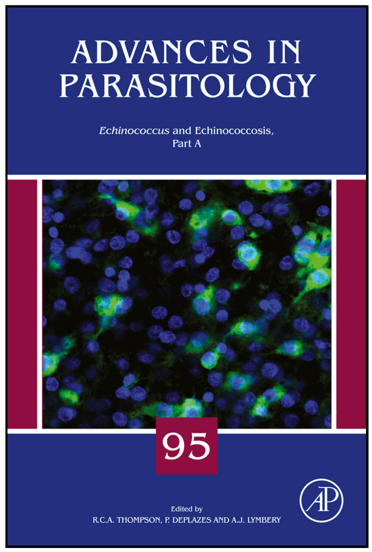

From Deplazes, P., Rinaldi, L., Alvarez Rojas, C.A., Torgerson, P.R., Harandi, M.F., Romig, T., Antolova, D., Schurer, J.M., Lahmar, S., Cringoli, G., Magambo, J., Thompson, R.C.A., Jenkins, E.J., 2017. Global Distribution of Alveolar and Cystic Echinococcosis. In: Thompson, R.C.A., Deplazes, P., Lymbery, A.J., (Eds.), *Echinococcus* and Echinococcosis, Part A, pp. 315–493.
ISBN: 9780128114711

Academic Press

CHAPTER SIX

Global Distribution of Alveolar and Cystic Echinococcosis

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Advances in Parasitology, Volume 95
ISSN 0065-308X
http://dx.doi.org/10.1016/bs.apar.2016.11.001

Echinococcus and Echinococcosis, Part A, First Edition, 2017, 315–493

Abstract

Alveolar echinococcosis (AE) and cystic echinococcosis (CE) are severe helminthic zoonoses. *Echinococcus multilocularis* (causative agent of AE) is widely distributed in the northern hemisphere where it is typically maintained in a wild animal cycle including canids as definitive hosts and rodents as intermediate hosts. The species *Echinococcus granulosus, Echinococcus ortleppi*, *Echinococcus canadensis* and *Echinococcus intermedius* are the causative agents of CE with a worldwide distribution and a highly variable human disease burden in the different endemic areas depending upon human behavioural risk factors, the diversity and ecology of animal host assemblages and the genetic diversity within *Echinococcus* species which differ in their zoonotic potential and pathogenicity. Both AE and CE are regarded as neglected zoonoses, with a higher overall burden of disease for CE due to its global distribution and high regional prevalence, but a higher pathogenicity and case fatality rate for AE, especially in Asia. Over the past two decades, numerous studies have addressed the epidemiology and distribution of these *Echinococcus* species worldwide, resulting in better-defined boundaries of the endemic areas. This chapter presents the global distribution of *Echinococcus* species and human AE and CE in maps and summarizes the global data on host assemblages, transmission, prevalence in animal definitive hosts, incidence in people and molecular epidemiology.

1. GENERAL INTRODUCTION

Alveolar echinococcosis (AE) and cystic echinococcosis (CE) are zoonotic diseases caused by *Echinococcus* spp. transmitted from carnivores. The history of these two distinct diseases has been reviewed in chapter 'Historical Aspects of Echinococcosis' by Eckert and Thompson (2017). In this chapter, the causative agents of human CE (a complex of several species with additional genotypes) are referred to using the well-recognized genotype terminology (G1−G10), although a more formal taxonomic nomenclature has now been proposed by Thompson (2017) in chapter 'Biology and Systematics of *Echinococcus*'. Human AE is caused by geographically distinct strains/genotypes of *Echinococcus multilocularis*.

In this chapter, we will focus on the distribution of CE in humans and animal intermediate hosts, as well as intestinal *Echinococcus granulosus* infections in definitive hosts. For *E. multilocularis*, the chapter focuses mainly on the distribution in canid definitive hosts (predominantly foxes outside North America and parts of Asia) and on AE in humans.

Since the last publications focusing on the global distribution of *Echinococcus* spp. (Schantz et al., 1995; Eckert et al., 2001) a considerable amount of evidence is now available documenting in much more detail the changing distribution of both AE and CE. This chapter attempts to give a general overview on the current distribution and epidemiology of both diseases but refers to some key reviews for more detailed information and citations. In addition, the authors present in this review many sources of information which are not easily available (e.g., the so-called grey literature) or had to be translated from original languages (e.g. Russian).

Finally, for more detailed information on the ecology of *Echinococcus* spp., including the different cycles and host ranges involved [see chapter: Ecology and Life Cycle Patterns of *Echinococcus* Species by Romig et al. (2017) and chapter: Echinococcosis: Control and Prevention by Craig et al. (2017)].

The burden of human echinococcosis can be expressed in terms of disability adjusted life years (DALYs). The global burden of disease of AE is estimated to be 18,200 cases per annum, resulting in approximately 666,000 DALYs (37 DALYs per case) (Torgerson et al., 2010). However, 91% of cases and 95% of the DALYs were estimated to be in China. Thus, there are approximately 1600 cases of AE per annum in Europe, Russia and central Asia resulting in 33,000 DALYs or 21 DALYs per case. Survival analyses of French and Swiss AE patients have shown that modern treatments such as resection of liver lesions followed by prolonged therapy with benzimidazoles can result in survival of AE patients similar to those of healthy populations (Torgerson et al., 2008; Piarroux et al., 2011). Where treatment options are available, the burden in terms of DALYs is modest because of the improved prognosis; for example, in Switzerland, there is a total burden of approximately 78 DALYs per annum due to AE, or 3.7 DALYs per case, 10 times less than the global estimate (Torgerson et al., 2008). This is one important factor for the predominance of the global burden in China, where the majority of cases were estimated to occur in resource poor communities on the Tibetan plateau, thus inflating the DALYs per case. In central Asia this is likely to be similar (Torgerson, 2017).

The latest estimate for the global burden of CE is 188,000 new cases per annum resulting in 184,000 DALYs (0.98 DALYs per case (Torgerson et al., 2015). The much lower human health burden of CE compared to AE is entirely due to the low mortality rate of CE relative to AE. However, it is important to note that as the lifecycle of CE in many countries involves livestock intermediate hosts, there can be economic and animal health repercussions beyond that of AE.

A comprehensive review of peer-reviewed literature was undertaken to record the current distribution at global, continental, regional, national, provincial, departmental (or any jurisdiction), administrative levels regarding *E. multilocularis* in wild canids (primarily foxes) and *Echinococcus* spp. causing CE in humans and intermediate hosts.

Relevant data on the prevalence/incidence of *E. multilocularis* and *E. granulosus* were identified through a combination of (1) structured searches of electronic bibliographic databases, (2) additional searches of the 'grey' literature, including unpublished studies and government and international reports (e.g., WHO, OIE, etc.) and (3) direct contact with researchers and health managers.

The online databases PubMed and SCOPUS were used to identify relevant studies for *E. multilocularis* and *E. granulosus s.l.* with the keywords "*Echinococcus multilocularis, Echinococcus granulosus*, alveolar echinococcosis, cystic echinococcosis and current and former country names." No restrictions were placed on publication dates and language. Researchers were contacted when additional information was required or when data needed to be disaggregated.

Studies were included if they provided (1) the number of people/animals surveyed, (2) the number of positive cases, (3) details about the methodology of diagnosis and (4) details of the geographical site where they were conducted, including the administrative level. Studies reporting only prevalence/incidence data without provision of the denominator were also included as these can be used to delineate the limits of transmission of AE or CE.

A repository of data in excel was created to collect all the information and a geographical information system was developed using Arc-GIS 10.2.2 software (ESRI, Redlands, CA, United States) to produce maps.

The data and maps produced for this chapter offer the potential to improve the spatiotemporal targeting of control measures and to enhance the cost-effectiveness of integrated disease control programmes for *E. multilocularis* and *E. granulosus* in definitive and intermediate hosts. However, we should take into account the limits and bias of these maps due to the fact that the real prevalence, incidence and burden of CE and AE are difficult to estimate. This is due to the patchy distribution of CE and AE within transmission areas, the high proportion of asymptomatic infected individuals and symptomatic patients living in resource-poor areas with logistical and/or economic constraints, who never reach medical attention, and the unknown effect of underreporting of diagnosed cases. This last aspect is primarily due to the widespread lack of mandatory notification of echinococcosis overall (reviewed in Rossi et al., 2016).

2. GLOBAL DISTRIBUTION OF *ECHINOCOCCUS MULTILOCULARIS*

2.1 General information

2.1.1 Global distribution

Although generally considered a parasite of the northern hemisphere, criteria for designation as an endemic region for *E. multilocularis* cannot be consistently defined largely due to marked global differences in surveillance effort and detection capacity, as well as variability in host assemblages and prevalence.

The most widely used systems for detection of genetic variability of *E. multilocularis* are the microsatellite EmsB and mitochondrial gene sequences. Due to its high discriminative power, EmsB has been primarily used for the study of local diversity in Europe (Knapp et al., 2008, 2009). Our present understanding of the global genetic structure of the parasite has been initially established using concatenated sequences of the mitochondrial *cob*, *nad2* and *cox1* genes (Nakao et al., 2009; Gesy et al., 2013), as well as by using *cox1* sequences alone (Konyaev et al., 2012a, 2013). Initially, haplotypes of mt DNA sequences were thought to cluster in correlation with geographical regions, forming 'European', 'Asian', 'Mongolian' and 'North American' clades (Nakao et al., 2009). More recent data, still limited by inadequate geographical and numerical sampling coverage, demonstrate that variants of the 'European' clade are widespread at least in western Canada (Gesy et al., 2013; Massolo et al., 2014; Gesy and Jenkins, 2015), 'Asian' haplotypes are reported in western Russia and St. Lawrence Island, Alaska, and isolates clustering most closely with the North American (Alaskan) N1 genotype were found in arctic parts of Siberia (Konyaev et al., 2013), Svalbard, Norway (Knapp et al., 2012) and St. Lawrence Island, Alaska (Nakao et al., 2009) (Table 1). The diversity of *E. multilocularis* in the circumpolar North is recently reviewed in Davidson et al. (2016).

The ecosystems where *E. multilocularis* occurs are as diverse as arctic tundra, high altitude grassland, but also agricultural and urban landscapes [characterized by Romig et al. (2017) in chapter: Ecology and Life Cycle Patterns of *Echinococcus* Species].

Occurrence in definitive hosts (foxes and other canids) was used to define endemicity for areas of Europe and North America. From Turkey, Central Asia and large parts of Russia and China, human data on AE were considered the most reliable source of information. Infections in rodent intermediate hosts were considered as an indication of endemicity

Table 1 Confirmed occurrence of *Echinococcus multilocularis* haplotype assemblages in animal and human hosts

E. multilocularis haplotypes	Confirmed presence	References
Asian haplotypes	Japan (Hokkaido); China (Sichuan); Mongolia, Kazakhstan; Russia (European part, southern Siberia); United States (Alaska, St. Lawrence Island)	Nakao et al. (2009), Ito et al. (2010), and Konyaev et al. (2013)
Mongolian haplotype	China (Inner Mongolia); Mongolia; Russia (Southern Siberia)	Nakao et al. (2009), Ito et al. (2010), and Konyaev et al. (2013)
North American (N1) haplotype	United States (Alaska, St. Lawrence Island); Norway (Svalbard); Russia (Northern Siberia)	Nakao et al. (2009) and Konyaev et al. (2013) Knapp et al. (2012)
North American (N2) haplotype	United States (Indiana, South Dakota, Minnesota)	Nakao et al. (2009) Yamasaki et al. (2008)
	Canada (Saskatchewan)	Gesy and Jenkins (2015)
European haplotypes	Europe (Austria, Belgium, France, Germany, Western Russia, Slovakia); Canada (British Columbia, Alberta, Saskatchewan)	Nakao et al. (2009), Konyaev et al. (2013), Gesy et al. (2013), Massolo et al. (2014), and Gesy and Jenkins (2015)

in a few cases. Fig. 1 depicts the global endemic area of *E. multilocularis* based on data mainly from wild canid definitive hosts.

2.2 *Echinococcus multilocularis* and alveolar echinococcosis in Europe

There are multiple, related mitochondrial haplotypes of *E. multilocularis* in Europe (Nakao et al., 2009), and microsatellite analyses have shown even more significant biogeographic genetic variability (Knapp et al., 2009).

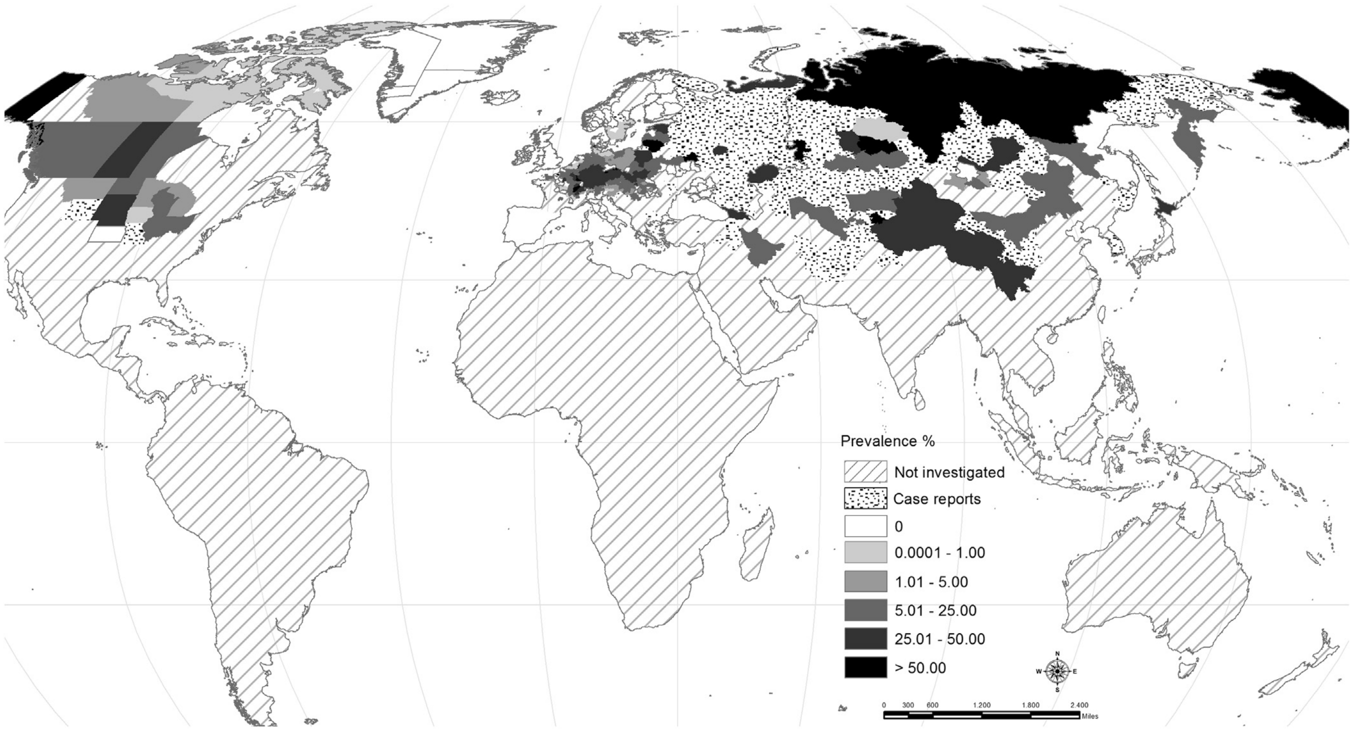

Figure 1 ***Current global distribution and prevalences of Echinococcus multilocularis in the main wild canid definitive hosts.*** In addition, in areas where data of wild canids are missing, case reports of AE in intermediate hosts or in humans as well as infections in other definitive hosts are given as *dotted areas*. For published details of the distribution/prevalence in the different countries/jurisdictions, see detailed maps (Figs. 2–4), Supplementary Material (Tables S1–S3) in Appendix A and text. Note that a positive finding in any host, study or jurisdiction renders the whole jurisdiction endemic.

Convincing evidence for the emergence of AE in Europe has been collected over the last 10 years (Gottstein et al., 2015). An expansion of the Central European endemic area has been observed to the north, west and to the east (see Fig. 2). Data generated in the last 20 years document that the Central European endemic area is connected to old known endemic areas in Eastern Europe and Asia. An emergence of AE has been documented in the Baltic region (Marcinkutė et al., 2015) with high prevalences in foxes and increasing numbers of human AE cases. The changes in parasite transmission have been associated with a drastic increase of fox populations in both rural and urban areas in Europe (Deplazes et al., 2004; Hegglin et al., 2015). Due to the long incubation period, increased incidences of AE can be expected in some known endemic areas and new cases can be expected in areas only recently discovered to be endemic. On the other hand, the epidemiological situation on the southern border of the Central European

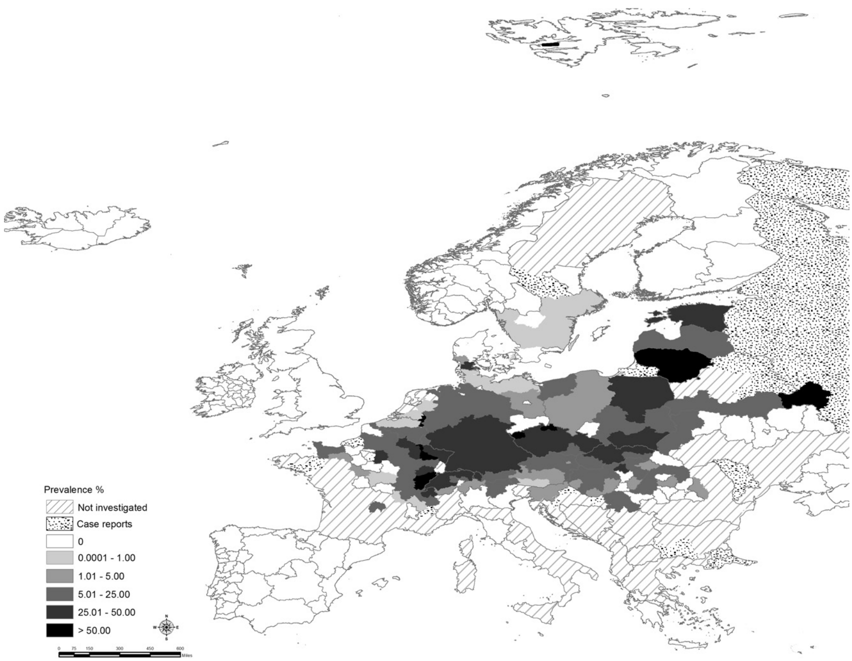

Figure 2 ***Current distribution of Echinococcus multilocularis in foxes (*****Vulpes vulpes, Vulpes lagopus*****) in Europe.*** Areas with case reports of AE in intermediate hosts or humans are approximately given as *dotted areas* if data of definitive hosts were missing. The detailed information (prevalence data in each jurisdiction) is listed in Table S1 of the Supplementary Material.

endemic area (Rausch, 1967) seems to be more stable but the endemicity has not been investigated intensively in all southeastern regions. South Europe is regarded as free of *E. multilocularis* but, in most of the areas, studies focusing on *E. multilocularis* have not been performed. For the situation in the European part of the Russian Federation, see Section 3.3.1.

2.2.1 Central Europe: France, Belgium, The Netherlands, Luxembourg, Germany, Switzerland, Czech Republic, Austria, Northern Italy

2.2.1.1 Transmission and host assemblages

Transmission of *E. multilocularis* in the 'old' endemic area of Central Europe is mainly based on the red fox as definitive host and voles (*Microtus arvalis* and *Arvicola* spp.) as intermediate hosts (Raoul et al., 2015), see chapter: Ecology and Life Cycle Patterns of *Echinococcus* Species by Romig et al. (2017).

There is evidence in many areas of Central Europe not only of a range expansion but also of an increase of the parasite prevalence in foxes (e.g., in Germany and The Netherlands) (Romig, 2002; van der Giessen, 2005). Simultaneous rapid increases of fox population densities with associated prevalence of *E. multilocularis* resulted in an estimated 10-fold increase of the parasite density in southwestern Germany (Romig et al., 2006). Red fox populations have increased throughout Europe in the last decades in all habitats, but especially in urban areas (Deplazes et al., 2004; Hegglin et al., 2015). Transmission of *E. multilocularis* is determined by host ecology (such as predator–prey preferences, defecating behaviour, activity patterns of definitive hosts and host dietary preferences). Key intermediate hosts have been identified for only central study areas in Europe and on Svalbard Island (Raoul et al., 2015); for most of the other areas there are insufficient data concerning rodent population composition and predation by definitive hosts. Therefore, it is difficult to understand the transmission patterns or predict changes in parasite abundance or distribution (such as range expansion). In the last few decades, an expansion of the endemic area was confirmed in the western, northern and eastern parts of Central Europe (Fig. 2); however, it is possible that the parasite was present at low prevalences in the past and is only newly detected in these areas. In some endemic areas, significant increases in prevalence have been demonstrated.

Besides foxes and voles as the key species involved in the cycle, the raccoon dogs (*Nyctereutes procyonoides*) as wild definitive hosts and muskrats (*Ondatra zibethicus*) as intermediate hosts may be of local significance, but their role in maintaining the cycle has not been well studied [see chapter:

Ecology and Life Cycle Patterns of *Echinococcus* Species by Romig et al. (2017)] (Bruzinskaite-Schmidhalter et al., 2012). Domestic dogs with patent infections have been found in several areas and may play an important role for parasite transmission to humans; however, most probably, they are not significant for maintaining the cycle in Central Europe (Deplazes et al., 2011). Cats, with low worm burdens and correspondingly low egg excretion (Kapel et al., 2006), are probably of negligible zoonotic significance in the maintenance of the *E. multilocularis* life cycle (Deplazes, 2015).

The ecology of *E. multilocularis* in rodents has been investigated in depth in a few focal areas in Europe; however, systematic investigations over large areas have not been done. For reviews, see [Raoul et al., 2015; chapter: Ecology and Life Cycle Patterns of *Echinococcus* Species by Romig et al. (2017)].

2.2.1.1.1 Infections in animals In large parts of Central Europe, *E. multilocularis* is present in red fox populations with average prevalences ranging between 0.1% and 50% (Fig. 2), for prevalences see Table S1 in Supplementary Material. A considerable amount of data has been accumulated in the last decade especially for foxes in Germany. Prevalence data for many countries can be retrieved from the EFSA Scientific Opinion on *E. multilocularis* infections in animals (EFSA, 2015b). However, temporal and spatial prevalence variations can be highly significant, and prevalence estimates are furthermore dependant on the population structure, the sampling method, the sample size and the sensitivity of the diagnostic methods. Therefore, differences in prevalences should not be over interpreted. Continuous monitoring of fox populations for *E. multilocularis* is not considered to be justified for the endemic area in Central Europe (Conraths and Deplazes, 2015).

As shown in Fig. 2, lower prevalences are generally found on the border of the endemic area. This might reflect low fox densities (such as in alpine areas) or low population densities of key intermediate hosts, but in most areas, it is not known if the recent findings represent a stable epidemiological situation with ecological factors limiting parasite transmission, and/or range expansion. In one study area in the Southern Alps of Switzerland, a stable epidemiological situation over more than 20 years was described, with the *E. multilocularis* endemic area determined by the southern border of the *M. arvalis* distribution (Guerra et al., 2014). Reports of autochthonous human AE in two patients between 1906 and 1922 from South Tyrol (Hosemann et al., 1928) suggest that recent reports of *E. multilocularis* in foxes in this region is a new detection and not a recent range expansion from the north (Manfredi et al., 2002; Casulli et al., 2005).

In **France**, between 2005 and 2010, a large-scale survey of foxes was conducted in 42 departments (representing almost all of northeastern France). The prevalences varied widely among departments, from 0% to 54% (mean prevalence 17%) (Combes et al., 2012).

Some eastern regions of the **Netherlands** are highly endemic, with prevalence in foxes reaching close to 60% in Limburg (Maas et al., 2014), while no records of infected foxes are known from the western parts of the country (EFSA, 2015b).

High prevalence in foxes is reported from **Luxembourg** and the southern parts of **Belgium**, while prevalence approaches 0% towards the north of **Belgium** (EFSA, 2015b).

In **Switzerland**, a clear gradient is apparent between the well-known high endemic areas in the northern and western cantons where prevalence estimates range from 44% to 53% and low endemic areas in the central (alpine) areas as well as the southern and southwestern cantons (prevalence range 2–12%) (EFSA, 2015b).

For **Austria**, older data show a clear division with high prevalence in the west (Vorarlberg, Tyrol) and low prevalence in the remaining country. Temporal changes are unclear, because surveys in different parts of Austria were done in different time periods (EFSA, 2015b).

In **Italy**, positive records in foxes are limited to the provinces of Trento and Bolzano (South Tyrol), while surveys further south and west (including Lombardy and Aosta) had negative outcomes (EFSA, 2015b).

In **Germany**, investigations of fox infection started in the late 1970s, initially centering on the southern parts of the country which were known to be endemic due to the occurrence of human AE cases (Zeyhle et al., 1990). Up to the present, data on the infection status of close to 100,000 foxes were gathered from all federal states of Germany (except for the cities of Bremen and Hamburg), which show a clear temporal and spatial structuring. Prevalence before 1995 was generally lower than after, and prevalence estimates in the elevated and mountainous regions of southern and central Germany were in both periods higher than in northern and eastern Germany. Studies on fox infection after 1995 resulted in prevalence estimates of 40.4–55.5% (Bavaria), 37.0% (Baden-Württemberg), 2.4% (Brandenburg), 35.9–40.5% (Hesse), 14.4 (Lower Saxony), 16.1–36.8% (North Rhine-Westphalia), 33.8% (Rhineland-Palatinate), 1.4–19.0% (Saxony-Anhalt), 0.0% (Schleswig-Holstein) and 30.9% (Thuringia).

Only older data with negative results are available from Berlin and Saxony [Table S1 and EFSA (2015b)]. *Echinococcus multilocularis* prevalence in urban fox populations is generally lower than in surrounding rural landscapes; examples are Stuttgart [17.3% (Deplazes et al., 2004)] and Munich [20.2% (König and Romig, 2010)]. Direct comparison of prevalence estimates between individual studies is often difficult due to the application of diagnostic methods of different test parameters. Studies, demonstrating a temporal prevalence increase after 1990, are available for the states of Baden-Württemberg (Romig, 2002), Lower Saxony (Berke et al., 2008) and Thuringia (Staubach et al., 2011). Apart from foxes, *E. multilocularis* worms and metacestodes were recorded from raccoon dogs; domestic dogs; domestic and wild cats; several species of voles, muskrats, coypu and various dead-end hosts such as wild boar or zoo animals [lit. in (EFSA, 2015b) and see chapter: Ecology and Life Cycle Patterns of *Echinococcus* Species by Romig et al. (2017)].

