B. procyonis,* the ability to identify a raccoon latrine and manage the risk can help prevent human infections. FBH can be readily controlled through food education and by implementing food standards and treatment for imported and locally grown foods. In summary, the overall message is that while globalisation, urbanisation, and climate change will impact on the spread of zoonotic helminths, appropriate awareness of the risk they pose will help in the future control and prevention of the human diseases they cause.

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