In the **Czech Republic** the prevalence of *E. multilocularis* in foxes ranges between 14% and 62%, with an average of 33% (Pijáček, 2011).

Based on recently improved diagnostic strategies, patent *E. multilocularis* infections have been diagnosed in dogs and cats in Switzerland, Czech Republic, Germany (Hegglin and Deplazes, 2013) and France (Umhang et al., 2014b). Prevalence of <1.5% was recorded in privately owned rural and urban pet dogs, but higher prevalences of 3–8% were found in dogs with free access to rodent habitats such as farm dogs and hunting dogs (Hegglin and Deplazes, 2013). Based on the prevalence of 0.3% in a representative dog population, the probability for an individual dog becoming infected at least once during 10 years was estimated at 8.7%. Large investigations of faecal samples sent to a private laboratory revealed *E. multilocularis* eggs in 0.13% of dogs from northern Germany and 0.35% in dogs from southern Germany (Dyachenko et al., 2008). Given that rural dogs with higher infection risk are less likely to receive veterinary care, this figure is probably an underestimate. Considering the total dog population (approximately 5.4×10^6 dogs) in Germany, approximately 13,000 are expected to be infected.

The prevalence of *E. multilocularis* in domestic or wild cats in Europe (determined by necropsy) ranged between 0% and 5.5% (Deplazes, 2015). Cat infections are characterized by low worm burdens and strongly reduced worm development, resulting in lower egg production as compared to foxes or dogs. Prevalences for patent *E. multilocularis* infections of 0.4–5% in cats were determined by PCR in several European countries (Dyachenko et al., 2008; Deplazes et al., 2011; van Asch et al., 2013). Therefore, the role of the cat for maintaining the cycle, or for zoonotic risk, is of low significance (Deplazes, 2015).

Pigs are susceptible to *E. multilocularis* oncosphere invasion but subsequent metacestode development is restricted resulting in dead calcified lesions without protoscoleces (Deplazes et al., 2005). Infections in pigs are therefore of no transmission significance but may represent a marker for the environmental contamination with eggs of *E. multilocularis*, especially pigs fed with grass or animals with outdoor access. In Switzerland, 10% of pigs kept outdoors are presented with liver lesions caused by *E. multilocularis* (Sydler et al., 1998). In Germany, contamination of forage stored in the open or straw litter was estimated to be the most likely source of infection in four farms (Bottcher et al., 2013).

Of veterinary importance is AE in dogs and a variety of captive nonhuman primates. In Central Europe, severe and often lethal liver infections in dogs have been regularly diagnosed since 1988 (Corsini et al., 2015; Deplazes and Eckert, 2001). Such infections can easily be diagnosed by necropsy and histology (as for humans) (Deplazes and Eckert, 2001), and therefore this may indicate an increased exposure of the dog population to this parasite. Based on the relatively large dog population and high prevalences of adult cestode infection in foxes, the susceptibility of dogs for AE is estimated as very low. Similar to dogs, lethal AE has been diagnosed in captive primates (Deplazes and Eckert, 2001), including lemurs (Umhang et al., 2013a), macaques (*Macaca* spp.) (Tappe et al., 2007), western lowland gorillas (Wenker and Hoby, 2011) and chimpanzees (*Pan troglodytes*) (Federer et al., 2016), white-handed gibbons (*Hylobates lar*) and squirrel monkeys (*Saimiri sciureus*). Based on the small numbers of primates exposed and the numerous cases described, the susceptibility of monkeys including apes to AE exacerbated by the infection pressure in captivity is considered to be very high.

2.2.1.1.2 Alveolar echinococcosis in humans Central Europe has been a known core endemic area for AE since the end of the 19th century [for historical review see chapter: Historical Aspects of Echinococcosis by Eckert and Thompson (2017)]. Historically, human AE cases distinct from CE were reported first from the Jura and Alps. Between 1982 and 2000, 599 AE cases (42% in France, 24% in Germany, 21% in Switzerland, 13% in other countries) were registered in the 'EurEchinoReg' project in Central Europe (Kern et al., 2003). For a comprehensive review of the AE situation in Europe, see (Vuitton et al., 2015). In most European countries, human AE and infections in animals are notifiable (not the case for human AE in Denmark, Switzerland and the Netherlands) (Vuitton et al., 2015). For Germany, however, it was estimated that the national surveillance system failed to detect 67% of AE cases over 3 years (Jorgensen et al., 2008).

Most recently there is clear evidence of increasing incidences of AE in **Switzerland**, parts of France, Germany and Austria (Gottstein et al., 2015). Yearly, around 150−200 new AE cases are expected to be diagnosed in Central Europe, with the regional annual incidences (AE cases/10^5 inhabitants) varying between 0 and 8.1 (Vuitton et al., 2015). In Switzerland the overall yearly AE incidence has increased significantly from 0.1 (1993−2000) to 0.26 (2001−05) (Schweiger et al., 2007); thereafter, the incidences persisted at the higher level until 2012. Most of the cases are found in highly populated areas around the largest cities of the country and not in the lower populated mountain areas (Deplazes P., unpublished data). In **Austria**, a pronounced increase in cases was recorded: 2.8 new cases per year between 2000 and 2010 and 13 in 2013. The annual incidence in Vorarlberg with 372,001 residents was 0.08 cases during 1991−2000 which increased to 0.32 cases during 2001−10. In Tyrol (710,048 residents), annual incidences varied from 0.17 (1991−2000) to 0.07 (2001−10) to 0.56 per/10^5 inhabitants in 2011. Only sporadic cases are recorded in the other seven Austrian provinces (Schneider et al., 2011).

In **Germany**, notification of human AE became compulsory in 2001, and the number of AE cases per year (based on data from the Robert-Koch-Institut, 'SurvS tat@RKI 2.0, https://survstat.rki.de') have been increasing steadily from 21 (in 2001) to 47 in 2015. In contrast, the number of CE cases and cases of undetermined echinococcoses has remained rather stable over the same period. The data reported through this system are considered to lead to a substantial underestimate of the true situation (Jorgensen et al., 2008).

In **France**, geographic clustering of AE cases has been well documented based on data from a population-based registry. High-risk areas included the Massif Central and the northeastern regions of the country, where most cases either resided in villages or towns or had farming or gardening activities (Piarroux et al., 2013). A recent study in France based on AE cases between 1982 and 2007 confirmed that the risk of AE was associated with mountain climates/landscapes (Piarroux et al., 2015).

In the **Czech Republic**, the examination of 1892 patients between 1998 and 2014 revealed 20 AE cases, the first two diagnosed in 2007 (Kolářová et al., 2015).

For Switzerland, the annual burden of AE was estimated to be 78 DALYs, or approximately 3.7 DALYs per case, with a median cost of €109,000 per case (Torgerson et al., 2008). Survival analysis on databases of French and Swiss AE patients has shown that advances in diagnosis, staging and state of the art treatments [chapter: *Echinococcus*–Host Interactions at Cellular and Molecular Levels by Brehm and Koziol (2017)] can result in survival of AE patients nearly comparable to the unaffected general population (Torgerson et al., 2008; Piarroux et al., 2011).

2.2.2 Western and Northern Europe: Iceland, Ireland, United Kingdom, Norway, Sweden, Finland and Denmark

2.2.2.1 Transmission and host assemblages

E. multilocularis transmission has been known to be occurring since 1997 in Denmark (DK), in Sweden (SE) since 2011, and on the Svalbard Archipelago of Norway since 1999 (Wahlstrom et al., 2015). Main definitive hosts for *E. multilocularis* in DK and SE are red foxes (possibly raccoon dogs in Jutland, DK). No *E. multilocularis* lesions have been documented in small mammals in the Great Copenhagen area (0/719) (Wahlstrom et al., 2015). Recently, in southern Sweden, for the first time, *E. multilocularis* was detected in voles (*Arvicola amphibius* and *Microtus agrestis)* (Miller et al., 2016).

Transmission in Svalbard is restricted to a limited area of a few square kilometres. The parasite cycles between the only definitive host species, the indigenous arctic fox (*Vulpes lagopus)* and the introduced sibling vole (*Microtus levis*) as intermediate host, in which prevalence can be up to 100% in overwintered males (Henttonen et al., 2001). The *E. multilocularis* haplotype in this area was distinct from the European haplotypes (Table 1). Furthermore, the low polymorphism identified among 27 metacestode isolates supports the hypothesis that *E. multilocularis* was introduced to Svalbard with Arctic foxes and that introduction of the intermediate hosts enabled the local life cycle to become established (Knapp et al., 2012).

2.2.2.2 Infections in animals

The few data published in this area have been comprehensively reviewed (Wahlstrom et al., 2015). In **Denmark**, *E. multilocularis* was detected for the first time with very low worm burdens (<50 worms) in 3/340 foxes (0.9%) from the Greater Copenhagen area during investigations starting in 1997 (Kapel and Saeed, 2000). In 2011, the parasite was confirmed in Southern Jutland in 13/41 foxes (32%, worm burdens up to 1527) and in two raccoon dogs and in 2014 in 4/97 (4.1%) foxes around 100 km north of the first finding in Grindsted (Wahlstrom et al., 2015).

In **Sweden**, a national screening program including more than 3800 foxes was initiated in 2000. Prevalences between 0.1% and 0.9% were detected since 2011 (Fig. 2), with worm burdens up to 1235 (Wahlstrom et al., 2015). Furthermore, south of the first findings, *E. multilocularis* was found in Smaland (Miller et al., 2016). In a recent study of 1566 rodents from four regions in Sweden, *E. multilocularis* metacestodes were detected in the liver of 1 of 187 *M. agrestis* (0.5%) and 8 of 439 (1.8%) *A. amphibius,* but none of 655 *Myodes glareolus* or 285 *Apodemus* spp. were infected (Miller et al., 2016). In both infected species, protoscoleces were present, indicating their competence as intermediate hosts. There was a high local prevalence (6/9 rodents) in an endemic focus (a single field) despite the overall low national prevalence in foxes of <0.1%. In **Norway**, the parasite was not detected in 3405 red foxes investigated between 2000 and 2014. Similarly, 2759 red foxes and 2353 raccoon dogs investigated in **Finland** between 2000 and 2014 were free of *Echinococcus* (Wahlstrom et al., 2015).

So far no data support the endemicity of *E. multilocularis* in **Ireland**, the **United Kingdom** or **Iceland**. In the United Kingdom, the parasite has been found in a captive beaver (Barlow et al., 2011) and a macaque monkey (Boufana et al., 2012), both imported from southern Germany. Presently it is compulsory to treat all dogs and cats that are imported into the UK (https://www.gov.uk/take-pet-abroad/tapeworm-treatment-dogs) or Ireland with praziquantel to prevent the establishment of the parasite (Torgerson and Craig, 2009).

2.2.2.3 Alveolar echinococcosis in humans

As of the end of 2015, no putative autochthonous AE cases have been described in Western and Northern Europe; however, single imported cases in humans were reported from Denmark, United Kingdom and Sweden (Wahlstrom et al., 2015). Interestingly, AE cases have been reported in Russian districts (e.g., Murmansk) and neighbouring eastern Finland (see Section 2.3.1).

2.2.3 Eastern Central Europe: Poland and Baltic countries, Belarus, Ukraine, Moldova, Slovakia, Hungary

2.2.3.1 Transmission and host assemblages

First descriptions of *E. multilocularis* in **Belarus, Ukraine** and **Moldova** go back more than 50 years, with the parasite reported in rodents in Belarus

(Shimalov, 2011), red foxes in Ukraine in 1957 and rodents from Moldova in 1961 (Bessonov, 2002). In **Poland**, *E. multilocularis* was detected for the first time in red foxes in 1994 (Malczewski et al., 1999).

In the countries of the Baltic region (i.e., **Lithuania**), the first report of *E. multilocularis* in animals was described in 2003 in one of the five investigated muskrats (Marcinkutė et al., 2015). Transmission of *E. multilocularis* has so far not been well documented but a *Microtus* sp. was found to be infected in this area (Sarkunas M., personal communication). In definitive hosts, no infections were recorded in 164 foxes and 10 raccoon dogs in 1964 or in 122 foxes and 58 raccoon dogs in 1976 [see (Marcinkutė et al., 2015)]. The parasite was detected for the first time in foxes in 2001 (Bruzinskaite-Schmidhalter et al., 2012). Interestingly, the first case of human AE dates back to 1997 in Lithuania before the first detection in animals. In contrast, in **Latvia** and **Estonia**, *E. multilocularis* was first detected in foxes in 2003 (Marcinkutė et al., 2015).

Detection of *E. multilocularis* in red foxes in the **Czech Republic** and **Slovakia** in the 1990s confirmed that the geographic distribution of the parasite was much wider than that had been previously thought (Dubinsky et al., 1999; Martinek et al., 2001). Later, prevalences up to 27.6% were recorded in red foxes in **Hungary** (Tolnai et al., 2013). Data regarding occurrence of the parasite in intermediate hosts in these three countries are scarce; larval stages were detected in the bank vole (*M. glareolus*) in the Czech Republic and in muskrat (*O. zibethicus*) in Slovakia (Martínek et al., 1998; Miterpáková et al., 2006).

2.2.3.2 Infections in animals

Initial investigations in **Poland** of 2951 red foxes between 1993 and 1998 revealed an overall prevalence of the tapeworm of 2.6%, with the highest regional prevalence (11.8%) recorded in northeastern parts of the country (Malczewski et al., 1999). The results of recent investigations including more than 1500 red foxes from 15 of 16 Polish counties revealed a mean prevalence of 16.5%, ranging from 2% in western and southwestern Poland to 50% in eastern and southern parts of the country (Karamon et al., 2014b). Adult worms were also detected in 2 of the 148 dogs examined (1.4%) (Karamon et al., 2016) and larval stages in 10 (0.8%) of the 1250 pigs with liver lesions (Karamon et al., 2014a).

In **Lithuania**, average countrywide *E. multilocularis* prevalence was 59% in 269 foxes, with worm burdens up to 20,924; the prevalence was 53% in the suburban area of Kaunas (Bruzinskaite-Schmidhalter et al., 2012). In the same study, 8% of 85 raccoon dogs were infected. In two other studies, 2 (0.8%) of 240 and 4 (1.1%) of 360 dogs excreted *E. multilocularis* eggs, further calcified *E. multilocularis* lesions were found in 3 (0.5%) of 685 pig livers (Marcinkutė et al., 2015).

Prevalence of *E. multilocularis* was 31.5% in a recent survey of 108 red foxes in **Estonia**, while only 1.6% of 249 raccoon dogs from the same study area were infected (Laurimaa et al., 2016a,b, 2015). In **Latvia**, *E. multilocularis* was described in foxes, wolves and raccoon dogs (Marcinkutė et al., 2015; Bagrade et al., 2008) and recently in 73 (17%) of 430 foxes and 17 (5.6%) of 305 raccoon dogs, therefore documenting a high endemicity in this country (Bagrade et al., 2014).

In **Belarus**, descriptions of *E. multilocularis* in a variety of rodents go back to the 1960s (Shimalov, 2011). Infected red foxes were found between 2001 and 2003 in the central and the southern part of the country [cited in (Marcinkutė et al., 2015)].

In the **Ukraine**, a well-documented historically endemic area, new data are available from Kharchenko et al. (2008). These authors examined a total of 164 red foxes: 52 originating from the south steppe regions, 93 from the North Polissya regions and 19 from western Ukraine. Only animals from western parts of the Ukraine, namely Volyn and L'viv regions, were infected with *E. multilocularis*.

The distribution of *E. multilocularis* in foxes is well documented in **Slovakia**. According to surveys between 2000 and 2010, the parasite is widespread, and average prevalences in foxes reached 30.3%. The highest prevalences were detected in northern Slovakia and the mountainous areas of central Slovakia, where the prevalence ranged between 30% and 60% (Miterpáková and Dubinský, 2011).

In **Hungary**, surveys conducted in 2008 and 2009 revealed an average prevalence of 11% in 840 red foxes. Positive animals originated from 16/19 Hungarian counties and also from suburban areas of the capital Budapest (Casulli et al., 2010a). In the period of 2012–13, the prevalence decreased to 7.9% in 772 red foxes, with mean intensity of infection of 243 worms/animal (Tolnai et al., 2013).

2.2.3.3 Alveolar echinococcosis in humans

In **Poland**, a total of 121 cases of AE have been confirmed between 1990 and 2011, with a steady increase in annual incidence. While a total of 55 patients were diagnosed in the years 2005–09, 23 new cases were reported in 2010–11 alone. The highest number of patients came from the

Warmińsko-Mazurskie province (Nahorski et al., 2013), where the highest prevalence in red foxes was also documented (Karamon et al., 2014b).

Human AE has been diagnosed in patients from the whole Baltic region. In **Lithuania**, there were 178 patients registered in the period of 1997–2014, and the incidence of the disease (per 10^5 inhabitants) increased from 0.03 in 2004 to 0.57 in 2009 and to 0.74 in 2012 (Marcinkutė et al., 2015). In **Latvia**, 29 cases of AE have been reported between 1996 and 2010 (Tulin et al., 2012). To date, only 13 patients with echinococcosis have been registered in **Estonia**, but the *Echinococcus* species involved was not identified (Marcinkutė et al., 2015); however, according to EFSA (2015a) three AE cases were registered in 2013.

Data on human echinococcosis in **Belarus** are scarce; only two patients with AE were reported, one from Brest and the second from the Mogilev region (Marcinkutė et al., 2015). The real situation with regard to human AE in **Ukraine** and **Moldova** is unknown; no data have been published in the literature so far.

The first two human cases of AE in **Slovakia** were recorded in 2000. In 2004, another two patients were reported. Since then, every year a few new cases of AE have been detected; and to date at least 50 patients with confirmed diagnoses have been documented (Antolova et al., 2014; Antolova D. personal communication).

Although a human case of AE had been reported in **Hungary** in the past (Horvath et al., 2008), the first autochthonous case of the disease was confirmed only recently (Dezsényi et al., 2016).

2.2.4 *Southeastern Central Europe: Slovenia, Croatia, Serbia, Romania, Bulgaria, other Balkan countries and European part of Turkey*

2.2.4.1 Transmission and host assemblages

Information about the occurrence of *E. multilocularis* in Southeastern Europe is fragmented and needs further investigation. In **Slovenia**, *E. multilocularis* was recently detected in red foxes (Vergles Rataj et al., 2010) and in northern Serbia in red foxes and golden jackals (Lalošević et al., 2016). The absence of *E. multilocularis* from neighbouring regions is likely an artefact for lack of investigations, and systematic studies are particularly required from Croatia, central and southern Serbia, southern Romania and Bulgaria. Indeed, preliminary molecular investigations confirmed positive foxes in northern **Croatia** (Beck R. personal communication). In **Romania**, *E. multilocularis* was for the first time detected in rodents between 1991 and

1995 (Sikó et al., 1995); subsequently, positive red foxes were found in the northwestern part of the country (Siko et al., 2011). In neighbouring **Bulgaria**, the metacestode stages were described in *Chionomys nivalis* and *Myodes glarelous* in the 1980s (Genov et al., 1980; Kolářová, 1999). From the European part of **Turkey** (Thrace) an old report of an infected fox with *E. multilocularis* was convincingly documented (figure shows a mature worm with genital pore anterior to the middle) (Merdivenci, 1963) (for the Asian part of Turkey see Section 2.3.3). Furthermore, a few cases of AE have been proposed from **Greece**, but the diagnostic criteria or the origin of the patient have not been well documented. *Echinococcus multilocularis* has not been described so far in **Bosnia-Herzegovina**, **FYROM** (former Yugoslav Republic of Macedonia), **Kosovo** and **Montenegro**.

Based on the fragmented and often anecdotal nature of the information, the epidemiological situation for *E. multilocularis* in southeastern Central Europe remains largely undetermined.

2.2.4.2 Distribution in animals

In **Slovenia**, several papers suggested that *E. multilocularis* was present in mostly atypical intermediate hosts (cattle, piglets) without convincing evidence [cited in Brglez and Kryštufek (1984)]. For example, histological findings in an unusual rodent intermediate host (*Apodemus flavicollis*) of an agglomeration of 2 mm vesicles filled with reddish (rose) fluid in the liver, mesentery, and other abdominal organs, in the absence of protoscoleces, is not sufficient to document an *E. multilocularis* infection. However, *E. multilocularis* was for the first time found in foxes hunted during 2002–05 in all regions of the country, with an overall prevalence of 2.6% (Vergles Rataj et al., 2010).

In a recent survey in the Vojvodina province of northern **Serbia**, 17.9% of 112 foxes and 14.3% of 28 golden jackals were found infected (Lalošević et al., 2016). An infected beaver that had been found earlier in central Serbia was apparently introduced from southern Germany (Cirovic et al., 2012).

In **Romania**, *E. multilocularis* metacestodes were identified by morphological criteria and the presence of protoscoleces in 0.45% of 442 *C. nivalis*, in 0.44% of 120 *M. arvalis*, in 0.51% of 1172 *Arvicola terrestris* and in 1.67% of 120 *M. glareolus* (Sikó et al., 1995). Between 2007 and 2010, *E. multilocularis* was identified in 27 (4.8%) of 561 red foxes from 15 Transylvanian counties (southeastern Romania), with the highest prevalence (10.5–14.6%) in the counties bordering Hungary and Ukraine (Siko et al., 2011, Fig. 2).

2.2.4.3 Alveolar echinococcosis in humans

In **Slovenia**, a serological study including 1263 patients suspected of having echinococcosis, revealed 9 seropositive cases with a species-specific Western blot; based on these data, a mean annual incidence for seropositive persons of 0.09 cases/10^5 inhabitants was calculated (Logar et al., 2007).

According to Siko et al. (2011), two cases of human AE have been diagnosed in patients from **Romania**, from the northwestern and the central parts of the country. Although Genov et al. (1980) mentioned the finding of human AE in **Bulgaria**, convincing evidence is still lacking (Kolářová, 1999). In **Greece**, sporadic cases have been published earlier and one confirmed case was registered in the European Echinococcosis Register (1996–2000) (Kern et al., 2003), but travel histories are not well documented.

2.3 *Echinococcus multilocularis* and alveolar echinococcosis in Asia

Echinococcus multilocularis is widespread across northern Asia with the endemic region covering most of Russia, central Asia and western China (Torgerson et al., 2010). Most of the burden of AE is in this region with over 90% of the global burden occurring in China alone (Fig. 3, Table S2 in Supplementary Material). In some rural communities, AE prevalences may be over 5% and represent the highest burden of any disease (Budke et al., 2004). As the disease is fatal in the absence of treatment, these represent extraordinarily high incidences of disease which are not reported in official data. Further north, in some districts of Siberia large numbers of human AE cases have been reported since the 1950s. In recent years there is increasing evidence that AE is becoming an increasing public health problem in central Asia, particularly in Kyrgyzstan where hundreds of cases are reported annually (Usubalieva et al., 2013; Raimkylov et al., 2015; Abdybekova et al., 2015).

The parasite is also actively transmitting on the northern Japanese island of Hokkaido. There are only sporadic reports of cases from northern India or Pakistan which appears to be the southern limit of the parasite distribution.

2.3.1 North Asia and the Russian Federation

2.3.1.1 Transmission and host assemblages

Most parts of the **Russian Federation** are considered endemic for *E. multilocularis* (Fig. 3, Table S2 in Supplementary Material). Based on data of human AE (Bessonov, 1998), parts of southern Siberia (e.g., Altai, Omsk and Tomsk), central Yakutia and parts of the Far East are regarded as highly

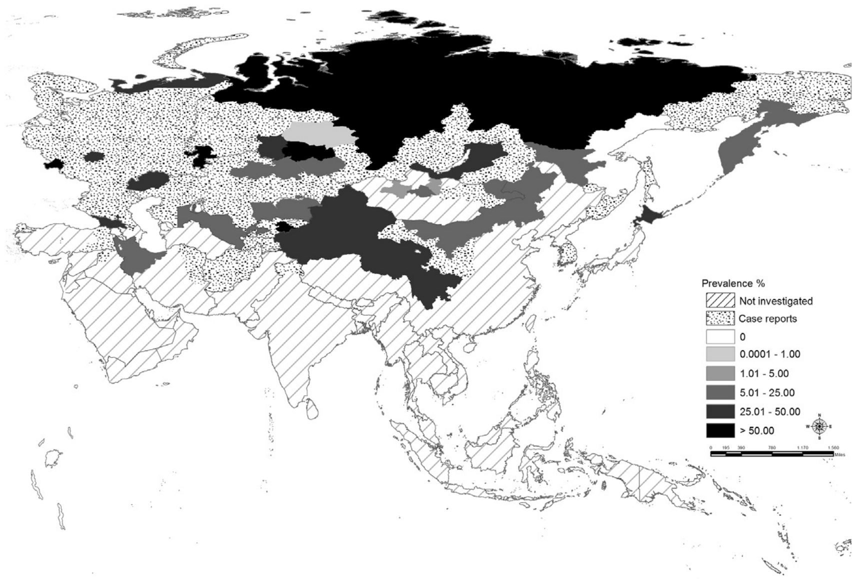

Figure 3 ***Current distribution of Echinococcus multilocularis in foxes (*****Vulpes vulpes; Vulpes ferrilata, Vulpes corsac, Vulpes lagopus*****) in Asia.*** Areas with case reports of AE in definitive and intermediate hosts or humans are approximately given as *dotted areas* if data of foxes were missing. The detailed information (prevalence data in each jurisdiction) is listed in Table S2 of the Supplementary Material.

endemic areas. In the temperate zones of Russia, red foxes represent the main definitive hosts, although the wolf, raccoon dog and the domestic dog may regionally contribute to the life cycle of *E. multilocularis* (Bessonov, 1998; Konyaev et al., 2012a). In red foxes, high prevalences are reported from Omsk and Novosibirsk areas and from the Tyva steppe bordering Mongolia (Fig. 3). Various voles, hamsters, squirrels (Konyaev et al., 2012a), pikas and bobak marmots have been identified as potential intermediate hosts [see chapter: Ecology and Life Cycle Patterns of *Echinococcus* Species by Romig et al. (2017)] but the ecological significance of these species is not well documented.

In the Russian Federation (see Table 1), haplotypes of four assemblages of *E. multilocularis* have been confirmed: a European haplotype from a captive monkey (Moscow Zoo), an Asian haplotype in western Siberia and European Russia, the Mongolian haplotype on an island of Baikal Lake and in the Altai Republic and the North American (N1) haplotype in Yakutia (Konyaev et al., 2013).

2.3.1.2 Infections in animals

Echinococcus multilocularis has been reported in foxes (*Vulpes vulpes*) in a number of studies in the **Russian Federation** covering a wide geographical area. In Kamchatka a prevalence of 15% was documented (Tranbenkova, 1992), and the prevalences recorded from the Far East were 22.6% (19 of 84 foxes) in the Amur region (Yudin, 2012) and 15–40% in the Buryatia region (Mazur and Fomina, 2012). In the Altay region (southern Siberia), 20 of 91 foxes were infected (Pomamarev and Kostykov, 2012). In Krasnoyarsk, 47 of 54 (Abuladze, 1964) and in Novosibirsk 89 of 162 foxes were infected (Lukashenko and Zorikhina, 1961). In European Russia, prevalences were 33% in foxes from Ryazan (SE of Moscow) (Andreyanov, 2011), 17% from Nenets (Arctic coast of European Russia) (Sorochenko, 1972) and 26% from the Ingushetia region bordering the Caucasus (Pliyeva and Uspenskii, 2006). In Bryansk, one of the westernmost provinces bordering the Ukraine and Belarus, 26 of 51 foxes were reported to be infected by Machulski in 1949, cited in Abuladze (1964).

High prevalences in arctic foxes (*V. lagopus*) have been described in northern Russia, approaching 100% in Yakutia (Kokolova, 2007). A prevalence of 64% in Nenets has been reported (Sorochenko, 1972) and a prevalence of 40% (20 of 50 foxes) was reported in Krasnoyarsk by Mamedov in 1960 (Abuladze, 1964).

Infections in wolves have been reported in Kamchatka (Tranbenkova, 1992) and the Amur region (Yudin, 2012), raccoon dogs in Ryazan (Andreyanov, 2011) and *Lynx lynx* from the Altay region (Pomamarev et al., 2011). Intermediate hosts reported in Russia include muskrat (*O. zibethicus*), suslik (*Spermophilus* spp.), rats (*Rattus norvegicus*), *Apodemus uralensis* and *M. arvalis* from the Caucasus (Pliyeva and Uspenskii, 2006; Kabardiev et al., 2014); lemmings (*Lemmus sibiricus*), house mice (*Mus musculus)* and *Myodes* spp. from Siberia (Kokolova, 2007); and *M. arvalis* and *Apodemus* in south European Russia (Kirillova and Kirillov, 2008).

2.3.1.3 Alveolar echinococcosis in humans

Obtaining accurate data on the number of human cases of AE in the **Russian Federation** is difficult. Data from the sanitary epidemiological service indicate approximately 500–600 cases of echinococcosis per annum but does not report AE and CE separately (Federal Centre of Hygiene and Epidemiology, 2006–10). However, other sources indicate that, between 2007 and 2012, 224 of these echinococcosis cases were AE – 37 per annum (Anonymous, 2013). In contrast, a systematic review of published and unpublished Russian literature and public health reports estimates over 1000 cases per year (Torgerson et al., 2010). This includes a report of 3274 cases of echinococcosis (diagnostic criteria not indicated) in Russia in 2002, representing a threefold increase since 1995 (Bishnevski et al., 2007), which is consistent with the incidence of echinococcosis reported in Russian immigrants residing in Germany (Torgerson, 2017). Several large echinococcosis case studies in Moscow and other cities indicated that the ratio of CE to AE cases was approximately 2:1 [for example Abdullaev et al. (2006) and Lysenko et al. (2006)]. Contemporary and older reports indicate large numbers of cases of AE with a wide geographical distribution, including 147 cases in Novosibirsk (Kabardiev et al., 2014); 52 cases between 2000 and 2010 in Bashkortostan (Pantieleiev et al., 2011); 350 cases between 1961 and 1998 in Kirov in the Volga basin in European Russia (Dhuravliev et al., 2000); 17 cases between 2003 and 2010 in a clinic in Perm, between Moscow and the Urals (Kotelnikova et al., 2011); 197 cases between 1969 and 2013 in one hospital in Tomsk (Zaytsev, 2013); and 38 cases between 2007 and 2012 in Krasnoyarsk district (Rukopisi and Zaitsiev, 2015). In Krasnodar, which borders the Black Sea, both AE and CE are being reported in significant numbers (Anonymous, 2013).

Recent government reports (available at http://rospotrebnadzor.ru) also indicate cases (numbers not reported) in the Belogorod, Bryansk, Chelyabinsk, Mariy-El, Mordovia, Murmansk, Nizhegorod, Omsk, Samara, Saratov, Smolensk, Sverdlovsk, Udmurt, Ulyanovsk and Yaroslav districts. Interestingly, Murmansk district has a border with both Norway and Finland where human AE has not yet been reported.

Furthermore, there is older literature from the time of Soviet administration, including a study in Kamchatka describing 350 cases over an unspecified time period (Nabokov and Vasiliev, 1978), 130 cases from Novosirbisk in the 1960s (Bregadze and Kogan, 1962), and 996 cases between 1950 and 1968 in Sakha (Yakutia) giving an annual incidence of 9.2 cases per 10^5 (Isakov, 1982).

2.3.2 Caucasus and Central Asia: Kazakhstan, Kyrgyzstan, Uzbekistan, Armenia, Azerbaijan and Georgia

2.3.2.1 Transmission and host assemblages

Echinococcus multilocularis has long been known throughout the former Soviet Union. In Central Asia, human AE was thought to be rare and sporadic with few case reports and little surveillance data. However, the first case in

Kyrgyzstan was reported in 1948 (Kuttubaev et al., 2004). Reports of animals date from at least 1957 (Gagarin et al., 1957).

Human AE, along with CE, appears to be emerging in central Asia. After the dissolution of the Soviet Union in 1991, increase in populations of both stray and owned dogs, poverty, and opportunities for scavenging of rodents have been linked to high prevalences of *E. multilocularis* in dogs (Van Kesteren et al., 2013; Ziadinov et al., 2008). This may translate to increased risk of zoonotic transmission due to the close contact between dogs and humans (Torgerson, 2013). Dog owners may have higher odds of being affected by AE than non-dog owners (Torgerson P., personal communication).

2.3.2.2 Infections in animals

There is very limited information on *E. multilocularis* in animals in the three republics in the Caucasus. In 1989, three of 13 wolves examined in the Sheki-Zaqatal region of northern **Azerbaijan** were infected with *E. multilocularis* (Elchuev, 1989). In **Georgia** (Kurashvili, 1966) a prevalence of 30% of *E. multilocularis* was reported in foxes.

In **Kyrgyzstan**, AE was first reported in rodents (Gagarin et al., 1957); subsequently, the parasite was described in *Microtus* spp. and *O. zibethicus* (reviewed by Abdyjaparov and Kuttubaev, 2004). Recent studies have revealed *E. multilocularis* in 20% of dogs in communities with opportunities to scavenge or hunt rodents (Ziadinov et al., 2008). Red foxes, normally considered the natural definitive hosts of this parasite, have been reported to have a prevalence of infection of over 65% in the Naryn region of Kyrgyzstan (Ziadinov et al., 2010). Thus, conditions that allow infection of dogs from the natural cycle favour the onward transmission to humans.

In **Kazakhstan**, *E. multilocularis* infections in foxes and wild rodents have been described for several decades and have long been known to be distributed over most of the country (Abuladze, 1964). In the arid regions of Kazakhstan, characterized by desert or semidesert landscape, foci of AE in rodents are associated with water and are aggregated around oases. Elsewhere, the parasite is more widely distributed in mountainous and steppe habitats (Shaikenov, 2006; Shaikenov et al., 2004). Other reports (see Table S2 in Supplementary Material) estimate 8.3% of foxes infected in the Zhambul region, 23% of foxes infected in the Pavlodar region, 25% of foxes from the Almaty region, and more recently, 28.5% in west Kazakhstan. A prevalence of 5% of *E. multilocularis* in dogs has been described in the mountainous region of south east Kazakhstan (Stefanic et al., 2004; Torgerson, 2013).

In **Uzbekistan**, *E. multilocularis* has been found in 8.6% of foxes from the Amu-Darya delta and lower river valley in Karakalpakstan. The parasite has also been found in small mammals (*Ondatra, Rhombomys* and *Meriones* spp.) from the same area (Kairov, 1976). Older literature documented *E. multilocularis* in 1 of 678 dogs and 19 of 189 foxes (10%) originating from nine districts of Uzbekistan (Sadikov, 1963).

2.3.2.3 Alveolar echinococcosis in humans

There are no available data on human AE from the Caucasus, **Uzbekistan** or **Turkmenistan**.

Human AE has been known in Central Asia for several decades. For example Arslanova (1962) reported 33 cases of AE in 19,837 autopsies performed between 1941 and 1957 in southern **Kazakhstan**. More recently, 46 cases of AE were reported in a single surgical centre in Almaty between 2006 and 2014, and estimates from Kazakhstani expatriats are in the region of 34 cases per annum or 0.2 cases per 10^5 per year (Abdybekova et al., 2015).

In **Kyrgyzstan**, the number of cases of human AE (confirmed by histology on lesions removed at surgery) has increased from 0 to 2 cases per year in the 1990s to 148 cases reported in 2013, or 2.6 cases per 10^5 inhabitants per year. In some districts the incidence is as high as 58 cases per 10^5 per year (Usubalieva et al., 2013; Raimkylov et al., 2015). The estimated human burden of echinococcosis in Kyrgyzstan for 2013 is 11,915 (4.547–29.544) DALYs for AE and a further 1.742 (1.056–2.723) DALY for CE (Counotte et al., 2016). The burden of echinococcosis is roughly one-third of the burden of HIV which was estimated to be 38,870 (21,261–64,297) DALY in 2010 (Ortblad et al., 2013).

In **Tadjikistan**, a surgeon from Dushanbe reported treating 19 AE cases between 2010 and 2013 (Akhmedov et al., 2013). However, these figures are likely prone to underreporting and underdiagnosis (Mathers et al., 2007; Welburn et al., 2015).

2.3.3 Middle East: e.g., Iran, Turkey

AE is rare in tropical and subtropical areas of the Middle East (ME). However, in higher latitudes of the region, AE is more frequent and the parasite may be undergoing geographical range expansion to the south

(Geramizadeh et al., 2012). No report of *E. multilocularis* has been documented from **Syria, Jordan, Lebanon, Palestine, Israel** or the **Arabian Peninsula**.

In **Iran**, *E. multilocularis* was first reported in the early 1970s, with 10% of the red foxes infected in Moghan plain of the northwestern parts of the country (Mobedi and Sadighian, 1971). Since then a number of human AE patients have been documented, and prevalence was 22.9% in red foxes and 16% in jackals. However, attempts to identify rodent intermediate hosts have not been successful in the northwest (Zariffard and Massoud, 1998).

New foci of AE have been reported from Khorasan Razavi province (northeastern Iran) in 2007 and 2010 (Fattahi Masoom and Sharifi, 2007; Berenji et al., 2007; Raisolsadat, 2010). A captive spider monkey (*Ateles geoffroyi*) is also believed to have died of AE in the same area (Borji et al., 2012b). All wild carnivores examined, including three foxes, nine jackals, one hyena and one wolf, and five of 77 dogs (6.5%), were positive by PCR (Beiromvand et al., 2011). A number of small mammal intermediate hosts including *Microtus transcaspicus, Ochotona rufescens, M. musculus, Crocidura gmelini* and *Apodemus witherbyi* have been identified in this region (Beiromvand et al., 2013). These findings indicate autochthonous transmission of *E. multilocularis* in the region and document the zoonotic risk.

In **Iraq**, a human case of AE has been reported from the north, in Zakho near the Iraqi–Turkish border (Al-Attar et al., 1983). However, no animal reservoir has yet been identified.

Large parts of **Turkey** are considered as highly endemic for *E. multilocularis*. In animals, there is one report of an infected red fox (Merdivenci, 1963) from the European part of the country (Thrace), and more recently from Central Anatolia (Nevşehir, Kayseri) and Thrace, PCR on fox environmental samples was positive for *E. multilocularis* (Gürler A.T., personal communication). Since 1939, approximately 500 human cases of AE have been documented in more than 60 studies in Turkey. Cases of AE have been frequently reported especially from eastern Anatolia. Between 1980 and 1998 more than 200 new AE patients were identified (Altintas, 1995, 2003, 2008; Miman and Yazar, 2012; Uysal and Paksoy, 1986). During 1980–2000, an incidence of 0.4 cases/10^5 has been recorded in southeastern Anatolia including Diyarbakır, Sanliurfa and Batman provinces (Uzunlar et al., 2003). During the decade 2000–10, 162 human AE cases have been documented, with more than 86% of the patients from eastern and southeastern parts of Turkey (Miman and Yazar, 2012). Based on the relatively rare occurrence of cerebral AE cases (3–4% brain involvement), about

100 liver AE cases are expected to occur annually in Turkey (Torgerson et al., 2010). AE has been recognized as an emerging zoonosis in Turkey and, from a public health point of view, it has been recently made reportable in the country (Altintas, 2008).

2.3.4 North East Asia: China, Mongolia, Korea, Japan

2.3.4.1 China

2.3.4.1.1 Transmission and host assemblages *Echinococcus multilocularis* is present over much of central and western China, but is thought to be absent from eastern China (Fig. 3). Regions known to be endemic for this parasite are inner Mongolia in the north and further north east as far as Heilongjiang. In northwestern China, endemic provinces include Gansu, Qinghai, Ningxia and Xinjiang. In southwestern and central China, the western part of Sichuan province and the eastern part of the Tibet Autonomous Region (TAR) are endemic (Feng et al., 2015).

These endemic areas are mainly in the less densely populated areas of China. Thus, endemic provinces represent nearly two-thirds the area of China, but only 16% of the Chinese population. Within these provinces, *E. multilocularis* transmission risk is variable and seems best predicted by landscape features that support population outbreaks of particular small mammal species rather than species diversity (Giraudoux et al., 2013b). These provinces are also largely coendemic for AE and CE, although at the local level, one may predominate.

The history of AE in China is reviewed by Vuitton et al. (2011). The first human cases of AE were recognized in Xinjiang in the far west of China as early as 1956, with a report of six clinical cases published in 1965. In Qinghai province the first reported case was in 1959. In Gansu there were several reports also published in the 1960s. It was initially believed that the disease was rare and sporadic in China, as elsewhere, but by the 1980s it was clear that there were areas of China with large numbers of human cases. In 1992 a large focus of human AE in central China was published (Craig et al., 1992). Since then there have been numerous reports of AE in some communities in central and western China, where AE is a major cause of disease burden (Budke et al., 2004).

2.3.4.1.2 Infections in animals The first reports of *E. multilocularis* in canids occurred in the 1990s. Prevalence values ranging between 15% and 60% have been reported in red foxes (*V. vulpes*) in Xinjiang, Ningxia (Guyuan) and Qinghai and Inner Mongolia (Jiang, 1998; Wang et al., 2008).

The Tibetan fox (*V. ferrilata*) has been described as an important definitive host in the eastern part of the Tibetan plateau [Qiu et al., 1999; cited in Vuitton et al. (2003)]. In Sichuan province, *E. multilocularis* was detected in 35% of 94 faecal samples of Tibetan foxes collected in the environment (Jiang et al., 2012) and further east, in Qinghai province, 4 of 12 Tibetan foxes were infected (Wang et al., 2008). Evidence is accumulating that the Tibetan fox rather than the red fox is the more important definitive host on the Tibetan plateau (Tsukada et al., 2014). Transmission in the TAR and in other Tibetan regions (Feng et al., 2015) includes a wildlife cycle with Tibetan foxes (*V. ferrilata*) and microtine and/or ochotonid small mammal species (Raoul et al., 2006). Furthermore, the role of domestic dogs in AE transmission in TAR is probably similar to that described in Tibetan communities in northwest Sichuan (Giraudoux et al., 2013a; Vaniscotte et al., 2011).

Isolates of *E. multilocularis* from foxes in Qinghai province are genetically identical to those found further east in Sichuan province (Feng et al., 2013). In the province of Inner Mongolia, it has been reported that 19 of 151 (13%) corsac foxes (*Vulpes corsac*) were infected with *E. multilocularis*.

The parasite has been reported at high prevalence in dogs in a number of studies, particularly from the Tibetan Plateau. In Shiqu County, western Sichuan Province, prevalence was 12% of 372 dogs purged with arecoline, probably closer to 15% when adjusted for the insensitivity of purgation (Budke et al., 2005a, 2005b; Hartnack et al., 2013). Further studies in the same area found 23% of 142 samples of dog faeces positive for *E. multilocularis* (Vaniscotte et al., 2011). In Ganzi County, also in Sichuan province, 8 of 23 dogs were positive for *E. multilocularis* following necropsy (Huang et al., 2008).

Further west in Qinghai region, 16 dogs (of an unreported sample size) were found infected with *E. multilocularis* (Ma et al., 2015a). In Gansu province, 6 of 59 dogs from Zhang County were found to be infected (Shi, 1995). A more recent study from Gansu found four of 74 dogs (5.4%) infected (Zhao et al., 2009). Only one infected dog (of 30 examined) was found in Xinjiang (Zhang et al., 2006).

A number of studies have documented small mammal intermediate hosts infected with *E. multilocularis* over much of the endemic region of China. These include *A. amphibius* in Xinjiang and *Lepus oiostolus* from Sichuan and Qinghai (Wang et al., 2008); *Meriones unguiculatus* in Inner Mongolia; *Microtus ilaeus*, *Lasiopodomys brandti* and *Neodon irene* in Inner Mongolia, Xinjiang and Sichuan (Wang et al., 2008; Tang et al., 2004); *M. musculus* in Xinjiang (Wang et al., 2008); *Eospalax fontanierii* in Ningxi and Gansu and *Ochotona curzoniae* in Sichuan and Qinghai (Wang et al., 2008); 2009); *Ochotona daurica* in Gansu, *Spermophilus dauricus* in Ningxia, and *Spermophilus erythrogenys* in Xinjiang (Wang et al., 2008). Prevalences range from 0.01% for *M. musculus* to approximately 10% for *Ochotona* (Wang et al., 2008).

2.3.4.1.3 Alveolar echinococcosis in humans Over 90% of the global burden of AE occurs in China, with over 16,000 cases annually (Torgerson et al., 2010). Because the main endemic areas of AE are frequently in the economically most disadvantaged and remote areas, precise numbers of human cases are not reported and government surveys grossly underestimate the true number of cases. There are very few studies which directly report numbers or incidence of new cases of AE; one hospital in Xinjiang reported 159 AE cases over a 10-year period (Wang et al., 2015a). The best estimates of incidence are based on ultrasound prevalence studies (Table 2) combined with the size of the populations at risk, the duration of disease, and the case fatality ratio. Where there are inadequate or no treatment options available, which is true for most endemic areas of China, the disease is likely to run a fatal course within 10 years of diagnosis (Torgerson et al., 2008). In total, close to 60,000 individuals have been examined in ultrasound studies with AE prevalences ranging from under 1% to 8%. Regional variation is marked; prevalence was >8% in some individual small communities, while only three cases of AE (of 257,823 people) were detected in Gannan autonomous prefecture in Gansu after the commencement of an echinococcosis control programme (Wang et al., 2015c). Prevalence was 0.5% (114 of 20,730) in children between the ages of 5 and 15 years in Qinghai province, which is remarkably high because of the long latent period of the disease, indicating a high infection pressure from a very early age (Cai et al., 2012). Estimates of the regional annual incidences of AE (Torgerson et al., 2010) are provided in Table 3.

Epidemiological analysis indicates that usually only a small part of the general population is at risk (such as Tibetan pastoralists). In the TAR, which covers 1.23 million square kilometres with a population of 2.81 million (2.3 inhabitants) per square kilometre, reports of AE date back to 1977 and since then 22 AE cases have been documented (Feng et al., 2015). From these data, the incidence of AE was estimated to be between 0.6 and $2.8/10^5$ inhabitants. However, a pilot mass screening in Dingqing in eastern TAR indicated the prevalence of human AE to be 4.7%. Thus, locally, AE might be a serious public health problem

Table 2 Population studies of alveolar echinococcosis (AE) in rural China (all cases were confirmed by diagnostic imaging)

Region	AE cases	Population size studied	References
Gansu	84	2482	Bartholomot et al. (2002)
Gansu (Zhang County)	65	1312	Craig et al. (1992)
Gansu (Minle County)	1[a]	362	Han et al. (2015)
Ningxia (Xija, Guyuan and Haiyuan Counties)	96	4778	Yang et al. (2007)
Ninxia (Xija County)	20	221	Yang et al. (2006)
Qinghai	39	1549	Yu et al. (2008)
Qinghai (Darlag County)	141	1723	Han et al. (2009)
Qinghai (Chindu, Zeko and Garde Counties)	31	3703	Schantz et al. (2003)
Qinghai (Maqing County)	34	1561	Ma et al. (2015b)
Qinghai[b]	114	20,730	Cai et al. (2012)
Qinghai (Zhiduo County)	2	979	Wu et al. (2007)
Sichuan	60	705	Wang et al. (2004)
Sichuan (Ganzu autonomous prefecture)	308	8512	Tiaoying et al. (2005)
Sichuan (Ganzi and Shiqu Counties)	223	7138	Wang et al. (2006)
Tibet Autonomous Region[c]	12	1511	Feng et al. (2015)
Xinjiang (Hobukesar Mongolian Autonomous County)	4	421	Li et al. (2013a)

[a]Additional cases of AE were found by examining records of local hospitals.
[b]Survey only done in children between 5 and 15 years of age.
[c]Three counties of Lhasa prefecture. All the AE cases were in Dingqing County (12 of 232 investigated) with a local prevalence of 5.2%.

in some counties, similar to Tibetan communities in northwest Sichuan and southwest Qinghai provinces. Based on this prevalence of 4.7%, a much higher national prevalence can be estimated as shown in Table 3.

2.3.4.2 Mongolia, Korea, Japan

In **Mongolia**, AE is less common than CE (Ito and Budke, 2015). *Echinococcus multilocularis* has been documented in wild canids (red foxes and wolves) in northern Mongolia (Ito et al., 2013). Apart from one infected vole (*Microtus limnophilus*) from Khovd Province (Gardner et al., 2013), the key intermediate hosts of *E. multilocularis* are unknown and require further study. The first description of AE in humans dates back to 1982

Table 3 Alveolar echinococcosis in China, estimated number of cases per annum in various provinces

Province	Population at risk (million)	Estimated prevalence	Estimated median number of new cases per year	Annual incidence per 10^5 inhabitants
Gansu	3.6	2.9%	7676	2
Heilongjiang[a]			<10	0.02
Inner Mongolia	3.0	0.02%	44	0.2
Qinghai	5.4	1.0%	3766	67
Ningxia	1.2	2.0%	1770	2.7
Sichuan	0.92	3.6%	2390	2.9
Tibet Autonomous Region	2.7	0.1%	172	5.5
Xinjiang	5.8	0.2%	811	3.5

[a]Four cases have been reported in Heilongjiang in 1994 (Wang et al., 2008). Since then there is no additional information from this province.

(Ito and Budke, 2015). So far five cases of AE have been documented in four provinces, mainly in the northwest of Mongolia (Ito and Budke, 2015). Molecular studies from metacestodes of three AE patients revealed both Asian and the Mongolian *E. multilocularis* haplotypes (Ito et al., 2010).

Korea is not considered endemic for *E. multilocularis*. However, a recent report described AE in a 41-year-old woman who had never visited a known endemic area (Kim et al., 2011). Data from North Korea are not available.

In **Japan**, the first human case of AE was diagnosed in 1937 in a woman from Rebun Island, around 9 to 13 years after the introduction of foxes for vole control and fur production (Ito et al., 2003). However, the infection has since been eliminated successfully from the island. A probable independent introduction of Asian haplotypes of *E. multilocularis* happened in eastern Hokkaido, where AE cases in humans have been diagnosed continuously since 1965 (reviewed in Schantz et al., 1995; Ito et al., 2003). Based on longitudinal studies, during the 1980s the parasite dispersed geographically and, during the 1990s, it became increasingly prevalent in the fox population. The whole island of Hokkaido is now regarded as endemic for *E. multilocularis* (Ito et al., 2003). With the urbanization of fox populations, the *E. multilocularis* life cycle has been established in highly populated areas, for example, in Sapporo (Ito et al., 2003). The grey-sided vole (*Myodes rufocanus*) which is present in large populations in forests and scrubland is regarded as the main intermediate host [for details, chapter: Ecology and Life Cycle Patterns of *Echinococcus* Species by Romig et al. (2017)].

Data from recent monitoring programs in Hokkaido revealed intestinal *E. multilocularis* infections in 635/1933 foxes investigated by necropsy during 2009–13 [Japanese Infectious Agents Surveillance (2014) Vol. 35 p.183 (written in Japanese)]. Furthermore, intestinal *E. multilocularis* infections have been detected in raccoon dogs, but the epidemiological role of this species is not known. Between 1966 and 1999, intestinal infections were diagnosed in 99 of 9849 (1%) of domestic dogs investigated, a prevalence similar to European endemic areas. Prevalence of intestinal infections in cats of up to 5.5% are recorded, but are considered of little zoonotic significance due to the absence of mature eggs [cited in Ito et al. (2003)]. Infertile *E. multilocularis* lesions have been systematically detected in a variety of slaughtered animals [e.g., in 0.1% of pigs (n = 18 million) or in 0.15% of horses (n = 15,583) (Takahashi and Mori, 2001, cited in Ito et al. (2003)]. Furthermore, severe and often lethal AE cases have been detected in a variety of monkeys [cited in Ito et al. (2003)]. These animal infections document a high environmental contamination with *E. multilocularis* eggs in the Hokkaido endemic area.

The epidemiology of human AE in Japan has been comprehensively summarized (Ito et al., 2003). From 1937 to 1997, 373 AE cases have been documented, and until 2002, 10–20 new cases were registered per year in a total population of around 6 million in Hokkaido. In a study including 134 human AE patients, cattle and pig farming and the use of well water were identified as risk factors for human infection (Yamamoto et al., 2001). Based on data from the Japanese National Institute of Infectious Diseases (http://www.nih.go.jp/niid/ja/survei/2085-idwr/ydata/5672-report-ja2014-20.html), between 2010 and 2014, on average 16 new cases have been diagnosed in Hokkaido (incidence of 0.3 AE cases per 10^5 inhabitants per year).

2.3.5 South Asia: Afghanistan, Pakistan, India, Nepal and Bhutan

Single AE cases have been documented in the north of South Asia, but the southern distributional limit is still unclear (Fig. 3).

In **India**, an isolated case of AE was reported from a man from the hill regions of Kashmir (Aikat et al., 1978), but no animal reservoir has yet been identified. In a few other case reports from India the patients originated from a known endemic area or no data were given.

Epidemiological investigations are needed to determine the status of AE in **Afghanistan and Pakistan**. A 67-year-old immigrant from Afghanistan was diagnosed with hepatic AE in the UK (Graham et al., 2002). Considering that AE is established in neighbouring northeastern Iran, *E. multilocularis* is probably present in parts of Afghanistan.

For **Nepal**, no evidence was found for the occurrence of AE in a systematic review (Devleesschauwer et al., 2014) and no data are available concerning AE in **Bhutan** (N. K. Thapa, Ministry of Agriculture & Forests, Thimphu, Bhutan).

2.4 Africa

Records of AE in northern Africa are based on macroscopical descriptions, histopathology, radiological imaging and serology of three autochthonous patients who never travelled abroad from Tunisia (Schantz et al., 1995) and Morocco (Maliki et al., 2004), respectively. No positive samples were found in a coprodiagnostic survey of wild canids (Lahmar et al., 2009a), in necropsied jackals and foxes (Lahmar et al., 2014a), or from postmortem examination of livers and lungs from wild boars in the selected areas in Tunisia (Lahmar S., personal communication). Therefore, for the nations south of the Mediterranean Sea, the presence of *E. multilocularis* remains to be confirmed.

2.5 North America

2.5.1 Mexico, United States of America, Canada and Greenland

Within North America, northwestern Canada, northwestern Alaska, and the northcentral United States have long been considered endemic for *E. multilocularis*. Historically, two disjunct regions were recognized: the Northern Tundra Zone (NTZ) and the North Central Region (NCR) (Eckert et al., 2001). The NTZ consists of the northwestern coastal regions of Alaska and of the western Canadian Arctic, essentially corresponding to the range of Arctic fox (*V. lagopus*); however, the parasite has not been reported in the Yukon Territory or in the Canadian Arctic east of Hudson's Bay, possibly due to lack of sampling effort and low prevalence (Jenkins et al., 2013; Rausch, 1995).

The NCR was considered the southern portion of the three Canadian prairie provinces (Alberta, Saskatchewan and Manitoba) and northcentral American States (Montana, North Dakota, South Dakota, Nebraska, Minnesota, Iowa, Wisconsin, Illinois, Michigan, Indiana, Ohio and Missouri) (Fig. 4). Evidence for endemicity of *E. multilocularis* in Wyoming (indicated

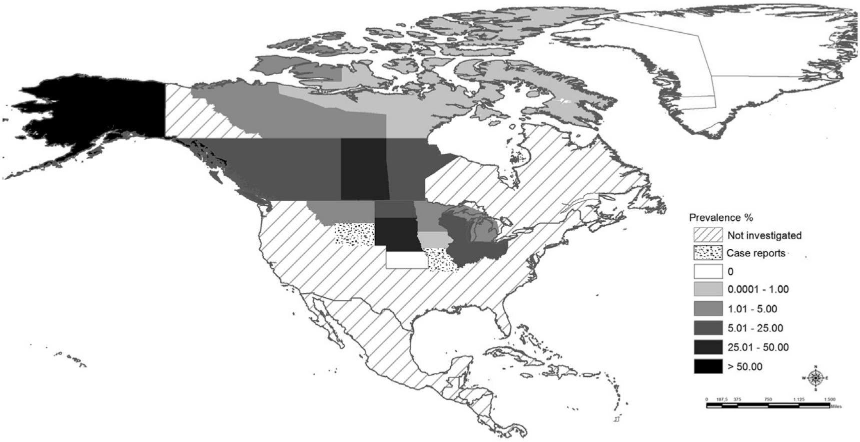

Figure 4 ***Current distribution of Echinococcus multilocularis in foxes (*****Vulpes vulpes, Vulpes lagopus, Urocyon cinereoargenteus*****), coyotes (*****Canis latrans*****) and wolves (*****Canis lupus*****) in North America (Canada, Greenland, United States).*** Areas with case reports of AE in intermediate hosts are approximately given as *dotted areas* if data of definitive hosts were missing. The detailed information (prevalence data in each jurisdiction) is listed in Table S3 of the Supplementary Material.

as case report on map) and Missouri is based on one unusual intermediate host and unpublished data in red fox (*V. vulpes*), respectively (Kritsky et al., 1977; Schantz et al., 1995). Central Indiana remains the southern limit of the parasite based on published data (Melotti et al., 2015).

Definition of the NCR now needs to reflect that the geographic range of the parasite appears to be expanding at western, eastern and northern distributional limits, although it is possible that new detections are, at least in part, a result of increased sampling effort and targeting of definitive hosts (DH) other than foxes. At its western distributional limits in Canada, it was recently detected as AE in a dog in 2009 and, subsequently, adult cestodes were found in coyotes (*Canis latrans*) in central British Columbia (Gesy et al., 2013; Jenkins et al., 2012). At its eastern distributional limits, the parasite has been recently detected as AE in dogs in southern Ontario, Canada, in 2012 and in wild canid definitive hosts in Illinois, Indiana, Ohio, and Michigan in the United States in the 1990s (Melotti et al., 2015; Skelding et al., 2014; Storandt and Kazacos, 1993). North of the northern distributional limit of the NCR in Canada (essentially corresponding to the northern limit of the prairie ecozone), the parasite had been considered absent in the boreal region separating the NTZ and the NCR (Schantz et al., 1995); however, the parasite has recently been detected in wolves (*Canis lupus*) in taiga and boreal regions of the southern Northwest Territories and northern British Columbia (Gesy et al., 2014; Schurer et al., 2014a, 2016).

In **Greenland**, *E. multilocularis* has not been reported. Although arctic foxes are present, the only potential rodent intermediate host (collared lemming, *Dicrostonyx rubricatus*) is not considered particularly suitable (Holt et al., 2005; Jenkins et al., 2013; Rausch, 1995). The parasite has not been reported from the southern United States or **Mexico**. Egg resistance to freezing and susceptibility to warmth and desiccation may limit this parasite to the northern hemisphere, raising the possibility that climate warming in North America may cause this parasite to shift northwards (Mas-Coma et al., 2008; Schiller, 1955; Veit et al., 1995). However, the haplotypes of the parasite present in the NCR are presumably tolerant of warmer temperatures and may continue to expand in distribution where suitable wildlife hosts are present (Jenkins et al., 2011). Red foxes are moving further North and are outcompeting Arctic foxes (Hersteinsson and MacDonald, 1992), perhaps bringing with them more temperate-adapted haplotypes of the parasite.

2.5.1.1 Transmission and host assemblages

Recognition of *E. multilocularis*, initially called *E. sibiricensis*, as a distinct species from *E. granulosus* was accomplished based on laboratory studies in Alaska in the 1950s (Rausch and Schiller, 1951). *Echinococcus multilocularis* was initially thought to be genetically uniform across its circumpolar range, and indeed there is less genetic diversity within *E. multilocularis* than the *E. granulosus* species complex. With the advent of genetic characterization at more discriminatory mitochondrial DNA loci, we are now recognizing greater diversity within *E. multilocularis* around the circumpolar North and within North America (Gesy et al., 2014; Nakao et al., 2009). Although much of this diversity is in the form of single nucleotide polymorphisms, there are distinct genetic groupings and differences, as well as ecological and biological differences between populations of *E. multilocularis* in the NCR and NTZ. Together, this suggests that we may need to revisit the taxonomic status of these populations.

Although morphologically similar, early experimental infections demonstrated distinct developmental differences between NTZ and NCR isolates of *E. multilocularis* (Bartel et al., 1992; Rausch and Richards, 1971). This was supported later by recognition of genetic differences between the NTZ (North American N1 and Asian) and NCR (North American N2) haplotypes of the parasite (Nakao et al., 2009) which belied previous suggestions that the parasite was a recent introduction from the north. Most recently, European haplotypes and the North American N2 and closely related haplotypes have been identified in wildlife in the NCR and other regions of northwestern Canada, suggesting a complex mosaic of endemic and introduced haplotypes of *E. multilocularis* (Gesy and Jenkins, 2015). More work is needed to determine if these haplotypes circulate in different host assemblages and if they differ in zoonotic potential.

Transmission of *E. multilocularis* in North America mainly involves wild canid definitive hosts and rodent intermediate hosts. Rarely, transmission may involve domestic pets and people; for example, on St. Lawrence Island, Alaska, with spillover of the parasite from wildlife to domestic dogs and, through dogs, to people (Rausch and Schiller, 1956). There are distinct ecological groupings in the NTZ and the NCR. In the NTZ, the parasite cycles between Arctic fox as definitive hosts and arvicoline rodents (i.e., lemmings, voles) and shrews as intermediate host. Red fox and coyote are also present as far north as the Arctic coast in western North America (Naughton, 2012), but there has been little surveillance effort in these potential definitive hosts. In the NCR, red fox and coyote serve as definitive hosts and neotomine (deer mice) and arvicoline rodents (primarily voles) as intermediate hosts. Wolves are newly recognized definitive hosts in taiga and boreal regions of North America (Schurer et al., 2016), where the parasite was once thought to be absent due to low rodent densities. Wolves may thus connect the disjunct populations of *E. multilocularis* in the NTZ and NCR, due to their large home range sizes (75–2500 km^2, exceeding 75,000 km^2 in the Arctic) and dispersal distances (50–800 km) (Naughton, 2012).

Translocation of *Echinococcus* spp. into and within North America has likely occurred with introduction of European red fox (Kamler and Ballard, 2002), translocation (illegal) of foxes for hunting enclosures (Davidson et al., 1992), reintroduction of wolves for conservation purposes (Foreyt et al., 2009), and importation of pet dogs from Europe and other regions of the world (Davidson et al., 2012; Jenkins et al., 2012). The latter is particularly concerning (and likely to be ongoing) as there is no mandatory testing or treatment for *Echinococcus* in imported or translocated companion animals in the United States or Canada, in large part due to failure to recognize species and finer scale genetic differences within *Echinococcus* spp. (Lymbery et al., 2015). Regulatory bodies for animal health need to consider genetic diversity within *E. multilocularis* and marked regional differences in prevalence, and consider testing and/or treatment of imported dogs and translocated wild canids to prevent importation of foreign haplotype or dissemination into nonendemic regions (such as the Atlantic provinces and states).

2.5.1.2 Infections in animals

Adult cestodes of *E. multilocularis* have been reported from multiple locations in endemic regions of the continental **United States** and **Canada** from Arctic fox, red fox, coyote and wolves (Table S3 in Supplementary Material). There is only one report of *E. multilocularis* in grey fox (*Urocyon cinereoargenteus*), by Vande Vusse et al., in 1978, cited in Melotti et al. (2015). The most epidemiologically significant wild canid definitive host depends on relative host abundance, home range size and dispersal distance, and infection intensity. By species, study prevalence (from the literature cited in Table S3 in Supplementary Material) was, on average, 25% in red fox (range 0.5–75%), 24% in coyote (range 0.4–44%) and 27% in wolf (8–67%). By region, coyote is likely a more important definitive host than red fox in the NCR, due to higher (and increasing) relative abundance in urban and agricultural regions, larger home ranges (10–190 km^2) and dispersal distances (often more than 100 km) (Naughton, 2012). Increasingly, the parasite is reported at high prevalence and intensity in thriving urban coyote populations in western Canada (Catalano et al., 2012; Gesy, 2012; Gesy and Jenkins, 2015; Hildreth et al., 2000; Leiby et al., 1970; Liccioli et al., 2012; Melotti et al., 2015; Seesee et al., 1983; Storandt and Kazacos, 1993, 2012), paralleling the European situation with red foxes.

Trends in prevalence are difficult to analyse due to highly biased sampling, with intense focus on North Dakota and St. Lawrence Island. Schantz et al. (1995) reported a trend for prevalence to increase over time, but this is greatly influenced by study design and may change dramatically with new molecular techniques for coprodiagnosis. Prevalence varies seasonally, with reports lowest in winter and highest in summer in red fox in North Dakota (Kritsky and Leiby, 1978) and highest in autumn and lowest in spring in Arctic foxes on St. Lawrence Island (Rausch and Fay, 2002). There are also geographic differences. In the United States region of NCR, the highest prevalences (>20%) were reported in South Dakota, Nebraska and Indiana, and lowest (<5%) in Iowa, Michigan and Montana (see Fig. 4 and Table S3 in Supplementary Material). In Canada, prevalence was greater than 20% in canid definitive hosts in Saskatchewan, Alberta, and British Columbia, and less than 5% in two northern territories. Prevalence was much higher in Arctic foxes on islands in Alaska (average 67%, range 32−100%) than on the Alaskan mainland (7.5%, range 2−15%) and in the western Canadian Arctic (1.5%, range 1−2%) (Eaton and Secord, 1979; Gesy et al., 2014; Jenkins et al., 2013; Kirk, 2010).

In a highly endemic island system (St. Lawrence Island), 5−13% of dogs were positive for *E. multilocularis* on examination of intestines at necropsy (Rausch and Fay, 2002), and dogs were considered the primary source of human exposure to the parasite (Stehr-Green et al., 1988). Outside Alaska, neither adult cestodes nor eggs of *E. multilocularis* have been reported from dogs in North America. Molecular characterization of taeniid eggs from faeces found only *Taenia* spp. and *Echinococcus canadensis* in nine taeniid egg positive samples from 1086 shelter dogs from across Canada (Villeneuve et al., 2015). While dogs are theoretically a good definitive host for *E. multilocularis*, so far in North America they are more commonly reported as aberrant intermediate hosts and are thus sentinels of environmental contamination rather than a source. More studies are needed to determine the true prevalence in dogs (as definitive hosts and intermediate hosts) in North America, as well as canine risk factors for exposure (breed, age, urban vs rural, predatory behaviour, immune status, access to areas used by wild canids, etc.).

There have been only two reports of naturally infected cats serving as definitive hosts for *E. multilocularis* in North America, one in Canada (Saskatchewan) and one in the United States (North Dakota) (Leiby and Kritsky, 1972; Wobeser, 1971). Gravid segments were reported in one cat in North Dakota. This reinforces that the parasite is uncommon in cats, and, combined with low infection intensities and fecundity in experimentally exposed cats (Kapel et al., 2006; Rausch and Richards, 1971), suggests that cats are an unlikely source of environmental contamination. There has been some effort to determine if wild felids (bobcats) are infected, but none has been found infected (Storandt et al., 2002).

Data on the incidence of AE in animal intermediate hosts are not routinely collected. The condition is not reportable to animal or human health authorities at the national level in Canada or the United States, although it is annually notifiable to the World Organization for Animal Health − OIE − by laboratories in both countries (http://www.inspection.gc.ca/animals/terrestrial-animals/diseases/annually-notifiable/eng/1305672292490/1305672713247; https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/monitoring-and-surveillance/sa_disease_reporting/ct_disease_list). Most reports are from targeted studies in wild rodents, opportunistic observations from trapped furbearers or case reports in domestic dogs, nonhuman primates in zoos, and people. Low prevalence in intermediate hosts, even in highly endemic areas, is the norm — if detected in rodents, this may be a better indicator of endemicity than detection in wild canid definitive hosts, as the latter have home range sizes of tens to thousands of square kilometres, and dispersal distances of hundreds of kilometres.

In the NTZ, *E. multilocularis* has been reported in ground squirrels (*Urocitellus parryii*), red-back voles (*Myodes rutilus*), tundra voles (*Microtus oeconomus*) and shrews (*Sorex jacksoni*) from St. Lawrence Island (Rausch and Schiller, 1956); reviewed in (Jenkins et al., 2013). Prevalence in voles on St. Lawrence Island ranged from 2 to 63% (reviewed in (Jenkins et al., 2013), and in spring could be as high as 80% before declining due to the 'wash-out' effect from uninfected young of the year (Rausch et al., 1990). The parasite is very rare in rodents in mainland Alaska, although it has been detected in <1% of brown lemmings (*Lemmus trimucronatus*) (Holt et al., 2005). There have been no reports in rodents in the Canadian Arctic; it was not detected in lemmings and voles in a region in the central Canadian Arctic with positive Arctic fox (Gesy et al., 2014).

In the NCR, the parasite has been reported from deer mice (*Peromyscus maniculatus*), house mice (*M. musculus*), meadow voles (*Microtus pennsylvanicus*), southern red backed voles (*Myodes gapperi*), bushy-tailed woodrats (*Neotoma cinerea*), and muskrats (*O. zibethicus*) (Gesy et al., 2013; Gesy and Jenkins, 2015; Holmes et al., 1971; Kritsky et al., 1977; Leiby et al., 1970; Liccioli et al., 2013). In the NCR, prevalence is so low and studies so few that geographic and seasonal trends are not readily apparent. In deer mice, the most successful intermediate hosts in the NCR, prevalence in 11 studies reporting nonzero values ranged from 0.5% to 22%, with an average of 5%. In meadow vole, average prevalence was 3% (range 0.8—6%) in five studies reporting nonzero values (references cited in Table S4 in Supplementary Material).

AE has recently been reported for the first time as a clinical issue in domestic dogs in Canada, with detection of a European haplotype in a dog native to central British Columbia in 2009, followed by detection in a dog native to southern Ontario in 2012, both previously considered nonendemic regions for *E. multilocularis* (Jenkins et al., 2012; Peregrine et al., 2012; Skelding et al., 2014). At present, four dogs with AE have been reported in southern Ontario since 2012 (Peregrine, 2015). Within the Canadian NCR, AE was detected in a dog from Manitoba in 2012, followed by six cases of AE in dogs from Alberta and Saskatchewan from 2014 to 2016 (two cases/year in each province) based on a search of the Prairie Diagnostic Services database in April 2016. This raises the possibility that introduced European haplotypes now established in wild canids may be responsible for the emergence of AE in dogs in both previously and newly endemic regions of Canada. Public health authorities in Canada, and possibly the northern United States, need to be vigilant for new human cases, as dogs could be serving as sentinels of a newly emerging threat to human health.

2.5.1.3 Alveolar echinococcosis in humans

Outside of Alaska, AE has not been considered a mainstream human health issue in North America. Reports of AE in North Americans in the literature are generally limited to case reports, reviews of hospitalization data, and serological/skin test studies (fraught with both false positives and negatives). Unfortunately, AE is not always distinguished from CE, and CE is a far more likely diagnosis. When AE is diagnosed, incomplete travel histories and a very low expected prevalence generally lead to assumptions that most cases are foreign acquired.

In **Canada**, prior to 2013, only one autochthonous case has been reported. This case was an Icelandic immigrant in Manitoba in 1935 (James and Boyd, 1937). In 2013, an immunocompromised patient from rural west-central Alberta presented with AE. The cyst material typed as European, despite no history of travel to Europe (Massolo et al., 2015). A recent review of hospitalization data in Canada found 16 AE cases between 2002 and 2011, most commonly reported in liver and as metastases to multiple sites (Schurer et al., 2015). A similar review found 12 cases of AE between 2001 and 2014, all in regions endemic for *E. multilocularis* (British Columbia, Alberta, Saskatchewan and Ontario) (Massolo et al., 2014). Both studies significantly underestimate the true prevalence of AE, as the type of echinococcosis was not reported in 191 and 251 cases, and because the estimates did not adjust for cases that did not seek medical treatment. Regardless, the geographic distribution of human cases of AE overlaps with the known distribution of *E. multilocularis* in wildlife in Canada, and the possibility of endemic transmission should not be dismissed out of hand.

In the **United States, Alaska** has historically been a hotspot for autochthonous cases of human AE, with a few cases on the northwestern coast of mainland Alaska (Castrodale, 2003). Testing for AE using serology, skin tests, medical imaging and biopsy is reviewed in Jenkins et al. (2013), Rausch and Schiller (1956) and Wilson et al. (1995). The incidence of AE on St. Lawrence Island based on serosurvey has been as high as 98/100,000 (Schantz et al., 1995). From reported data, there were a total of 54 human cases of AE between 1947 and 1986 in Alaska, and no cases of AE from 1987 to 2010 [reviewed in Jenkins et al. (2013)]. Between 2010 and 2014, there were five reported cases, mostly from interior and southeastern regions of Alaska, more likely to be CE than AE (http://epibulletins.dhss.alaska.gov/Bulletin/DisplayClassificationBulletins/42).

Recent characterization of cyst material from voles on St. Lawrence Island (Nakao et al., 2009) and eggs from Arctic foxes on the North Slope of Alaska (Kirk, 2010) as Asian haplotypes of *E. multilocularis* raise the possibility that the hyperendemic focus of AE in northwestern Alaska reflects higher zoonotic potential of Asian haplotype of the parasite, and not simply unique ecological and behavioural risk factors.

Outside Alaska, only one autochthonous case in the United States is reported from a resident of Minnesota in 1977 (Gamble et al., 1979) who was subsequently identified as the N2, or central North American, haplotype (Klein and Massolo, 2015; Yamasaki et al., 2008). This is the first and only report of zoonotic transmission of the N2 haplotype endemic to the NCR; there was no evidence of exposure in a serological survey of high risk people (trappers) in the United States region of the NCR (Hildreth et al., 2000).

Genetic differences between haplotypes of *E. multilocularis* present in the NCR and NTZ (notably St. Lawrence Island) could account for the historical lack of human cases of *E. multilocularis* observed in North America outside Alaska, despite relatively high prevalence in wild canids in the NCR. While it is possible that there is decreased opportunity for human exposure in the NCR, many indigenous and rural inhabitants of this region of North America hunt, trap, consume untreated surface water, keep dogs as pets and working animals, and harvest foods that could be contaminated with faeces of wild canids. Enhanced surveillance, epidemiological investigation and molecular characterization of cestodes from canid definitive hosts, and cysts from animal and human intermediate hosts of AE, are needed to better understand the biological significance of genetic diversity within populations of *E. multilocularis* in North America, and their potential to emerge along with changes in climate, landscape, and the wildlife/human interface.

3. GLOBAL DISTRIBUTION OF *ECHINOCOCCUS* SPP. CAUSING CYSTIC ECHINOCOCCOSIS

The global endemic areas of *Echinococcus* spp. causing CE based on data mainly from domestic intermediate hosts are depicted in Fig. 5.

3.1 North America: Mexico, United States, Canada and Greenland

3.1.1 Introduction and molecular epidemiology

CE in humans and intermediate hosts in North America is caused by wildlife-associated genotypes of *E. canadensis* (primarily in cervid intermediate hosts), and livestock-associated genotypes of *E. granulosus sensu lato* (sheep, swine and cattle intermediate hosts). *Echinococcus canadensis* (G8 and G10 – Table 4) has the greatest geographic distribution and prevalence in Canada, Alaska and the northern latitudes of the contiguous United States, where assemblages involve wolves (*C. lupus*) and cervids (especially moose, *Alces alces*; caribou, *Rangifer tarandus*; and elk, or wapiti, *Cervus canadensis*). *Echinococcus granulosus* (not genotyped) is maintained in a dog–sheep assemblage in western states of the United States. In Mexico, *Echinococcus intermedius* (G7) is maintained in a dog–swine assemblage, and there are isolated reports of *E. granulosus* (G1) and *Echinococcus ortleppi* (G5) (Table 4). While annually notifiable to the World Organisation for Animal Health (OIE) at the laboratory level, there is no formal surveillance in place for CE in animals (especially wildlife) in North America. Domestic livestock are routinely inspected at slaughter in the United States, Canada and Mexico; however, small ruminants (goats and sheep) are often slaughtered and sold at the 'farm gate', and would not be inspected. Wildlife hosts (canids and ungulates) are not routinely inspected, and cysts detected in ungulates at necropsy, the most conclusive method of detection, are often considered incidental findings. Intestines of wild canids are not routinely opened at necropsy due to the risk of zoonotic *Echinococcus* spp. in Canada and the United States.

Historically, human CE in northern North America was associated with the presence of sled dogs, which were a vital source of transport for indigenous groups. The incidence of CE declined as sled dogs were replaced with motorized transport (Rausch, 2003); however, northern and indigenous populations remain overrepresented, possibly due to the presence of large free-roaming dog populations, challenges in preventing dogs from scavenging and hunting and the limited access to commercial dog food or

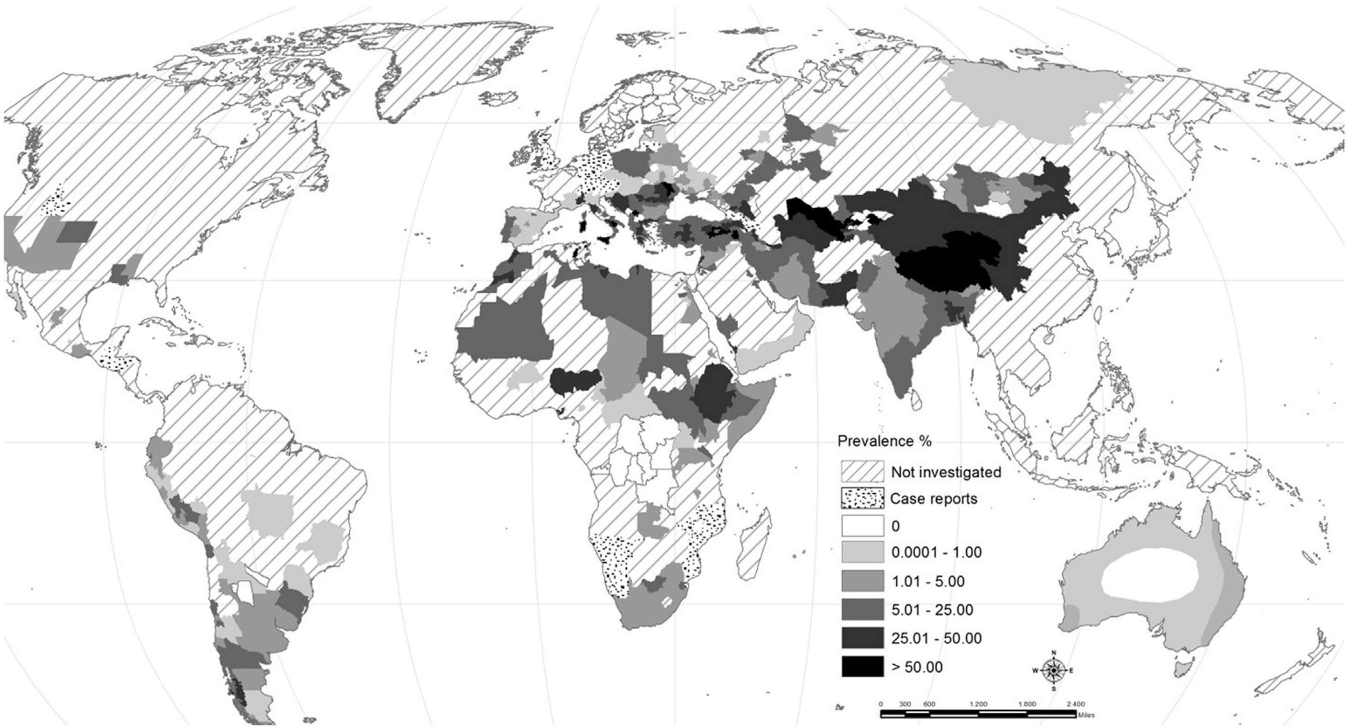

Figure 5 ***Current global distribution of Echinococcus spp. causing cystic echinococcosis in the main domestic intermediate hosts (not included are the cervid genotypes of Echinococcus canadensis and Echinococcus equinus).*** In addition, in areas where data of domestic intermediate hosts are missing, case reports of CE in wild intermediate hosts are given as *dotted areas* (see Fig. 12). For published details of the distribution/prevalence in the different countries/jurisdictions, see detailed maps (Figs. 6–13), Supplementary Material (Tables S5–S14) in Appendix A and text. Note that a positive finding in any host, study or jurisdiction renders the whole jurisdiction endemic.

Table 4 Genotypes of *Echinococcus* spp. causing cystic echinococcosis in North America: *Echinococcus granulosus* (G1), *Echinococcus ortleppi* (G5), *Echinococcus intermedius* (G7) and *Echinococcus canadensis* (G8, G10)

Country	Human	Canids	Cervids	Swine
Canada		G8[1,2] G10[1,2,3,4]	G8[4,5] G10[4,5]	
United States	G8[6]		G8[4,7] G10[4]	Historically present but eradicated
México	G5[8]	G7[9]		G1[10] G7[9,10,11]

[1] (Bryan et al., 2012); [2] (Schurer et al., 2014a); [3] (Himsworth et al., 2010); [4] (Thompson et al., 2006); [5] (Schurer et al., 2013); [6] (McManus et al., 2002); [7] (Lichtenwalner et al., 2014); [8] (Maravilla et al., 2004); [9] (Rodriguez-Prado et al., 2014); [10] (Villalobos et al., 2007); [11] (Cruz-Reyes et al., 2007).

cestocidal treatment. The epidemiological and geographical picture of human CE is somewhat unclear for North American countries because echinococcosis is not nationally reportable in people, and when data are available, species/genotype and source (autochthonous or foreign acquired) of CE in human cases is rarely reported. Efforts to estimate human incidence are also hampered by underdiagnosis, as infected individuals often remain asymptomatic for several years (or indefinitely with the cervid associated strains), before presenting with nonspecific clinical features. Furthermore, only two studies report the molecular characterization of domestically acquired human CE in North America (G8 in Alaska and G5 in Mexico), demonstrating a major gap in our understanding of distribution and risk (Maravilla et al., 2004; McManus et al., 2002).

3.1.2 The United States

Host assemblages and transmission: *Echinococcus canadensis* (G8 and G10) occurs in moose, caribou, white-tailed deer (*Odocoileus virginianus*), mule and black-tailed deer (*Odocoileus hemionus*), and elk, with sporadic or historical reports of *E. granulosus sensu lato* in mountain goats (*Oreamnos americanus*), swine, cattle and horses (Eckert et al., 2001; Hoberg et al., 1994; Jenkins et al., 2013; Ward and Bradshaw, 1956). *Echinococcus canadensis* G10 is present in moose in Washington state, and G8 in moose in Alaska, Minnesota and Maine (Bowles et al., 1994; Lichtenwalner et al., 2014; Thompson et al., 2006). Definitive hosts for *E. granulosus* in the United States include wolves, coyotes (*C. latrans*) and dogs (Eckert et al., 2001). The reintroduction of wolves to Idaho and Wyoming in the 1990s has been associated with an apparent increase of *E. canadensis* in wild cervids and canids, causing considerable conflict between livestock ranchers and conservation biologists (Foreyt et al., 2009). G8 has been identified in a human case of CE in Alaska (McManus et al., 2002). CE is not a major public health concern in the United States, and most recent cases are foreign acquired.

CE in animals: CE is reported in wild ungulates across Alaska and the northern states of the contiguous United States. In the 1950s, the prevalence of CE in Alaskan moose was approximately 20% (N = 124), with infected moose documented in the lower Matanuska River and the Anchorage–Palmer regions (Rausch, 1959). Surveys of caribou in Alaska during the same time period reflected a lower prevalence (0/200, 2/79, 3/63 and 4/67 animals investigated) (Rausch and Williamson, 1959; Rausch, 2003). A recent survey in the state of Maine found hydatid cysts in 39% of 54 moose, which was unexpected because CE was not thought to occur in the northeastern United States due to the absence of wolves (Lichtenwalner et al., 2014). Infected moose have also been observed in Minnesota and the state of Washington (Bowles et al., 1994; Thompson et al., 2006). A 25-year survey of CE in Californian deer reported a prevalence of 1.3% (Brunetti and Rosen, 1970). There are two reports of infected mountain goats in Alaska and in Idaho (Foreyt et al., 2009; Rausch and Williamson, 1959).

Currently in the United States, sheep are the only known intermediate host for livestock genotypes of *E. granulosus*, and the distribution is limited to focal areas of the western United States where incidence is low. In the last 30 years, large scale surveys of Utah slaughterhouses observed CE in 1.6–8.2% of sheep (Crellin et al., 1982; Loveless et al., 1978); this was confirmed by trace-back analysis from another facility reporting infected sheep in Utah (10%; N = 986), Colorado (7%; N = 15), New Mexico (17%; N = 35) and the Navajo reservation (New Mexico and Arizona; 16%; N = 115) (Schantz et al., 1977b). A similar survey of a California slaughterhouse that processed both in-state and out-of-state animals reported an overall prevalence of 4.8% (N = 22,720) (Sawyer et al., 1969). Reports of hepatic CE in swine and cattle in the southeastern United States date to the mid-20th century, when backyard swine production was common, and household dogs had close contact with livestock. Slaughterhouse surveys of swine reported prevalences of 0.9% (N = 33,174) and 6% (N = 8066) in Mississippi, and 5–20% in Louisiana (Hutchison, 1960; Ward and Bradshaw, 1956). Approximately 1% (N = 800) of cattle were infected (Ward and Bradshaw, 1956), but there are no recent records of CE in cattle. Swine CE is no longer thought to occur in the United States, which is likely attributable to improvements in biosafety and the move towards large-scale indoor production. However, the current consumer trend for outdoor, free-range production facilities and the concomitant spread of feral swine across the United States increase the risk for CE to establish in domestic assemblages, indicating the need for monitoring. There are only six American reports of CE in horses, only one of which was confirmed to be autochthonous and originated either in Virginia or Maryland (Hoberg et al., 1994).

The earliest record of an infected wolf was 1933, coinciding with observations of infected moose in Minnesota (Riley, 1933). Two decades later, necropsy of canids in Alaska demonstrated an infection prevalence of 30% (N = 200) for wolves and 4–22% for sled dogs (Jenkins et al., 2013; Rausch and Williamson, 1959; Rausch, 1960), with the latter acting as primary definitive hosts in agriculturally intensive regions (Rausch, 2003). In 2006, the finding of CE in a mountain goat prompted a survey of 123 wolves in Idaho and Montana, revealing an infection prevalence of 63% (Foreyt et al., 2009). Approximately half (53%) of infected wolves harboured more than 20,000 adult cestodes, 13% held between 2000 and 20,000 and 34% had less than 2000. The source of infection for these wolves remains unclear because wolves were historically extirpated from this region. There is some speculation that wolves reintroduced from Canada (Alberta and British Columbia) to the United States (Idaho and Wyoming) in the mid-1990s might have carried the cestode, despite treatment with praziquantel (a cestocidal agent) prior to their move (Foreyt et al., 2009; Johnson, 2001). Alternatively, definitive hosts (such as coyotes) could already have existed in the area, or infected wolves could have migrated naturally from Canada to the United States (Foreyt et al., 2009).

In the contiguous United States, where wolves are largely absent, coyotes likely play a role in transmission of *E. canadensis*. In the 1970s, 4% of 173 coyotes in seven counties in California harboured adult cestodes (Liu et al., 1970). The sympatric distribution of infected black-tailed deer (*Odocoileus hemionus columbianus*) provided evidence for a coyote–deer assemblage in this state (Brunetti and Rosen, 1970; Romano et al., 1974). Negative findings in coyotes from sheep-rearing regions suggest that coyotes may not play an important role in transmitting *E. granulosus* (Butler and Grundmann, 1954). Between 1892 and 1975, *E. granulosus* has been reported in dogs from Washington DC, Georgia, Tennessee, Kentucky, Mississippi, California, Utah and New Mexico (Pappaioanou et al., 1977). Sheep dogs imported from Australia in 1938 likely introduced *E. granulosus* to Utah, after which it spread to surrounding states (Crellin et al., 1982). The maintenance of a dog–sheep assemblage was confirmed by longitudinal surveillance of dogs and sheep in the 1970s, reporting adult cestodes in 11.3% (N = 839) of Utah dogs (Loveless et al., 1978), followed by detection in Navajo dogs (0.7% of 429) in Arizona and New Mexico (Schantz et al., 1977a,b). In the eastern United States where swine infection was historically present, postmortem examination of 9300 dogs identified only four infected animals, and small scale surveys of wild canids revealed no *Echinococcus* positive animals (Hutchison, 1960; Ward, 1965). Recent national surveys of intestinal parasites in dogs did not address *E. granulosus* (Gates and Nolan, 2009; Little et al., 2009).

CE in humans: CE is not an important cause of morbidity or mortality in the United States, and most cases are imported (Donovan et al., 1995). Overall, incidence of CE in people declined significantly in the latter half of the 20th century, which is attributed to the phasing out of sled dogs in Alaska, pathogen reduction in countries of origin for immigrants (e.g., Iceland, New Zealand), the development of cestocidal treatments, and the introduction of control measures in livestock in endemic foci (Katz and Pan, 1958; Loveless et al., 1978; Rausch, 2003). In Alaska, where CE is reportable, 193 cases were reported prior to 1980, but only eight cases were reported after 1990 (Hueffer et al., 2013). A comprehensive review of case reports between 1900 and 1974 identified 123 cases of autochthonous CE in the contiguous United States (Pappaioanou et al., 1977). Maps of the human incidence reflect the rise and decline of *E. granulosus* s.l. circulating in swine in the southeast followed by the introduction and control of CE in sheep in the west (Pappaioanou et al., 1977). Certain cultural groups (Mormons, Navajo and Zuni tribes and American-Basques) experienced higher rates of CE in the western states, largely due to the use of dogs in sheep herding and the practice of feeding sheep carcasses to these dogs (Araujo et al., 1975; Schantz et al., 1977a). Today, autochthonous cases are rare, with sporadic cases in Alaska, California and Utah (Moro and Schantz, 2009). Approximately one to four cases occur among Navajo tribes in New Mexico and Arizona each year (Moro and Schantz, 2009). An examination of death certificates issued for all states between 1990 and 2007 identified echinococcosis (CE and AE) in only 41 deaths and identified a greater frequency in males, Asian/Pacific Islanders, Hispanics, Native Americans and those aged 75 years or older (Bristow et al., 2012).

3.1.3 Canada

Host assemblages and transmission: Only *E. canadensis* (G8, G10) is present in Canada, and G10 appears to be more common in wildlife in western Canada based on limited sampling (Schurer et al., 2013, 2014a). Definitive hosts include wolves, coyotes, and dogs, while intermediate hosts are usually wild or captive-bred cervids. The two genotypes (G8 and G10) of *E. canadensis* occur in sympatric distribution in Canada and are widely distributed across the country, except for the Maritime Provinces, the island of Newfoundland and the High Arctic islands (Schurer et al., 2013; Sweatman, 1952). In intermediate hosts, G8 has been observed in elk (also known as wapiti or *Cervus canadensis*) in Alberta and muskoxen (*Ovibos moschatus*) in Nunavut; while G10 has been observed in moose, elk and caribou in Alberta, Saskatchewan, Manitoba and Quebec (Schurer et al., 2013; Thompson et al., 2006). Wolves infected by *E. canadensis* G8 are found in British Columbia, Saskatchewan, Manitoba and the Northwest Territories, and wolves infected by *E. canadensis* G10 are similarly distributed with the addition of Alberta (Bryan et al., 2012; Schurer et al., 2014a; Thompson et al., 2006). *Echinococcus canadensis* G10 is also present in domestic dogs in Saskatchewan (Himsworth et al., 2010). Coyotes (*C. latrans*) are competent definitive hosts for *E. granulosus* s.l. (presumably *E. canadensis*, but isolates from this host have not yet been characterized genetically). In people, CE is overrepresented in residents in the northern territories, and many cases elsewhere are assumed to be foreign-acquired; overall, it is not currently a major cause of morbidity or mortality in Canada.

CE in animals: Moose and caribou/reindeer (*R. tarandus*) are primary intermediate hosts for CE, and prevalence in these hosts is estimated at 42–47% and 1–21%, respectively, when only studies with sample sizes over 100 animals are considered (Rausch, 2003; Schurer et al., 2013; Sweatman, 1952). The most comprehensive survey of reindeer was conducted in the Northwest Territories in the 1950s, and 9.5% of 1664 animals had hydatid cysts (Choquette et al., 1957). Metacestodes are also commonly observed in elk (11–38%) and white-tailed deer (*O. virginianus*; 0–0.3%); however, cysts in these animals appear to be less fertile than cysts in moose and caribou, suggesting that they play a diminished role in the life cycle (Schurer et al., 2013; Sweatman and Williams, 1963). Other intermediate hosts include black-tailed and mule deer, muskoxen, and American bison (*Bison bison*), although these are less common (Rausch and Williamson, 1959; Schurer et al., 2013; Sweatman and Williams, 1963). Only historic records exist of hydatid cysts in horses and swine, and there are no records of naturally infected cattle or sheep in Canada (Sweatman, 1952; Sweatman and Williams, 1963). Industry losses due to CE are presumably low in

Canada, where captive-raised cervids can be infected, but not domestic livestock (sheep, cattle, goats).

Wolves are the primary definitive host for *E. canadensis* in Canada. Examination of 191 wolves from three western provinces and one territory reported both G8 (6%) and G10 (24%), with a median intensity of 2258 ± 24,397 cestodes (range: 15−149,600) (Schurer et al., 2016). Mixed infections of *E. canadensis* G8−G10 (5%) and G10-*E. multilocularis* (6%) also occurred. These estimates are consistent with older postmortem surveys of wolves (20−24%) in Ontario and the Northwest and Yukon Territories, but are lower than that reported in Alberta (72%) (Choquette et al., 1957; Freeman et al., 1961; Holmes and Podesta, 1968). The most recent helminth surveys of coyotes did not detect *E. granulosus* s.l. in Alberta, Saskatchewan or Newfoundland (Bridger et al., 2009; Catalano et al., 2012; Thompson et al., 2009). Previously, adult cestodes were observed in 0.5−9% of coyotes in Alberta, Manitoba and Ontario (median intensity of 13−675 cestodes per infected animal) (Freeman et al., 1961; Holmes and Podesta, 1968; Samuel et al., 1978). Contemporary surveys of dogs are generally limited to faecal assessments, most of which report only taeniid egg prevalence. Of the four Canadian studies where taeniid eggs were identified to species level, one detected *E. granulosus* s.l. in British Columbia, Alberta and Ontario, one detected *E. canadensis* (G10) in Saskatchewan (6%; N = 155), and two others did not detect *Echinococcus* in Saskatchewan (Himsworth et al., 2010; Schurer et al., 2014a; Villeneuve et al., 2015). A previous postmortem survey of 114 dogs collected from 28 indigenous communities in British Columbia, Alberta and the Northwest Territories detected adult *Echinococcus* spp. cestodes in 28% of animals (Miller, 1953).

CE in humans: Reports of human CE are found as early as 1883, and until the 1950s, most cases occurred in immigrants originating in European countries such as Iceland and Italy, where livestock strains were endemic (Cameron, 1960; Finlayson and Fergus, 1963). After this time, autochthonous cases were routinely detected as incidental findings during chest radiographs for tuberculosis screenings, with higher rates reported for northern and indigenous peoples than any other ethnic group (Lamy et al., 1993; Miller, 1953). Today, as there is no national surveillance, CE prevalence can only be estimated by integrating data from serosurveillance studies, hospitalization data and case reports. Serosurveillance in indigenous communities in Saskatchewan, Nunavut, the Northwest Territories and Quebec show exposure levels ranging from 0% to 48% (Jenkins et al., 2013; Schurer et al., 2014b). According to clinical records, annual CE incidence ranges from 0.72 to 1.4 clinical cases per million people with an overrepresentation of cases in the northern territories, although these rates are acknowledged as underestimates (Gilbert et al., 2010; Schurer et al., 2015). Hospital records suggest that cases of echinococcosis (CE and AE) are distributed across Canada (Massolo et al., 2014; Schurer et al., 2015). Gender (females > males), indigenous ethnicity and residence north of 55°N are considered contemporary risk factors for autochthonous CE (Gilbert et al., 2010; Jenkins et al., 2013; Somily et al., 2005).

Healthcare costs associated with CE have been calculated in Canada and are based on direct costs associated with medical treatment (e.g., medical imaging, surgery, chemotherapy, over-the-counter and prescription medications and hospitalization). On average, the healthcare system pays $8842 CAD (2015) to treat one case of CE. This does not include indirect costs associated with recurrent illness, long-term disability, mortality, income lost due to missed work, the cost to care for sick family members or transportation to obtain medical care, which can be significant for patients in remote or northern regions. Regional programs to prevent CE in people by dosing dog populations with praziquantel at 6-week intervals are not currently feasible from a financial perspective, even when indirect costs such as long-term sequelae are considered (Schurer et al., 2015). However, such prevention programs could become cost-saving in areas of localized outbreaks or in high-risk communities.

3.1.4 Mexico

Host assemblages and transmission: In Mexico, CE is predominantly maintained by the swine–dog assemblage (*E. intermedius,* G7) (Cruz-Reyes et al., 2007; Rodriguez-Prado et al., 2014; Villalobos et al., 2007). *Echinococcus oligarthra* has been found in a bobcat (Salinas-López et al., 1996). Reports of G1, *E. ortleppi* and *E. oligarthra* are uncommon, and there is little evidence to support their widespread distribution in México (Rodriguez-Prado et al., 2014). Only a single autochthonous human case has been reported and involved *E. ortleppi* (cattle strain, G5) (Maravilla et al., 2004). CE is not considered a public health priority in Mexico as the majority of human cases are foreign-acquired, and new cases occur infrequently (Eckert et al., 2001; Steta and Torre, 2009).

CE in animals: Slaughterhouse studies of swine have shown CE prevalence of 0.27% of 40,073 (Vargas Rivera et al., 1995), 6.5% of 2873 (Martínez-Maya et al., 1994) and 5% of 87 (Flisser et al., 2015) in the states of la Paz, Zacatecas and Oaxaca, respectively. The prevalence in cattle is far lower (0.1% of 3079), and CE was not detected in other livestock (sheep and goats) surveyed in the same studies (Martínez Maya et al., 1994; Rodriguez-Prado et al., 2014).

Parasite surveillance in the Federal District and the states of Queretaro, Zacatecas and México demonstrated that dogs were infected with adult *Echinococcus* stages. The infection prevalence was low in all studies (0.49−0.85%), and it is unclear whether wild definitive hosts also contribute to the life cycle (Eguia-Aguilar et al., 2005; Fernández and Cantó, 2002; Rodriguez-Prado et al., 2014).

CE in humans: Between 1990 and 1998, only 33 hospitalized cases with postoperative diagnosis of CE were reported in the yearbook statistics of the Mexican Ministry of Health. A small number of human cases have been reported in the literature in different states of Mexico (Cornejo-Juarez et al., 2013; Cortés Carrasco et al., 2002; Cruz Benítez, 2009; Orea-Martinez et al., 2013; Steta and Torre, 2009; Suarez et al., 1995; Valenzuela Ramos et al., 2010; Villarreal Jiménez et al., 1995). Only 11 cases in the last 60 years were autochthonous (Steta and Torre, 2009). The only molecular data available reported the presence of *E. ortleppi* (G5) in a single human case of CE (Maravilla et al., 2004). Serosurveillance of a suburban population close to a slaughterhouse that detected pigs with CE found that 15% of 200 participants had been exposed (Sánchez-González et al., 1997); however, it is important to consider that cross-reactivity with other cestodes in this kind of test can lead to false positives. Finally, ultrasound screening has shown cases of CE in 0.75% of 401 people in the State of Mexico (Mata-Miranda et al., 2007).

3.2 Central America

CE has been reported sporadically in humans in the past in countries of Central America, such as Guatemala, El Salvador, Honduras, Cuba, Panama (Sanchez et al., 1992; Sousa and Lombardo Ayala, 1965) and Costa Rica (Brenes Madrigal et al., 1977). However, local transmission and molecular data have not been documented for any of these countries. No new information is available regarding human CE in most of these countries, except in Cuba, with recent reports of both autochthonous and imported cases (Escalante et al., 2012; González Núñez et al., 2001).

Previous data described sporadic animal and human cases in Guatemala, El Salvador and Honduras. In recent years, a report of postmortem inspections of livestock in Haiti described CE as affecting mostly pigs (5.2%), but also sheep (2.1%), goats (0.9%) and cattle (0.3%). A high infection prevalence in dogs was detected in the same study (25%) (Blaise and Raccurt, 2007).

3.3 South America: Argentina, Bolivia, Brazil, Chile, Colombia, Ecuador, Paraguay, Peru, Uruguay and Venezuela

3.3.1 Host assemblages, transmission and molecular epidemiology

In South America, CE is known to occur with high prevalence in parts of Argentina (Patagonia, Pampas, Coast), Bolivia (southwest), Brazil (south), Chile (southland central valley regions and extreme south), Peru (central and southern highlands) and Uruguay (see Fig. 6 and Table S5 in the Supplementary Material). The disease has major human health and socioeconomic importance (Fig. 7 and Table S6) and has a high prevalence in livestock.

In South America, CE is maintained by domestic cycles of transmission that involve dogs and herbivores (sheep, swine, cattle, goats, horses and camelids) and multiple species/genotypes including *E. granulosus* (G1−3), *E. ortleppi* (G5) and *E. intermedius* (G6/7) (Table 5). Argentina hosts more strains than any other country, while Peru has the most human CE cases, despite underreporting. Human CE is associated with G1-3 in Argentina, Brazil, Chile, Peru and Bolivia; G5 in Argentina and Brazil; and G6 in Argentina, Chile and Peru. Intermediate hosts for G1−3 include sheep, cattle, goats, alpaca and swine with cattle the intermediate host for G5, goats for G6 and swine for G7.

The reservoir for G6 involves goats (Soriano et al., 2010) and infects humans in the Neuquén region (Guarnera et al., 2004; Kamenetzky et al., 2002), Rio Negro and Buenos Aires (Rosenzvit et al., 1999) and Catamarca. Dogs infected with *E. intermedius* (G6) have been reported in Rio Negro, Neuquén and Catamarca. *Echinococcus ortleppi* has been described in few isolated cases in animals and humans from remote areas of Argentina: Neuquén (South) (Guarnera et al., 2004) and Tucuman (North) (Kamenetzky et al., 2002). Infected animals include two cattle in Santa Fe and two dogs in Catamarca (Kamenetzky et al., 2002). The G7 genotype of *E. intermedius* has been described in pigs from Santa Fe (Rosenzvit et al., 1999) and Buenos Aires (Kamenetzky et al., 2002) and one dog in Neuquén (Kamenetzky et al., 2002); no human cases have been detected. In southern **Brazil**, *E. granulosus* has a sympatric distribution with *E. ortleppi* and with *E. intermedius* (G7) (Rio Grande do Sul State)

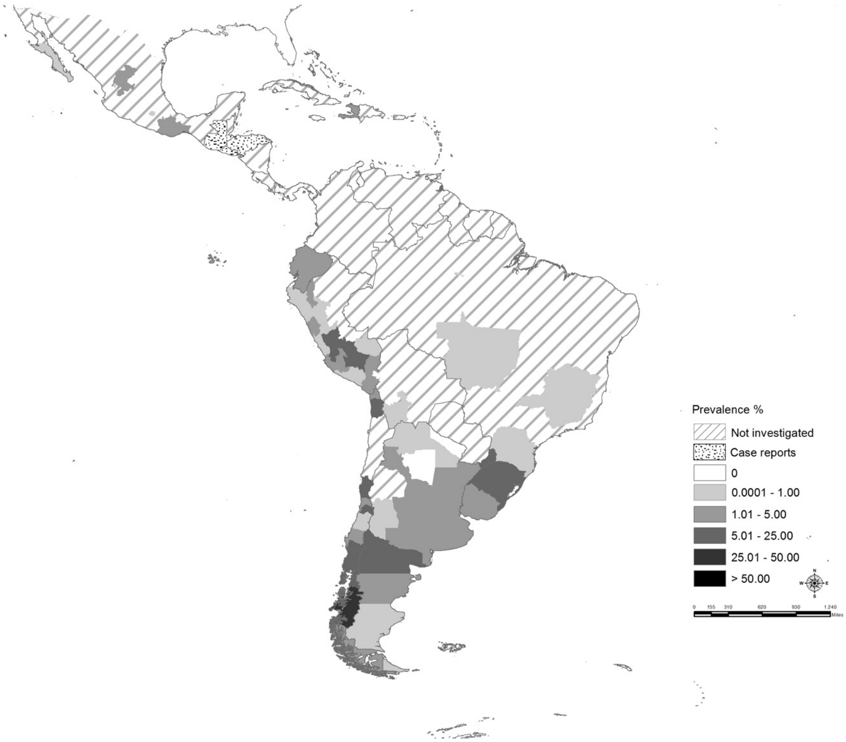

Figure 6 ***Current distribution of Echinococcus spp. causing cystic echinococcosis in domestic intermediate hosts (sheep, cattle and pigs) in Central and South America.*** The detailed information (prevalence data in each jurisdiction) is listed in Table S5 of the Supplementary Material.

(Balbinotti et al., 2012; de la Rue et al., 2006). A single human case of *E. ortleppi* was reported (de la Rue et al., 2011).

In **Chile**, a single case of *E. intermedius* (G6) has been reported in a study in which 19 other CE cases were *E. granulosus* (G1) (Manterola et al., 2008). A second study described the presence of *E. granulosus* in cattle (Espinoza et al., 2014). In **Peru**, *E. granulosus* is responsible for most animal and human infections (Moro et al., 2009; Sánchez et al., 2010; Santivanez et al., 2008); however, a few cases of *E. intermedius* (G6 and G7) have been reported in humans and pigs, respectively (Moro et al., 2009; Sanchez et al., 2012; Santivanez et al., 2008). Molecular data from **Uruguay** is

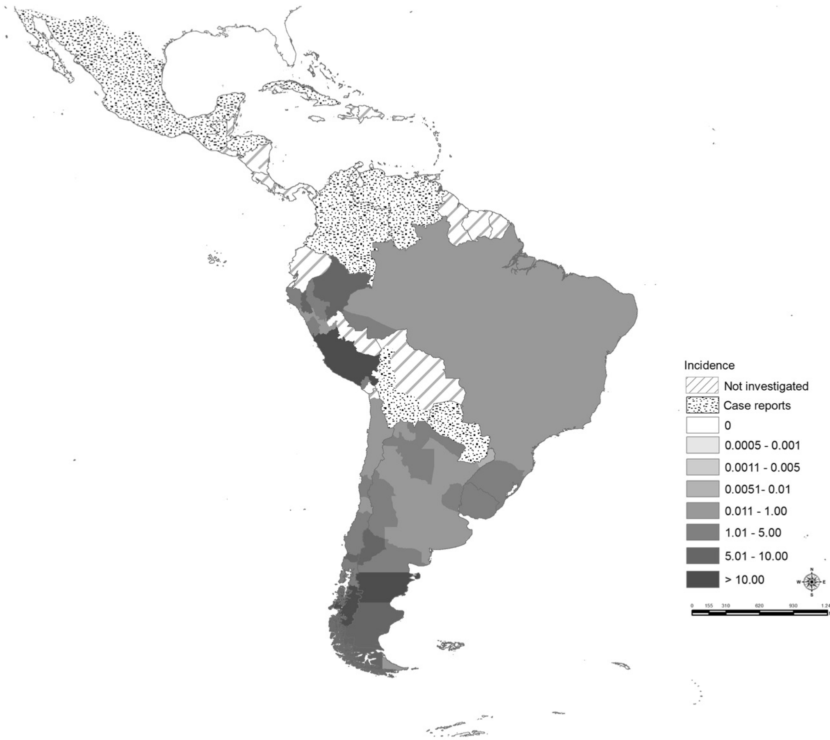

Figure 7 ***Current incidence of human cystic echinococcosis in Central and South America.*** The detailed information (incidence data in each jurisdiction) is listed in Table S6 of the Supplementary Material.

limited to a few samples included in studies reporting the genetic variability of *E. granulosus* in other South American countries. Five samples from cattle have been characterized as *E. granulosus* (G1) (Cucher et al., 2016; Kamenetzky et al., 2002), while two samples from cattle have been identified as *E. ortleppi* (Cucher et al., 2016). A similar situation is true for **Bolivia**, where molecular data is limited to a single report of *E. granulosus* (G1) in a person (Kamenetzky et al., 2002).

3.3.2 Infection in animals

In general, good documentation is available for livestock cases at post-mortem examination in most South American countries (Fig. 6) involved in the initiative for the control of CE led by the Pan American

Table 5 Genotypes of *Echinococcus* spp. causing cystic echinococcosis in South America: *Echinococcus granulosus* (G1−3), *Echinococcus ortleppi* (G5), *Echinococcus intermedius* (G6/7)

Country	Human	Dog	Sheep	Cattle	Goat (Go)/Alpaca (A)	Pig
Argentina	G1[1,2,3,4] G2[2,4] G5[2] G6[2,4]	G1[3,5] G6[5]	G1[4,5] G2[4] G3[5]	G1[1,3]	Go: G1[5] Go: G6[5]	G1[3] G7[4,5]
Brazil	G1[6] G3[6] G5[6]	G1[6] G3[6] G5[6]	G1[8]	G1[3,7,8] G5[3,7,8]		G1[9] G7[9]
Chile	G1[3,10] G6[10]			G1[3,11] G3[11]		
Peru	G1[12,13,14] G6[12,14]		G1[12,13]	G1[12,13]	A: G1[15] Go: G6[12]	G1[15] G7[12,15]
Uruguay				G1[1,3] G5[1]		
Bolivia	G1[3]					

[1] (Cucher et al., 2016); [2] (Guarnera et al., 2004); [3] (Kamenetzky et al., 2002); [4] (Rosenzvit et al., 1999); [5] (Soriano et al., 2010); [6] (de la Rue et al., 2011); [7] (Balbinotti et al., 2012); [8] (de la Rue et al., 2006); [9] (Monteiro et al., 2014); [10] (Manterola et al., 2008); [11] (Espinoza et al., 2014); [12] (Moro et al., 2009); [13] (Sánchez et al., 2010); [14] (Santivanez et al., 2008); [15] (Sanchez et al., 2012).

Health Organization (PAHO). However, the data regarding infection in dogs is scarce and no systematic surveillance is in place. In 2011, official abattoir inspections in **Argentina** (Trezeguet et al., 2011) reported the following prevalence of CE at the national level: 3% of 916,102 sheep, 1.6% of 3,273,864 pigs and 2.9% of 9,010,321 cattle. The most heavily infected regions for sheep were Rio Negro (21.9%), Buenos Aires (9.2%) and Chubut (2.2%), while infected swine were most frequently found in La Pampa (2.2%), Mendoza (1.8%), Buenos Aires (1.7%) and Santa Fe (1.1%). Infected cattle occurred most often in Rio Negro (19.1%), followed by Neuquén and Misiones (15%). Approximately, 2.5% of 1042 dogs sampled from 352 sheep farms from La Pampa, Neuquén, Rio Negro, Chubut, Santa Cruz and Tierra del Fuego were positive on copro ELISA (Cavagion et al., 2005). In Neuquén, the prevalence of infection in rural dogs is 12.4% (Pierangeli et al., 2010).

In **Brazil**, the most affected state is Rio Grande do Sul. There, 12% of cattle, 17% of sheep, and 11% of dogs (coproantigen test) have been found to be infected (de la Rue, 2008). The same report shows low levels of infection in cattle in other states of Brazil: 0.12% in cattle in Parana and 0.002% in Mato Grosso (de la Rue, 2008). Older data also showed a low level of infection in cattle in Minas Gerais (0.18%) between 1990 and 1994 (Sa et al., 1998). The only study of canine echinococcosis reported a prevalence of 27.7% in Santana do Livramento county, an endemic area in the state of Rio Grande do Sul (Farias et al., 2004).

In **Chile**, *E. granulosus* is the second leading cause of livestock viscera condemnation after the liver fluke *Fasciola hepatica*. In 2014, 28.9% of animals presenting an issue at meat inspection were infected with *E. granulosus*. Abattoir inspections report CE in 19% of cattle, 3% of sheep, 0.01% of pigs, 2.3% of horses and 3% of goats. The most affected regions are the Capital (Metropolitan Region), Los Lagos (X region), Araucania (IX region), Los Rios (XIV region), Aysen (XI region) and Magallanes (XII region) (SAG, 2015). In the IV region (Coquimbo), a coproantigen study of dog faeces demonstrated that CE transmission is not exclusive to rural areas [prevalences of 11.7% in city dogs, 5.9% in town dogs and 3.5% in rural dogs (Acosta-Jamett et al., 2010)].

In **Peru**, few studies have reported prevalence in livestock. In 1997, 82% of sheep and 32% of dogs were infected in Junin (Moro et al., 1997). A second study in the same area reported 46% (23/50) of dogs positive on coproantigen testing while 38% (13/34) of sheep were infected at postmortem examination (Moro et al., 1999). A study on abattoir workers and stray dogs from a nonendemic coastal city found 4 of 22 dogs positive while 3 of 32 human had liver CE (Reyes et al., 2012). Between 2009 and 2012, official data reported infection prevalence ranges of 3.61–6.12% for cattle and 6.55–10.44% for sheep (PAHO, 2015).

In **Uruguay**, from 2009 to 2014, the infection prevalence was 2.2–5.9% in sheep and 3.9–7.05% in cattle (PAHO, 2015). Surveillance of rural dogs using a coproantigen test revealed that approximately 4.3% were infected (Irabedra and Salvatella, 2010).

In **Ecuador**, CE has been described in 0.12% of 1658 cattle and 0.5% of 1790 pigs (Torres, 2012). A previous report showed a higher prevalence in pigs (13%) in a different area (Allaico, 2010). A number of other previous reports have been published showing prevalence in pigs (between 1.13% and 5.1%), cattle (0.21–11.8%) and sheep (0.04%) [reviewed in Allaico (2010)]. These data suggest that CE is an important problem in animals in Ecuador.

3.3.3 Infection in humans

Between January 2009 and December 2014, countries involved in the initiative for the control of CE in South America (Argentina, Brazil, Chile, Peru and Uruguay) reported 29,556 cases of CE, with the majority of cases in **Peru** (20,785). CE cases are usually underreported with a higher number in hospital records than reported each year. This is partly influenced by the different systems for notification of the disease in each country (see Fig. 7 and Table S6 in the Supplementary Material). Moreover, notification of human CE is not compulsory in all countries (PAHO, 2015).

In **Argentina,** between 2005 and 2010, the annual incidence was 0.95/100,000, with the highest incidence in Chubut (12.75/10^5 inhabitants), followed by Neuquén (8.14) and Santa Cruz (6.41) (Moral, 2010). Argentina has been a pioneer in South America implementing population ultrasound screenings as a tool to diagnose CE and also to assess the success of control programs. For example, in the Argentinean Patagonia, 87 (0.4%) cases were diagnosed after 22,793 ultrasound scans were performed in children from 6 to 14 years of age from 2000 to 2008 (Del Carpio et al., 2012). In Rio Negro, the overall prevalence of CE based on ultrasound was 7.1% (40/560) in 2009 (Bingham et al., 2014).

In **Brazil**, between 1981 and 1998, 701 CE cases underwent surgery in Rio Grande do Sul (Mardini and Souza, 1999). Between 1999 and 2002, 14, 8, 32 and 2 cases were registered respectively, and none from 2003 until August 2005 [reviewed by de la Rue (2008)]. Between 2009 and 2014, 91 cases were confirmed (PAHO, 2015). In this country the notification of the disease is not compulsory. According to data from the Brazilian government (DATASUS, 2013) there were 110 deaths due to echinococcosis between 1993 and 2013, assuming a case fatality rate of about 2% there would be 5500 cases in this period suggesting an incidence of 0.1/10^5 inhabitants per year for the whole country (DATASUS, 2013). Interestingly, with these data the highest incidence occurs in the state of Acre: 3.3/10^5 inhabitants per year in the west bordering Peru and Amazonas. Since there is no detailed cause of death in this report, it is possible that some of the cases are due to neotropical echinococcosis rather than CE. In Rio Grande do Sul the incidence was calculated at 1.1/10^5 inhabitants per year.

In **Bolivia**, CE is endemic in southwestern parts of the country. However, of the 106 CE cases recently reported (1998−2004), 83% originated from La Paz, suggesting that CE is increasing in eastern regions (Vera et al., 2004). This idea is supported by other reported cases in La Paz (Vera et al., 2006) and Cochabamba (Torrez Salazar et al., 2009). A study of hospitalized cases in children between January 1984 and February 1999 showed an increasing frequency of CE in La Paz city (Tamayo Meneses et al., 2004). Finally, in the locality of Tupiza, an increase in human cases of CE has been observed, with 238/1030 (18.8%) ultrasounds showing signs of CE and 23.9% of dog faeces positive to coproantigens (Villena and Uzqueda, 2011).

In **Chile**, according to the data from the Ministry of Health during 2009–14, the annual incidence was between 1.4 and 1.8/100,000, while the incidence based on the number of discharges in hospitals due to CE in the same period was between 4.68 and 5/100,000 (PAHO, 2015). The disease is present in the whole country (see Fig. 7 and Table S6), with highest prevalence in the regions where livestock production is concentrated including Aysen, Magallanes in the extreme south; Coquimbo in the north–central area and Araucania, Bio Bio, Los Rios and Los Lagos in the south part of the country (Martinez, 2011, 2014).

In **Peru**, there is no compulsory notification of CE; therefore, the number of cases is likely underestimated (PAHO, 2015). Incidence rates can reach between 14 and 43 cases/100,000 in the regions of Pasco, Huancavelica, Junin, Puno and Cusco (Cabrera, 2007). Official reports from the Ministry of Health based on registers at hospitals show an incidence between 7 and 8 cases/100,000 per year (Cabrera, 2007). A study using ultrasound and X-ray to detect CE reported a prevalence of 9.1% amongst 407 people in the central Peruvian Andes (Moro et al., 1997). Another study using ultrasound and serology in the same area reported a prevalence of 9.3% ($N = 214$) (Moro et al., 1999). In Canchayllo, a locality in the Peruvian highlands, ultrasound surveys detected CE in 4.9% of 309 subjects (Moro et al., 2005). Autochthonous transmission of *E. granulosus* occurs in Lima, based on findings of CE in 3/32 workers in unlicensed abattoirs, using a combination of abdominal ultrasound, chest X-rays and serology (Reyes et al., 2012).

In **Uruguay**, the incidence has decreased in recent years based on ultrasound studies in risk areas, from 6.5 per 1000 inhabitants in 2008 to 2.8 in 2013 (Irabedra et al., 2016). The incidence in the endemic areas is estimated between 1.3 and 3.8 cases/10^5 inhabitants (PAHO, 2015).

The remaining South American countries have not received much attention in the reporting of CE and epidemiological studies are limited (see Fig. 7 and Table S6 in the Supplementary Material). It is not known with certainty the incidence, prevalence or burden of CE in Colombia, Venezuela and Paraguay. In **Colombia**, the first case was reported in 1941 (Perez Fontana, 1949). Two other cases were reported in the following decade (Lichtenberger, 1957), and more recently, a single autochthonous case (Gómez et al., 2003). In **Venezuela**, the first case described in 1938 was not thought to be autochthonous (Gómez and Luna, 1938), and only nine autochthonous cases have since been reported (Guanipa et al., 1990). In **Paraguay**, the disease is rare, and there is only one record of autochthonous CE (Rodas et al., 2011).

3.4 Cystic echinococcosis in Europe

3.4.1 Introduction

For south and southeastern Europe, *E. granulosus* (sheep strain, genotypes G1–3) represents the principal causative agent of CE. *Echinococcus intermedius* (pig strain, G7) is the main human CE agent in the Baltic countries (Marcinkutė et al., 2015). Furthermore, two less pathogenic genotypes of *E. canadensis* (G8 and G10) have been documented in northern Europe (Oksanen and Lavikainen, 2015). Across Europe the actual prevalence of CE in animals or humans remains fragmented, partly due to the lack of efficient and dedicated reporting systems. In this regard, a European register was initiated within the FP7 HERACLES project aiming to provide prospective data on the epidemiology and clinical features of human CE (Rossi et al., 2016). Fig. 8 and Table S7 reports the current distribution of *Echinococcus* spp. causing CE in Europe (not including the cervid genotypes of *E. canadensis*). Information (incidence data) of CE in humans in Europe is reported in Table S8 of the Supplementary Material.

3.4.1.1 Western and Northern Europe: Iceland, Ireland, Great Britain, Norway, Sweden, Finland and Denmark

3.4.1.1.1 Host assemblages, transmission and molecular epidemiology After a successful control program, **Iceland** can be regarded as free of CE transmission since decades (Schantz et al., 1995; Sigurdarson, 2010).

The **United Kingdom** is endemic for *E. granulosus* (G1), and there is a long history of CE occurring in humans. For example, a likely case of CE was reported in 1785 at the Edinburgh infirmary (Risse, 2005). More recently the main foci of transmission have been in the Western Isles off the North West coast of Scotland and in Wales. Historically, *Echinococcus equinus* circulated in a typical foxhound–horse cycle (Thompson and Smith, 1975), but transmission is still documented in the UK (see later).

For the north of **Scandinavia**, the current epidemiological situation of the cervid strains (G8 and G10) of *E. canadensis* has recently been reviewed in

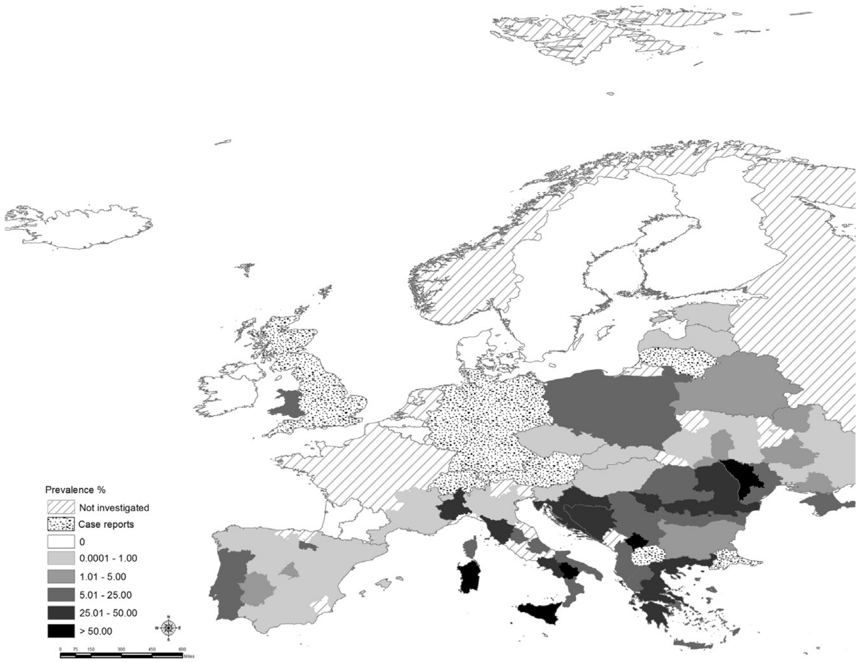

Figure 8 ***Current distribution of Echinococcus spp. causing cystic echinococcosis in domestic intermediate hosts (sheep, cattle, pigs and boar) in Europe.*** The detailed information (prevalence data in each jurisdiction) is listed in Table S7 of the Supplementary Material.

depth (Oksanen and Lavikainen, 2015). The cycle is mainly perpetuated between wolves as definitive and cervids as intermediate hosts (the involvement of working dogs has decreased). *Echinococcus canadensis* (G10) was identified in Finland in wolves, cervids and in one human (Oksanen and Lavikainen, 2015).

3.4.1.1.2 Infections in animals For the **UK** and **Ireland**, there is very limited data on the prevalence of *Echinococcus* spp. in animal hosts (see Fig. 8 and Table S7 in the Supplementary Material). However, in the UK *E. granulosus* (G1−3) has been found in dogs, sheep and cattle whilst *E. equinus* (G4) has been isolated from horses, dogs and from two captive mammals: zebra (*Equus burchellii*) and lemur (*Varecia rubra*) (Boufana et al., 2015b). In **Ireland**, *E. equinus* has been found in horses and dogs (Hatch, 1970; Kumaratilake et al., 1986). Ireland is not believed to be endemic for other species/genotypes of *E. granulosus* s.l. (Torgerson and Budke, 2003). In the north of Scandinavia, *E. canadensis* is found in cervids (1.2% in Finland, 1.6% in Sweden) and wolves (10–46% in Finland) (Oksanen and Lavikainen, 2015).

3.4.1.1.3 Cystic echinococcosis in humans In the **UK**, there were a total of 110 hospital admissions in Scotland with a diagnosis of CE between 1968 and 1989. The highest incidence values were recorded in the Western Isles (annually 2.5 cases per 10^5 inhabitants), Shetland (1.2) and Highland (0.2) (Braddick and Reilly, 1993). Between 1974 and 1983 the average annual incidence in Wales was $0.4/10^5$ with 0.02 cases in England. Within Wales, Powys and particularly Brecknock had the highest incidence of approximately 7 cases per 10^5 inhabitants (Palmer and Biffin, 1987). Because of the high incidence in Powys, a control programme was implemented in 1983 that led to the successful reduction in the cases of human CE in the area (Palmer et al., 1996). Unfortunately, the dog dosing programme was suspended in 1989 and since then there has been evidence of renewed transmission in animal hosts (Mastin et al., 2011). Nevertheless, generally human CE has been decreasing in incidence in the UK. Between 2005 and 2009, 52 cases were reported as confirmed CE ($0.03/10^5$ per year), although many of these cases were diagnosed in immigrants (Halsby et al., 2014). However, these might be underestimates as 227 hospitalizations and 2 deaths were attributed to CE in England between 2005 and 2009. No cases were reported from Scotland during this period. Other data demonstrated 46 cases of CE reported from 2008 to 2012 (European Centre for Disease Prevention and Control, 2013).

Ireland is believed to be nonendemic for *E. granulosus* and no reports of autochthonous cases of CE have been registered, although it is endemic for *E. equinus* (Torgerson and Budke, 2003).

In **Scandinavia,** human CE caused by *E. canadensis* (G8 and G10) involved primarily the lungs causing a relative benign disease; since the 1960s only one CE case caused by *E. canadensis* (G10) has been diagnosed in eastern Finland (Oksanen and Lavikainen, 2015).

3.4.2 Central Europe: Belgium, The Netherlands, Luxembourg, Germany, Switzerland, Austria and Czech Republic

In Austria, Germany and Switzerland, historically *E. ortleppi* (cattle strain, G5) was endemic (Eckert et al., 2001), and there are no recent findings published. Local transmission of *Echinococcus* genotypes causing CE has not been well documented in this area over the last decades. However, several CE cases in humans have been considered to be autochthonous in Austria and

Germany; and therefore parts of these countries have still to be regarded endemic areas with sporadic cases.

3.4.2.1 Infections in animals

No systematic data are available but slaughterhouse reports indicate that CE in livestock is nearly absent. In one case, G7 was identified in a cyst from a pig in **Austria** (H. Auer, personal communication). From **Germany**, *E. granulosus* findings date back to the 1970s, but no current data have been published. Sporadic cases of *E. granulosus* s.s. in sheep have been observed in the vicinity of Stuttgart, but infection sources are not clear (Romig, personal communication).

In **Switzerland**, *E. granulosus* is occasionally diagnosed in imported dogs and in single cases in ruminants. In one case, *E. granulosus* (G1) transmission in a sheep flock was observed (Deplazes P., personal communication).

Occasionally *E. equinus* has been diagnosed in Switzerland, Germany and Belgium but these cases are most probably imported. A case of CE in the lungs of a horse foaled and raised in Germany was documented, but sources of such rare cases are unclear (Blutke et al., 2010). In the **Czech Republic**, in the period of 2005 and 2007, CE was reported in 6 cows, 267 pigs and 33 sheep, considered sporadic relative to the total number of slaughtered animals (Svobodová, 2014).

3.4.2.2 Cystic echinococcosis in humans

Most of the CE cases diagnosed in humans have been classified as imported cases. For example, in the **Netherlands**, nearly 30 cases of CE in patients originating mainly from areas around the Mediterranean Sea are confirmed each year (Herremans et al., 2010). In Switzerland, no autochthonous CE cases are documented, and around 50 imported cases of CE are reported each year in immigrants.

For **Germany** the annual incidence (2001–13) of CE per 10^5 inhabitants was calculated to be 0.05 (of total 552 CE cases, 111 were in the autochthonous populations) (Torgerson, 2017). In a series of 37 CE patients with genotyped *Echinococcus* (35 *E. granulosus* s.s., 2 *E. intermedius* G7) treated in a southern German hospital between 1999 and 2011, only one patient (with G1 infection) originated from central Europe (Wagner, 2014). However, autochthonous infection may occur sporadically: for at least 2 out of 15 CE patients who grew up in Germany, diagnosed 1999–2008, there is no reasonable doubt that they acquired the infection locally (Richter et al., 2009).

In a retrospective investigation of CE in **Austria**, the majority (92%) of 23 autochthonous cases harboured cysts belonging to G7, while immigrants were mainly infected with G1 or G6. All in all, the annual incidence of CE in Austria was estimated to be 0.4 per 10^5 inhabitants (Schneider et al., 2010). Similarly, in the **Czech Republic**, CE is reported occasionally. Since 2005, 10 cases have been treated in two hospitals (Prague, Liberec); of these, only one is likely autochthonous (Stejskal et al., 2014).

3.4.3 Eastern Central Europe: Poland and Baltic countries, Belarus, Ukraine, Moldova, Slovakia, Hungary

3.4.3.1 Host assemblages, transmission and molecular epidemiology

In the Baltic region (**Lithuania, Latvia** and **Estonia**) CE has been known to occur since the beginning of the 20th century. For example, in Estonia the first description dates back to 1904 (Marcinkutė et al., 2015). So far, four genotypes have been identified (Table 6). In **Lithuania**, *E. intermedius* (the pig strain, G7) with a farm dog–pig cycle maintained by home slaughter practices has been predominantly observed in humans, pigs, cattle (sterile cysts) and in dogs (Bruzinskaite et al., 2009). The cervid strains of *E. canadensis* (G8, G10) transmitted by wolves as definitive hosts and cervid species as intermediate hosts have been identified in **Estonia** and **Latvia** (Marcinkutė et al., 2015); (Oksanen and Lavikainen, 2015) and *E. granulosus* (G1) was found in a dog in Estonia (Marcinkutė et al., 2015) but the importance of this cycle is not known. In **Poland**, CE also occurs in animals (mainly pigs) and in humans; in people, *E. intermedius* (G7) and *E. granulosus* (G1) have been confirmed (autochthonous origin could not be excluded in two patients with G1) (Dybicz et al., 2015; Marcinkutė et al., 2015).

In **Moldova**, **Ukraine** and **Belarus**, countries of the former Soviet Union, the presence of *Echinococcus* species causing CE as well as *E. multilocularis* has been known for several decades. The Republic of Moldova is recognized as a CE endemic area, where human disease is considered as a high-priority public health problem. Similarly, in the Ukraine human CE cases are reported regularly, while a few cases have been registered in Belarus.

In **Slovakia and Hungary**, CE had been known to occur regularly in the past, likely attributed to high prevalence in slaughtered pigs on many small breeding farms before the 1990s (Turčeková et al., 2009). Later, economic and social changes caused a decrease in the numbers of family farms,

Table 6 Genotypes of *Echinococcus* spp. causing cystic echinococcosis in eastern Central Europe: *Echinococcus granulosus* (G1–3), *Echinococcus equinus* (G4), *Echinococcus ortleppi* (G5), *Echinococcus intermedius* (G6/7) and *Echinococcus canadensis* (G8, G10) (no data found in the missing countries)

Country	Human	Dog	Wild canids	Cattle	Pig (P), Wild boar (Wb)	Sheep (S), Cervids (C)
Poland	G7 and G1[1]				P: G7[3]	
Estonia		G1[2]	G8[2] G10[2]			C: G8 and G10[2,4]
Latvia			G10[2]			
Lithuania	G7[5]	G7[2,5]		G7[2,5]	P: G7[2,5]	
Ukraine					P, Wb: G7[6]	
Moldova				G1[7] G3[7]		S: G1[7] S: G3[7]
Slovakia	G7[8] and G1–3★				P: G7[8]	

[1] (Dybicz et al., 2015); [2](Marcinkutė et al., 2015); [3] (Karamon et al., 2012); [4] (Moks et al., 2008); [5] (Bruzinskaite et al., 2009); [6] (Kedra et al., 2000); [7] (Umhang et al., 2014a); [8] (Turčeková et al., 2009); ★ Antolová D. unpublished data.

and pig husbandry moved almost exclusively indoors. Moreover, preventive measures and the improvement of veterinary meat inspection contributed to the decrease of human CE cases as well as the decline of CE in slaughtered animals.

3.4.3.2 Infections in animals

In **Lithuania**, **Estonia and Latvia**, *Echinococcus* species causing CE have been described in the past and were recently reviewed in Marcinkutė et al. (2015).

In **Estonia**, historically CE was reported in pigs, sheep and wild cervids (Marcinkutė et al., 2015). In more recent studies, *E. granulosus* has been found in Estonian wildlife including moose and roe deer (*Capreolus capreolus*) as intermediate hosts, with the grey wolf as definitive host. The Estonian Veterinary and Food Laboratory has only reported a few cases of CE in farm animals, e.g., in 2004, 4 of 444,084 pigs (0.0009%) and 8 of 6202 moose (0.1%) were infected. Cysts were also detected in 2 of 1787 imported reindeer (0.1%) in 2005, and in 1 of 53,903 cattle (0.002%) (Marcinkutė et al., 2015). In 2003, adult *Echinococcus* cestodes were detected in one of 26 grey wolves, and in 2004–05 CE was detected in the lungs of 16 (0.8%) of 2038 hunted moose (Moks et al., 2008). Of these, 11 belonged to genotype G8 and 5 to genotype G10. This was the first record of G8 in Eurasia (Moks et al., 2008).

In **Latvia**, historical data document a pig – dog life cycle which was considered typical for the region. Recent low prevalence (<0.2%) of echinococcosis in farm animals in the period 2004–07 and 2010 and no detected infections in dogs suggest that a cycle in domestic animals is not of relevance in Latvia (Marcinkutė et al., 2015). Intestinal *Echinococcus* stages detected in 1 (2.9%) of 34 wolves were later confirmed to be *E. canadensis* (G10). The populations of wildlife involved in the known *E. canadensis* (G10) life cycle are stable with a tendency to increase in Latvia (Marcinkutė et al., 2015).

In **Lithuania**, historic and recent data document mainly the presence of a pig–dog *Echinococcus* cycle. A recent study (2005–06) performed in the southwestern part of Lithuania detected CE in 13.2% (81/612) of pigs reared in small family farms and in 4.1% of those reared in industrial farms. Molecular analysis of isolated taeniid eggs revealed *Taenia* spp. in 10.8%, *E. intermedius* (G6/7) in 3.8% and *E. multilocularis* in 0.8% of the dogs investigated in the same area. In addition, three samples from the livers of humans, one sterile cyst from a cow, seven samples from pigs, and eggs from faeces of eight dogs were confirmed as *E. intermedius* (G6/7) (Bruzinskaite et al., 2009).

In **Poland**, CE has been documented in the past in pigs (4.5%), beef cattle (0.007%), sheep and goats (18.7%) (Derylo, 1998). According to more recent data, *E. granulosus* s.l. was detected in 4.1% of 267 pigs from southern Poland and the pig strain (G7) seems to be the most common in Poland (Dybicz et al., 2015).

Data from **Belarus**, published in 2000 and 2002, reported the occurrence of *E. granulosus* in 0.15% of cattle, 0.7–1.2% of sheep and 6–7% of pigs as well as in 5–6% of dogs (Malczewski, 2002). Furthermore, *Echinococcus* cestodes were detected in the intestines of 6/52 (11.5%) wolves (Shimalov and Shimalov, 2000).

In Ukraine (northeast), the presence of *Echinococcus* intestinal stages was documented in 6.25% of wolves (Kornyushin et al., 2011) and in 10.9% of dogs (Varodi et al., 2007). CE has been seen in 4/58 (5.2%) of wild boars and 1/400 red deer (0.7%) (Yemets, 2013). The highest prevalence in sheep occurs in the Crimea (21.3%) and Odessa regions (12.2%) (Litvinenko, 2015), whilst in cattle the highest prevalences are seen in Odessa (3.3%) and Kirovohrad regions (2.4%) (Litvinenko, 2012). In pigs the two districts with the highest prevalence are the Khmelnytskyi and Sumy regions (3.1% and 2.7%, respectively) (Litvinenko, 2013). Molecular analyses confirmed the presence of *E. intermedius* (pig strain, G7) in two pigs and a wild boar from Sumy region (Kedra et al., 2000).

In the **Republic of Moldova** a slaughterhouse survey was conducted in 2012 to estimate the prevalence of CE in cattle, sheep and pigs. The infection was highly prevalent in cattle (904/1525, 59.3%) and sheep (3450/5580, 61.9%), while no positive pigs (0/12,700) were found. The prevalence of infection was significantly higher in animals raised in private households than in those from collective farms (Chihai et al., 2016). In both cattle and sheep, only the occurrence of *E. granulosus* G1 and/or G3 was confirmed (Umhang et al., 2014a). In **Slovakia**, the annual prevalence of CE in pigs between 2000 and 2008 ranged from 0.02% to 0.13% (average: 0.08%), with decreasing tendency, especially after 2005 (Turčeková et al., 2009). Few data about the occurrence of intestinal *Echinococcus* spp. in carnivores are available; *E. granulosus*-like cestodes (genotype not determined) have been detected in two golden jackals (*Canis aureus*) in **Hungary** (Takacs et al., 2014).

3.4.3.3 Cystic echinococcosis in humans

For the **Baltic countries**, the historical and actual situations of CE have been reviewed in Marcinkutė et al. (2015). In **Lithuania**, incidences of clinical CE were estimated to be $0.03/10^5$ inhabitants in 1958 and 0.1 in 1960, but later in 2005 the incidence was 0.39 and it remained at a higher level of 1.11−1.15 for the years 2009−13 (Marcinkutė et al., 2015). As no obligatory notification of CE exists in Lithuania, and these data were recorded in two hospitals only, it can be assumed that the situation is underestimated in some districts. Most CE cases were registered from southeastern and northwestern areas of Lithuania with particularly high number of CE cases registered from the Vilnius district (Marcinkutė et al., 2015).

In **Latvia**, during the period 1999−2005, 29 CE cases were registered, but since 2001, an increase in human CE cases has been recorded. In the Infectology Centre of Latvia, 11 new cases were registered ($0.43/10^5$ inhabitants per year) in 2005 and subsequently, the number of diagnosed CE cases rose to 17 in 2008 ($0.77/10^5$), but decreased and remained stable in the period between 2009 and 2012 ($0.27-0.34/10^5$). Data of 93 patients with CE, diagnosed between 2002 and 2012, document the public health significance of CE in Latvia [Laivacuma and Viksna, cited in Marcinkutė et al. (2015)], but since echinococcosis is not a notifiable infectious disease in Latvia, the number of presently reported cases is probably underestimated.

To date, 13 cases of echinococcosis have officially been registered in humans in **Estonia** but AE and CE were not differentiated. However, based on clinical descriptions in two cases, CE can be suggested to be present in the country (Marcinkutė et al., 2015).

In **Poland**, a relatively low incidence of CE has been registered in recent years. In 2009 and 2010, 25 and 34 cases of CE were registered, respectively (incidence = 0.07 and $0.09/10^5$ inhabitants) (WHO, 2015, European Hospital Morbidity Database, World Health Organization Regional Office for Europe: http://data.euro.who.int/hmdb/). Most cases were reported in the Masovian province (33% of all reported cases, incidence $0.23/10^5$ inhabitants), and the smallest number in the Kuyavian-Pomeranian province (1 case, incidence $0.05/10^5$ inhabitants). More cases of echinococcosis (70%) were recorded in the countryside. In both rural and urban areas, women were more affected (86%) than men (Golab and Czarkowski, 2014; Waloch, 2012). Serological investigations (ELISA, Western blot) by the National Institute of Public Health confirmed CE in 162 patients of 5483 persons suspected of echinococcosis in the period of 2003 and 2010 (Wnukowska et al., 2011).

In **Belarus**, the incidence of CE appears quite low. In 2010−11, there were 20 cases reported (Anichkin and Martyniuk, 2012) resulting in an annual incidence of 0.1 cases per 10^5 inhabitants per year. In **Moldova**, CE seems to be of major importance; indeed 1770 human CE patients were reported between 2000 and 2010 (a mean of 177 per year) with an annual incidence of 4.9 CE cases per 10^5 inhabitants (Lungu, 2013).

In **Ukraine**, 2153 human CE cases were recorded between 2000 and 2013 (Litvinenko and Polokokovska, 2015) giving an annual incidence of 0.36 per 10^5 inhabitants. Nearly half the cases (986) were reported from the Odessa region which has an annual incidence of 2.9 cases per 10^5 inhabitants.

In **Slovakia**, human CE occurs sporadically, with a few cases reported to the Slovak Health Authorities every year, although most can be classified only as possible or probable cases. At the Institute of Parasitology of Slovak Academy of Sciences the diagnosis was confirmed in four patients between 2012 and 2015. In a woman from eastern Slovakia, *E. intermedius* (G7) was reported, while *E. granulosus* (G1−3) was recorded in one man. As the patient had travelled several times to Romania in the past, the case is not necessarily autochthonous (Antolovà D., personal communication). In **Hungary**, few case reports of echinococcosis or CE have been published (Casulli et al., 2010a; Csotye et al., 2011) and the origin of these patients is not documented.

3.4.4 Southern Europe: Portugal, Spain, France, Italy, Greece

3.4.4.1 Host assemblages and transmission

Echinococcus granulosus has been known in southern Europe since ancient times but it was only in 1801 that Rudolphi established the genus *Echinococcus*, the name referring to the small, round, 'spiny' protoscoleces found in the cysts (Romig et al., 2015).

Nowadays, CE remains the most important helminth zoonosis in southern Europe, causing serious consequences in terms of public health and the economy due to the considerable morbidity rates both in the public health sector and in livestock industries (Seimenis, 2003). The main way of transmission is through the domestic cycle, involving dogs as definitive hosts and farm livestock (especially small ruminants) as intermediate hosts. Eggs shed by infected dogs (especially free-roaming dogs living in rural areas) remain the most important source of infection for humans and other intermediate hosts. The role of wild animals in transmission has not yet been accurately studied (Seimenis, 2003). However, a wild animal cycle maintained among wild carnivores acting as definitive hosts (Gori et al., 2015; Guberti et al., 2004; Guerra et al., 2013) and wild boars as intermediate hosts have been documented in south-central Spain (Martin-Hernando et al., 2008), central

Italy (Busi et al., 2007) and the island of Corsica in France (Umhang et al., 2014c).

Risk factors for infection of intermediate and definitive animal hosts with *E. granulosus* have been recently reviewed by Otero-Abad and Torgerson (2013). The close proximity of humans to animals, traditional types of husbandry (especially for sheep and goats), clandestine home slaughter with insufficient facilities to destroy infected offal to which dogs have free access, and the high number of stray dogs and sheepdogs are some of the most important factors that allow the spread of CE in southern Europe (Garippa, 2006; Seimenis, 2003). In the Mediterranean area, pastoralism is a major occupation, with transhumance being very common. Usually, each rural family keeps one or more dogs for guarding, herding, hunting and/or companionship. These animals in some areas may be fed offal as food sources and/or have access to the location where animals are slaughtered as well as to livestock rearing areas and carcasses. The ability of dogs to roam freely is one of the most commonly reported risk factors for *E. granulosus* infection (Otero-Abad and Torgerson, 2013). Another important risk factor for *E. granulosus* infection is associated with the dog owner's lack of knowledge about parasite transmission or deficiencies in anthelmintic treatment. Additionally, the cultural and economic background of the owners has been found to be related to infection risk in dogs (Otero-Abad and Torgerson, 2013).

A particular epidemiological situation can be observed in southern Italy (Campania region), including the role of a sheep/dog cycle for the transmission of CE to cattle and water buffalo (Cringoli et al., 2007). In this region, illegal farm-slaughter of large ruminants is nearly absent and cattle and water buffaloes are slaughtered only in modern and efficient abattoirs, where the presence of canids is strictly forbidden. A study using geospatial tools confirmed the role of sheep in CE transmission based on the close proximity of sheep farms to positive bovines and/or water buffaloes, presumably because free-ranging canids with access to infected sheep carcasses contaminated the cattle/buffalo farms with *Echinococcus* eggs (Cringoli et al., 2007).

Control initiatives for CE in southern Europe started in the second half of the 19th century and have since been implemented in whole territories or in selected regions. However, to date CE has been successfully controlled at a national level only in parts of Cyprus (Economides et al., 1998). In other areas, the initiatives led only to a temporary reduction in animal and human CE prevalence (Magnino et al., 2014).

3.4.4.2 Molecular epidemiology

Four *Echinococcus* species including several genotypes have been documented so far to be circulating in southern Europe: *E. granulosus* (G1–3), *E. equinus* (G4), *E. ortleppi* (G5) and *E. intermedius* (G7) (Table 7).

Echinococcus granulosus (G1–3) is the species most frequently identified in domestic animals and humans in southern Europe (Beato et al., 2013; Busi et al., 2007; Gonzalez et al., 2002). Although the typical life cycle patterns involve livestock and domestic dogs, *E. granulosus* is also known to occur in wolves in Italy and Spain (Gonzalez et al., 2002; Gori et al., 2015) and in wild boars in Spain, Italy and Greece (Busi et al., 2007; Mwambete et al., 2004; Varcasia et al., 2007), highlighting that the wild animal cycle must be also taken into account in the epidemiology of *E. granulosus*.

Echinococcus equinus (G4) has been documented in horses from Spain and Italy (Gonzalez et al., 2002; Varcasia et al., 2008a) and *E. ortleppi* (G5) was found in cattle from Italy and France (Casulli et al., 2008; Grenouillet et al., 2014). In a study conducted in France (Casulli et al., 2008; Grenouillet et al., 2014), evidence of liver infections caused by *E. ortleppi* was reported in two humans.

Echinococcus intermedius (G6/7) is prevalent in France, Greece, Italy, Spain and Portugal in goats, pigs and wild boars. Furthermore, a study conducted with hunting dogs in Corsica showed the presence of *E. intermedius* (G6/7) in 1.2% of animals examined (Umhang et al., 2014c).

In southern **France**, the presence of *E. granulosus* (G1–3) in sheep and cattle has been documented (Umhang et al., 2013b) and, in Corsica, Grenouillet et al. (2014) and Umhang et al. (2014c,d) provided evidence of infection with *E. ortleppi* in cattle and humans and *E. intermedius* (G6/7) in pigs, wild boars and hunting dogs (Umhang et al., 2014c,d).

In **Greece**, *E. granulosus* was a dominant species in livestock, especially sheep, goats and buffaloes (Chaligiannis et al., 2015; Varcasia et al., 2007; Roinioti et al., 2016), and also in wild boars (Chaligiannis et al., 2015). Furthermore, *E. intermedius* (G7) was identified in goats (Chaligiannis et al., 2015; Varcasia et al., 2007) and in sheep (Roinioti et al., 2016).

In **Italy**, six genotypes have been identified in different hosts (Table 7), but their distribution was not uniform. *E. granulosus* (G1–3) is the species most frequently identified from intermediate and definitive hosts. In 2008, the presence of G2 in water buffaloes from southern Italy (a Mediterranean area) was reported for the first time (Capuano et al., 2006; Casulli et al., 2008; Rinaldi et al., 2008a), and Calderini et al. (2012) reported the occurrence of the G3 genotype in goats. *Echinococcus granulosus* (G1–3)

Table 7 Genotypes of *Echinococcus* spp. causing cystic echinococcosis in southern Europe: *Echinococcus granulosus* (G1–3), *Echinococcus equinus* (G4), *Echinococcus ortleppi* (G5), *Echinococcus intermedius* (G6/7) and *Echinococcus canadensis* (G8, G10) (no data found in the missing countries)

Country	Human	Dog (D), Wolf (W)	Sheep(S), Goat (G)	Cattle (C), Buffalo (B)	Equine	Pig (P), Wild boar (Wb)
France	G5[1]	G6/7[2]	S: G1–3[3]	C: G1–3[3] C: G5[1]		P and Wb: G6/7[4]
Greece			S: G1–3[5,6,21] S: G7[21] G: G1–3[5] G7[6]	B: G1–3[7]		Wb: G1–3[6]
Italy	G1–3[8]	D: G1–3★ W: G1–3[9]	S: G1–3[8] G: G3[10]	C: G1–3[8,9,10,11] C: G5[8,9,10,11] B: G1–3[9,12,13]	G4[14,15]	P: G1[11] P: G7[11] Wb: G1[8]
Portugal	G1–3[16]	W: G6/7[17]	S: G1–3[16,18] G: G1–3[16]	C: G1–3[16,18] C: G7[16]		
Spain	G1[19]	W: G1[19,20,21]	S: G1[19,20] G: G1[20] G7[20]	C: G1[20]	G4[19,20]	P: G1[19,20] P: G7[19] Wb: G1[20] G7[20]

[1] (Grenouillet et al., 2014); [2] (Umhang et al., 2014c); [3] (Umhang et al., 2013b); [4] (Umhang et al., 2014d); [5] (Chaligiannis et al., 2015); [6] (Varcasia et al., 2007); [7] (Chaabane-Banaoues et al., 2015); [8] (Busi et al., 2007); [9] (Casulli et al., 2008); [10] (Rinaldi et al., 2008b); [11] (Varcasia et al., 2006); [12] (Capuano et al., 2006); [13] (Rinaldi et al., 2008a); [14] (Scala et al., 2006); [15] (Varcasia et al., 2008a); [16] (Beato et al., 2013); [17] (Guerra et al., 2013); [18] (Beato et al., 2010); [19] (Gonzalez et al., 2002); [20] (Mwambete et al., 2004), [21] (Roinioti et al., 2016); ★ Cringoli G. unpublished data.

has been confirmed in dogs (Maurelli et al., 2015) and in humans (Busi et al., 2007) in the Campania region, *E. intermedius* (G7) in pigs in Sardinia (Varcasia et al., 2006), *E. ortleppi* in cattle in the Lombardy region (Casulli et al., 2008), and *E. equinus* in horses of Tuscany, Sardinia and Sicily (Scala et al., 2006; Varcasia et al., 2008a).

In southern **Portugal**, there is a predominance of *E. granulosus* (G1) both in ruminants and in humans (Beato et al., 2010, 2013). In the northern part of the country, *E. intermedius* (G7) in pigs seems to be more prevalent (Guerra et al., 2013). Recent data highlight the finding of the G7 genotype in wolves (Beato et al., 2013; Guerra et al., 2013) and in cattle (fertile cysts) in northern Portugal (Beato et al., 2013; Guerra et al., 2013). In **Spain**, molecular studies showed the existence of three species: *E. granulosus*, *E. equinus* and *E. ortleppi*.

3.4.4.3 Infections in animals

CE was widespread in **Cyprus** before the 1970s. Baseline data show that the parasite was present in 40−100% adult sheep, 20−50% cattle, 27−93% goats and 5−22% pigs (Economides et al., 1998) and very common (up to 40%) among dogs (Polydorou, 1983). A successful campaign of eradication was achieved from 1971 to 1985 including a drastic reduction of the dog population. After the division of Cyprus in 1974, the control program was consolidated in the Greek Cypriot sector and this part of the island is virtually free of CE transmission. In the Turkish Republic of Northern Cyprus, the control program was abandoned and CE remained endemic with a prevalence of about 40% in livestock (Economides and Christofi, 2000).

France is still considered an endemic area for CE (Fig. 8; Table S7 in Supplementary Material), but current prevalence of CE in intermediate hosts remains unknown due to the absence of official data reporting for the last 20 years (Umhang et al., 2013b). In 1989, a nation-wide slaughterhouse survey revealed the following CE prevalences in livestock in southern France: 0.42% in sheep and goats, 0.13% in cattle and 0.009% in pigs (Soule et al., 1995). In a 1994 survey, 0.31% of 43,148 cattle slaughtered in the Midi-Pyrenees were infected (Bichet and Dorchies, 1998). More recently, a cross-sectional study conducted in 2009−10 confirmed the low prevalence of CE in animals in France, with a total of 27 of 725,903 (0.00004%) positive sheep from the Alpes-de-Haute-Provence department and 4 of 138,624 (0.00003%) cattle from the Herault and Haute-Savoie departments (Umhang et al., 2013b). Moreover, 85% of the sheep cysts were fertile while none of the infected cattle exhibited fertile cysts, supporting that cattle do not play a role in transmission of *E. granulosus* (G1) in Europe (Umhang et al., 2013b). The main infected area was the south of France, where sheep breeding and traditional transhumance is concentrated. CE is historically present at high prevalence in Corsica, a French Mediterranean island, with 46% of sheep infected in 1960, and still 15% 20 years later (Umhang et al., 2014d). A recent slaughterhouse survey in Corsica showed a prevalence of 5.9% in pigs, and at the same time a similar prevalence of 4.0% in wild boars was reported (Umhang et al., 2014d). Interestingly, one of the four infected wild boars harboured fertile cysts, which highlights the potential role of this wild species as an intermediate host. More recently, a survey in Corsica revealed *E. intermedius* (G6/7) in 1.2% of hunting dogs (Umhang et al., 2014c).

In **Greece**, CE was widely prevalent long before the 1970s (Sotiraki and Chaligiannis, 2010). The prevalence of infection in farm animals was as high as 82% in cattle, 80% in sheep, 24% in goats and 5% in pigs (Sotiraki et al., 2003). In definitive hosts, prevalences were as follow: sheepdogs 50.4%, sentinel dogs 26.9%, hunting dogs 19.2%, urban stray dogs 9.3% and companion (pet) dogs 0−1% (Sotiraki et al., 2003). A control programme has been in force since 1984, and surveillance in livestock species since 1998 has documented prevalences of 31.3% in sheep, 10.3% in goats, 0.6% in pigs and 0% in cattle (Sotiraki et al., 2003). A survey conducted by Varcasia et al. (2007) in sheep and goats in the Peloponnesus area in southern Greece revealed prevalence values of 30.4% and 14.7%, respectively. Fertile cysts were found in 16.2% and in 7.4% of sheep and goats, respectively. Similar results were obtained by Christodoulopoulos et al. (2008) in sheep flocks in Thessaly (central) Greece from 2002 to 2006, with values of 39.3% (76.7% fertile cysts). Recently, Chaligiannis et al. (2015) conducted an epidemiological survey in different geographical regions of Greece (Thrace, Thessaly, Western and central Macedonia). In the Thrace region, hydatid cysts were found in 33.3% of sheep, while prevalences were 30.3% and 26.1% in sheep of western and central Macedonia, respectively. The highest CE prevalence was found in sheep of Thessaly (53.8%). While not detected in goats from Thrace and western Macedonia, 0.4% of goats and 42% of water buffalo in central Macedonia were infected. Fertile cysts were found in 6.4% of sheep, 3.2% of goats and 7.9% of buffaloes, but not in wild boars.

Regarding **Italy**, *E. granulosus* infection is prevalent in all parts of the country but regional differences (sporadic, endemic and hyperendemic areas) have been identified along a north-south gradient [reviewed in

Garippa (2006)]. CE has a sporadic distribution in northern regions where CE prevalence in farm animals are the lowest registered in Italy (<1%) (Manfredi et al., 2011). In central Italy CE is usually recorded in livestock with lower prevalence levels than in the southern regions. In Abruzzo and Tuscany, CE prevalences in sheep were 22% and 47%, respectively (Garippa, 2006). Regarding southern Italy, in Campania CE prevalence values were 33.3–75.0% in sheep (Cringoli et al., 2007; unpublished data), 10.4% in cattle (Rinaldi et al., 2008b) and 10.5% in buffaloes (Capuano et al., 2006), whereas in Basilicata 67.7% of sheep were affected (Cringoli et al., 2007; unpublished data) and further south in Calabria the prevalence is approximately 15% in sheep (Vincenzo Musella, University Magna Graecia of Catanzaro, Italy, personal communication). The highest CE prevalence was observed in Sardinia and Sicily at 75.0% (Scala et al., 2006) and 57.6% (Giannetto et al., 2004) with a fertility of 10.3% and 9.2%, respectively, whereas CE prevalence in cattle was 41.5% (fertile cysts 2.6%) and 67.1% (fertile cysts 4%) in the same areas (Garippa, 2006). CE has also been reported in different Italian regions in pigs, with a prevalence of 9.4–11.1% (Garippa et al., 2004; Varcasia et al., 2006) and 3.7% in wild boars (Varcasia et al., 2008b). A CE prevalence of less than 1% has been reported in horses (Varcasia et al., 2008a). In dogs, prevalence of *E. granulosus* is generally less than 6% (according to Garippa, 2006; Maurelli et al., 2015; Varcasia et al., 2011). Interestingly, *E. granulosus* was also isolated in 5.9–15% of wolves of northern Italy (Gori et al., 2015; Guberti et al., 2004). The role of the wolf as a definitive host for *E. granulosus* is confirmed in Italy in the Apennines.

In **Portugal**, CE has been recognized as a public health problem and is notifiable since 1987, but epidemiological studies are scarce. In the northern province of Trás-os-Montes, *E. granulosus* prevalences of 8–11%, 30% and 7–12% in swine, small ruminants and dogs were reported, respectively (de Carvalho and Guerra, 2014). Sheep, goats and cattle of the southern regions showed the highest rates of infection (de Carvalho and Guerra, 2014).

In **Spain**, CE is considered endemic, associated mainly with extensive or semiextensive sheep raising in the central part of the country, but *E. equinus* is also present (Carmena et al., 2008). Although specific control programs initiated in the 1980s have led to marked reductions in CE infection rates, the disease remains an important public health problem in the northeastern, central and western parts of the country. Updated data on the current prevalence of *E. granulosus* in definitive and intermediate hosts in Spain was given by Carmena et al. (2008). La Rioja and Aragon were the Autonomous Regions (ARs) with the highest prevalences for ovine/caprine CE, at 22.7%

and 2.0%, respectively. A similar prevalence trend and geographic pattern of disease was observed for bovine CE, with the Bask Country (3.8%) and Extremadura (2.2%) being the ARs with the highest prevalence of disease. In contrast, low CE prevalences (<0.1) in sheep, goats and cows were found in the Mediterranean and Cantabric coastal regions. In pigs, the mean prevalence of CE was 0.03%. Extremadura was the region with the highest infection rates for pigs (0.38%). The overall prevalence of *E. granulosus* infection in sheepdogs in the province of Alava was 8.0% and is considered a public health threat (Benito et al., 2006). As well, 15% of Iberian wolves harboured *E. granulosus* thus confirming the importance of a wild animal cycle (Sobrino et al., 2006).

3.4.4.4 Cystic echinococcosis in humans

CE is still regarded as an important zoonosis with a high burden of disease in southern Europe (see Table S8 in the Supplementary Material). Historically in **Cyprus**, an annual surgical incidence rate of 12.9 per 10^5 inhabitants was recorded. In the 'Greek sector' of the island, parasite transmission was controlled, resulting in very few human CE cases per year, whereas in the 'Turkish sector', the incidence remained high (8 cases per 10^5 inhabitants) (Economides and Christofi, 2000). In **France**, human cases of CE are most often considered to have been imported with immigrants (Umhang et al., 2013b). Corsica is the most important focus of human CE in France with an annual incidence of 1.3 cases per 10^5 inhabitants. In **Portugal**, the incidence of CE is variable with an increase from northern to southern regions, with the highest incidence in the area of Evora (3.2/10^5 inhabitants between 2004 and 2008) (de Morais, 2010). In **Spain**, the highest incidence of the disease occurs in the northeastern, central and western parts of the country, in the range of 1.1−3.4 cases per 10^5 inhabitants. Aragon, La Rioja and Castile-Leòn are the regions with the highest incidence of CE (3.41, 2.46 and 2.02 cases per 10^5 inhabitants). In contrast, coastal areas present relatively low incidence rates of human CE (Carmena et al., 2008). In **Greece**, after the CE control campaign, CE incidence has been dramatically reduced from 12.9 in 1984 (Sotiraki et al., 2003) to 0.25 per 10^5 inhabitants (ECDC, 2010). In **Italy**, human CE continues to be a public health concern with an annual incidence of 1.6/10^5 inhabitants. The highest average incidence rates were observed in Sardinia and Sicily, 6.8/10^5 and 4.0/10^5 respectively, followed by the south regions with an average incidence of 1.9/10^5 but as high as 5.4/10^5 in Basilicata and the central regions with an incidence of 1.07/10^5 inhabitants (1.65 in Latium). The average incidence in the northwest and the northeast of Italy were lower, with a registered incidence of $0.47/10^5$ and $0.36/10^5$ inhabitants, respectively (Brundu et al., 2014).

Each case of CE results in a mean of 0.97 DALYs (Torgerson et al., 2015). With over 1000 cases per year in both Italy (Brundu et al., 2014) and Spain (Herrador et al., 2016), it can be seen that there will be at least 2000 DALYs per annum due to CE in these two countries. These countries dominate the disease burden of CE in southern Europe simply because of their large size and relatively large numbers of cases of CE. The burden in other endemic countries in the region can easily be seen from the relative incidence or numbers of cases reported above.

3.4.5 Southeastern Central Europe: Romania, Bulgaria, Serbia, Croatia, Slovenia, Bosnia and Herzegovina, Kosovo, FYROM and Albania

3.4.5.1 Host assemblages, transmission and molecular epidemiology

CE is a major public health problem in many countries of the Balkan region, particularly in Romania. Predominantly *E. granulosus* (genotypes G1-3) have been confirmed in southeastern Central Europe (Table 8). The first human case of CE was mentioned in **Romania** in medical annals of 1862. Later, the disease was reported regularly throughout the whole country with 3,072 cases registered between 1987 and 1991 (Neghina et al.,

Table 8 Genotypes of *Echinococcus* spp. causing cystic echinococcosis in southeastern Central Europe (no data found in the missing countries): *Echinococcus granulosus* (G1−3), *Echinococcus equinus* (G4), *Echinococcus ortleppi* (G5), *Echinococcus intermedius* (G7)

Country	Human	Dog(D), Wild canids (Wc)	Sheep (S), Red deer (Rd)	Cattle	Swine (S), Wild boar (Wb)
Bulgaria		Wc: G1[1]	S: G1[1]	G1[1]	S: G1[1]
Romania	G1−3, G7[2]		S: G1−3[3] Rd: G7[4]	G1−3[3]	Wb: G7[4]
Serbia	G1, G7[5]		S: G1 cited in[6]	G1, G7 cited in[6]	S: G1, G7 cited in[6]
Kosovo		D: G1−3[7]		G1[9]	
Albania		D: G1[8]			

[1] (Breyer et al., 2004); [2] (Piccoli et al., 2013); [3] (Mitrea et al., 2014); [4] (Onac et al., 2013); [5] (Maillard et al., 2009); [6] (Bobic et al., 2012); [7] (Sherifi et al., 2011); [8] (Xhaxhiu et al., 2011); [9] Sherifi K. and Deplazes P. unpublished data.

2010). The disease is frequently found in domestic and wild intermediate hosts, particularly in cattle, sheep, wild boars and deer.

In **Bulgaria**, CE is still prevalent in all parts of the country. After a control campaign in the 1960s, a considerable decrease in the annual CE incidence (from $6.5/10^5$ inhabitants to $2.0/10^5$ inhabitants) was observed between 1971 and 1982. Later, between 1996 and 2013, the average annual incidence increased to $6.7/10^5$, and Bulgaria is now considered to have the highest morbidity rate of human CE in EU state members (Todorov and Boeva, 1999; Jordanova et al., 2015). G1 has been reported in both definitive and intermediate hosts in the country (Breyer et al., 2004).

The first report of echinococcosis in **Serbia** dates back to 1899. CE was very rarely diagnosed before the World War II, but numbers increased later on, and in 1997 the incidence was estimated to be 0.21 per 10^5 inhabitants (Bobic et al., 2012). So far, *E. granulosus* (G1) has been reported in humans, sheep and swine, and *E. intermedius* (G7) in humans and swine (Colovic, 2009; Maillard et al., 2009) (Table 8). Interestingly, infections in swine were of major significance in the past (Dakkak, 2010); however, recently infections in sheep might be of higher relevance (Bobic et al., 2012). As in other Balkan countries, home slaughtering is still an important risk factor for the transmission of CE in Serbia. According to the Statistical Reports of Serbia, only 30–33% of swine, 40–47% of cattle and 5–7% of sheep were slaughtered in abattoirs after 2005. Investigations of *E. granulosus* in dogs in Serbia have not been conducted/published so far, but they are assumed to serve as definitive hosts.

In **Croatia**, CE is recognized as a public health problem, but data on the spread of the parasite are rather limited. The region of Dalmatia that covers the eastern coast of the Adriatic sea is historically known as an endemic area. The incidence of human CE in Croatia decreased from 28.3 per 10^5 inhabitants between 1940 and 1950 to 4.2 per 10^5 inhabitants in the 1990s, but in some communities, the prevalence in domestic animals increased (Morovic, 1997). Wild boars also play a role in transmission of the parasite in Croatia (Rajkovic-Janje et al., 2002).

Only limited information on CE is available from **Bosnia and Herzegovina**, **Macedonia** and **Kosovo**. In these Balkan countries, the dog populations are not registered, and free roaming and stray dogs have easy access to uncooked offal and carcasses. Furthermore, the lack of knowledge of CE and the absence of strategic deworming of dogs contribute to the persistence of the infection pressure even in hunting and pet dogs. Based on the scarce data available, the predominant intermediate hosts are sheep and cattle (with a high percentage of sterile cysts). In contrast to Serbia, infections in pigs have so far not been documented in the three other Balkan countries. In **Kosovo**, besides professional slaughtering in abattoirs, home slaughtering of sheep and cattle for private meat consumption is traditionally performed not only by farmers but also by a large part of the population in rural and urban areas. Transmission of CE is linked mainly to home slaughtering and the feeding of infected organs to dogs. Many old sheep are slaughtered, particularly during Eid al-Adha (Feast of Sacrifice), and this celebration is followed by a pronounced increase of taeniid infections in dogs, including *E. granulosus* (Alishani et al., 2017).

In **Albania**, *E. granulosus* has been described for more than 60 years in intermediate and definitive hosts. Only recently infected dogs have been identified in the area surrounding Tirana (Xhaxhiu et al., 2011) and interestingly, a high proportion of human CE cases originated from Tirana in the last few years. Reasons for this peri-urban infection risk were suggested to be aggressive urbanization, sanitary and garbage disposal problems, and the presence of sheep and dogs inside landfills and in the city itself (Pilaca et al., 2014).

3.4.5.2 Infections in animals

In **Romania**, CE is frequently found in domestic (Fig. 8 and Table S7 in Supplementary Material) and wild intermediate hosts. Cysts were observed in 29.0−34.4% of cattle and 47.1−54.7% of sheep surveyed. Positive findings were also documented in wild boars (12.4%) and red deer (9.5%) in which *E. granulosus* (G1) and/or *E. intermedius* (G7) were confirmed (Mitrea et al., 2014; Onac et al., 2013).

In **Bulgaria**, CE prevalence values recorded in 2009 were 0.1% in pigs, 5.1% in cattle, 7.0% in sheep and 10.5% in goats (EFSA, 2011). Analysis of 24 isolates from definitive (jackal, wolves) and intermediate hosts (cattle, sheep, pigs) revealed the presence of *E. granulosus* (G1) in Stara Zagora county of Bulgaria (Breyer et al., 2004).

From **Slovenia**, low prevalences of CE in animals were reported (Fig. 8 and Table S7 in Supplementary Material). In 2009, CE was recorded in less than 0.1% of 123,760 cattle and 295,960 pigs examined and none of 9759 sheep, 450 goats and 1426 equines (EFSA, 2011). However, the data from humans in eastern Slovenia (see below) suggest ongoing CE transmission.

In **Serbia**, CE continues to be endemic, mainly in sheep (Fig. 8 and Table S7 in Supplementary Material), but despite predictions, neither official data nor those from clinical studies indicate its re-emergence (Bobic et al., 2012). In fact, a gradual decrease in the prevalence of CE during the last few decades has been identified in livestock (from 14% to 1% in sheep, from 13% to 2% in cattle and from 9% to 4% in swine (Bobic et al., 2012). However, the authors suggest that underreporting of CE at slaughterhouses, structural and economic reorganization and/or closing of abattoirs and an increase in home slaughtering in the last 20 years have to be considered.

Data about the occurrence of *Echinococcus* spp. in **Croatia** are scarce. CE was commonly found in livestock in Croatia in the 1950s until the 1970s, with prevalence values of 10−40% in cattle, 40−80% in sheep and up to 30% in pigs. In the 1980s, high variation in prevalences in sheep from 5% to 88% was found, and in 1991, 14% of stray dogs were positive for *E. granulosus* (Ecca et al., 2002). In eastern Croatia (Slavonia) CE was detected in 2 of 47 wild boars (*Sus scrofa*) collected in 2000 and 2001 (Rajkovic-Janje et al., 2002), documenting the possible involvement of wild animals in the life cycle.

In **Bosnia and Herzegovina**, a retrospective study based on unpublished data reported a high CE prevalence in cattle (27.2%) and sheep (80.3%). A more recent study confirmed CE in 22% of cattle and 65% of sheep (approximately 2000 animals in total) (Zuko and Obradović, 2014).

Regarding **FYROM (Former Yugoslav Republic of Macedonia)**, CE is thought to be endemic in intermediate hosts and humans, but no published data are available for this country.

In **Kosovo**, the prevalence of *Taenia* spp. and *E. granulosus* (sheep strain, G1−3) was 7.5% and 1.3%, respectively, in naturally infected pet dogs, sheepdogs and hunting and stray dogs (Sherifi et al., 2011). The occurrence of CE in slaughtered cattle from all over the country was high (72%), indicating a high environmental contamination with *E. granulosus* eggs (Hamidi et al., 2010).

In **Albania**, *E. granulosus* intestinal infections in dogs have been documented over more than 60 years (Xhaxhiu et al., 2011). In a recent study (2004−09), necropsy of 111 dogs revealed infections with *Taenia hydatigena* in 16.2% and with *E. granulosus* (G1) in 2.7%, suggesting transmission via free access of dogs to carcasses of intermediate hosts (Xhaxhiu et al., 2011). Studies covering the whole country revealed 1347/6051 (22.2%) of cattle and 168/603 (27.8%) of sheep positive for CE (Zanaj, 1997). According to abattoir surveys, CE has been present in Albania for decades with highly variable prevalences (5−75%), primarily in sheep and cattle rather than goats and swine [citations Xhaxhiu et al. (2011)].

3.4.5.3 Cystic echinococcosis in humans

According to the WHO, the highest annual incidence (per 10^5 inhabitants) of CE between 2001 and 2010 was reported for Bulgaria (range 3.88−9.27), followed by the FYROM (0.3−1.89), Bosnia and Herzegovina (0.32−1.06) and Croatia (0.23−0.81), whereas the lowest incidence was reported for Hungary (0.05−0.13) (Torgerson, 2017).

In **Romania**, 451 cases (including 82 children) were diagnosed during 2004−10 in the counties of Arad, Hunedoara, Caras-Seeverin and Timis. The yearly incidence was $3.4/10^5$ adults and $3.1/10^5$ children (Vlad et al., 2013). Hospital discharge data indicate 1730 cases of CE in 2012 which represents an incidence of 6.6/105 (European Hospital Morbidity Database − http://data.euro.who.int/hmdb/). Although some of these may be recurrent cases, rather than new cases it does indicate the massive scale of human CE in Romania.

In **Bulgaria**, 291−596 human cases of CE per year were recorded in the period of 2003−12, with an annual incidence ranging between $3.95/10^5$ and $8.14/10^5$ inhabitants (Rainova et al., 2014). According to official data from the National Centre of Infectious and Parasitic Diseases, the average incidence of the disease was steady ($4.45/10^5$ inhabitants) in the years 2009−14 (Muhtarov, 2014; Piccoli et al., 2013).

In **Slovenia**, cases of echinococcosis are reported sporadically, and often without differentiation between AE and CE. The number of reported AE/CE cases decreased from nine cases ($0.44/10^5$ inhabitants) in 2009 to eight cases (0.39) in 2010 and 2011, and six cases (0.29) in 2012 and 2013 (EFSA, 2015a). Seroepidemiological surveys performed in 2002−06 on 1323 suspected CE patients revealed 127 (9.6%) seropositive individuals originating mostly from the eastern part of the country, historically known as a CE endemic region (Logar et al., 2008). In 2012, 12 cases ($0.54/10^5$) were reported in the European Hospital Morbidity database.

In **Croatia**, one of the historically high endemic area of the country is Dalmatia although there has been a decrease in the CE incidence from the mid-1950s until 1990 (Morovic, 1997). Since 1965, reporting of CE to the Epidemiology Reference Centre of the Croatian National Institute of Public Health (CNIPH) has been mandatory, and based on these data, the annual number of reported cases of CE in Croatia varied between 4 and 35, with an increasing tendency until 2004 and a decrease thereafter (Tabain et al., 2011). For Croatia, an annual CE incidence (2001−10) of 0.23−0.81 per 10^5 inhabitants was reported (WHO, 2010) and 74 cases are reported in 2013 in the WHO European Hospital Morbidity Database = $1.2/10^5$ http://data.euro.who.int/hmdb/.

A seroepidemiological survey conducted on 540 patients with cystic liver disease revealed seropositive reactions for CE in 3.9% of the patients, thus confirming that CE still circulates in Croatia (Tabain et al., 2011).

For **Serbia**, a recent comprehensive retrospective study (Bobic et al., 2012) reported a total of 409 officially reported human CE cases (1998–2010) in contrast to 820 clinical cases described during this period. The annual incidence of CE in official records of the Institute for Public Health ranged from $0.38/10^5$ to $0.63/10^5$ inhabitants but is likely to be higher due to underreporting. The European Hospital Morbidity Database (http://data.euro.who.int/hmdb/) reported 252 cases of CE in 2013 or $3.2/10^5$ inhabitants. As this is a WHO database (i.e., UN), it may also include data from Kosovo.

No trend in the incidence of infection among adults was observed, but the number of CE cases in children continuously decreased. Females and patients from rural areas were more frequently infected. Differences in the geographic distribution of CE cases with a lower incidence in the central part of Serbia were also documented (Bobic et al., 2012).

In **Kosovo**, 163 CE patients from all over the country (75% living in rural and 25% in urban areas) were treated at the University Clinical Center of Prishtina between 1999 and 2001. Based on these data, a minimal average annual incidence of $2.7/10^5$ inhabitants was calculated (Alishani et al., 2017). However, this incidence probably underestimates the real epidemiological situation as many CE cases have been detected in patients who originated from Kosovo but now live in other European countries such as Germany or Switzerland.

Bosnia and **Herzegovina** is recognized as endemic for CE and after the war (1992–95), human surgical incidence increased, especially in cities that were under siege during that period [cited in Dakkak (2010)]. Furthermore, a recent preliminary study mentioned in Zuko and Obradović (2014) showed high seroprevalences in this country. For **Bosnia** (based on WHO reports), 34 cases per year have been registered (2003–10) resulting in an annual incidence of 0.7 CE cases per 10^5 inhabitants (Torgerson, 2017). Only fragmented information is available for **FYROM**, with an incidence of $0.3–1.89/10^5$ inhabitants recorded in the WHO report (cited in Torgerson (2017)).

In a recent study performed in 2005–11 in **Albania**, 333 CE cases have been diagnosed and treated in the only tertiary (university) medical hospital of the country (UHC, Tirana). Based on these data, a minimal annual incidence of 1.5 clinical CE cases per 10^5 inhabitants was reported (Pilaca et al., 2014).

3.5 Asia (including Eastern Europe)

3.5.1 North Asia: Russian Federation

3.5.1.1 Host assemblages, transmission and molecular epidemiology

Echinococcus species are widespread throughout Russia (see Figs. 9 and 10). They have been described in people, farm animals, dogs and wildlife such as moose, reindeer and wolves (Table 9). As shown in Table 9, *E. granulosus* (genotypes G1–3) and *E. canadensis* (G8, G10) have been confirmed in the European Russia and the Altai region. In Yakutia, G1 has been reported in sheep, and *E. intermedius* (G6) and *E. canadensis* (G8, G10) have been found in wild ungulates (including reindeer and elk) and wolves (Konyaev et al., 2013). An unusual case of CE in a domestic cat from St. Petersburg was caused by *E. granulosus* G1 (Konyaev et al., 2012b). *E. intermedius* (G7) has been reported from Armenia (Snabel et al., 2009).

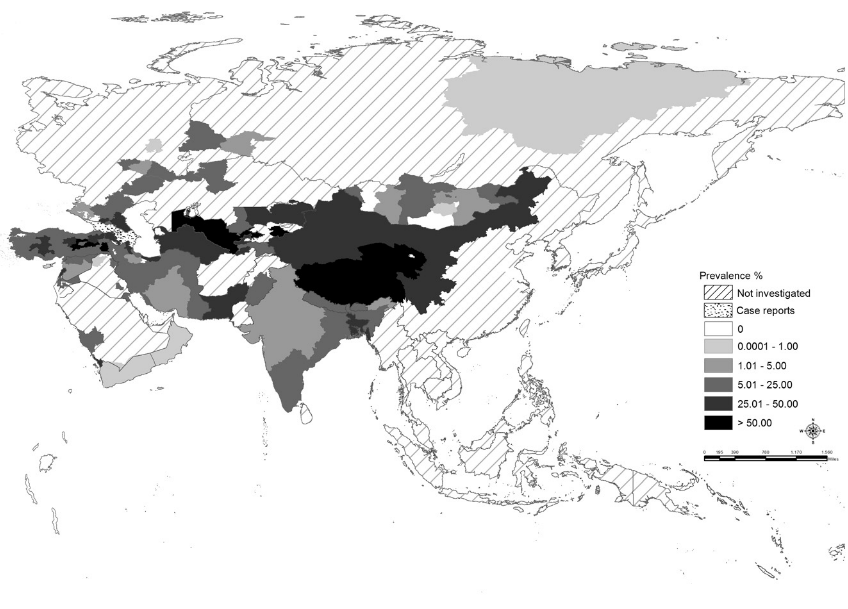

Figure 9 ***Current distribution of Echinococcus spp. causing cystic echinococcosis in domestic intermediate hosts (sheep, cattle, goats, pigs, buffaloes and yaks) in Asia.*** The detailed information (prevalence data in each jurisdiction) is listed in Table S9 of the Supplementary Material.

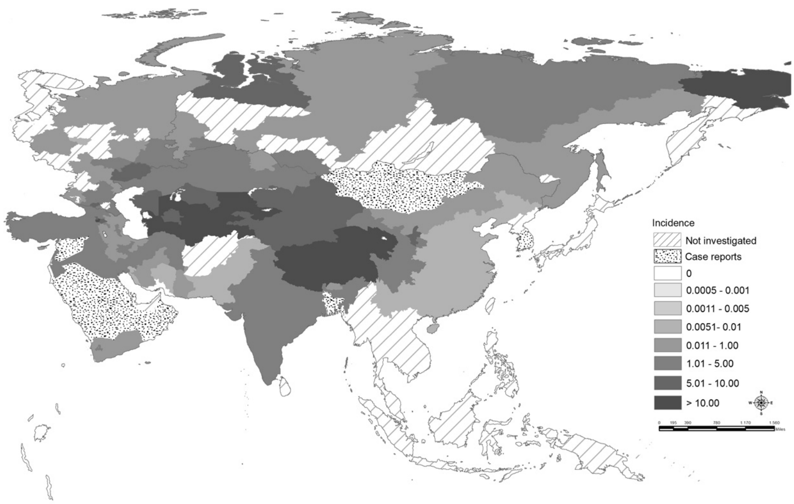

Figure 10 ***Current incidence of human cystic echinococcosis in Asia.*** The detailed information (incidence data in each jurisdiction) is listed in Table S10 of the Supplementary Material.

Table 9 Genotypes of *Echinococcus* spp. causing cystic echinococcosis in North Asia (including the European part of Russia), Central Asia and Caucasus (no data found in the missing countries): *Echinococcus granulosus* (G1−3), *Echinococcus equinus* (G4), *Echinococcus ortleppi* (G5), *Echinococcus intermedius* (G6/7) and *Echinococcus canadensis* (G8, G10)

Country	Human	Wolf (W), Dog (D)	Sheep (S), Goat (G)	Cervids	Pig	Cattle	Other
Russian Federation	G1−3, G6 G10[1,2]	W: G6 and G10[1]	G1−3[1]	G6, G8, G10			Cat: G1[3]
Kazakhstan		D: G1, G6/7[4,5,6]					
Kyrgyzstan		D: G1, G4, G6/7[7]					
Armenia	G1−3[8]		S: G1−3[8]		G7[9]	G1−3[8]	

[1] (Konyaev et al., 2013); [2] (Sharma et al., 2013); [3] (Konyaev et al., 2012b); [4] (Stefanic et al., 2004); [5] (Boufana et al., 2015a); [6] (Trachsel et al., 2007); [7] (Ziadinov et al., 2008); [8] Ebi, Gevorgyan H.S., personal communication; [9] (Snabel et al., 2009).

3.5.1.2 Infections in animals

Infection of animals with CE is widespread in Russia and reflects the wide distribution of human cases observed (see Figs. 9 and 10 and Tables S9 and S10 of the Supplementary Material). In the far south of the Caucasus, prevalences in sheep and cattle are between 20% and 30% (Dyachenko et al., 2014; Fiapsheva et al., 2007; Makhiyeva et al., 2010, 2012; Pliyeva and Uspenskii, 2006; Zhekamukhova et al., 2012). Dogs in this area are also highly infected, with prevalences of up to 70% (Bersanukayeava et al., 2013; Pliyeva and Uspenskii, 2006).

In the district of Kalmykia in Russia, 8.3% of sheep have been reported to be infected (Lazarev, 2010). Infection in cattle in Krasnodar has been reported at 4% (Shevkoplyas and Lopatin, 2009) and 2% in Samara Oblast (Uspenskii et al., 2013). Pigs also appear to be frequently infected in Russia: 3.5% in Krasnodar (Shevkoplyas and Lopatin, 2009) and 11% in Ulyanovsk (Romanov and Mishonkova, 2010).

In the region of the Urals, approximately 20% of sheep are infected in Orenburg (Belimenko and Khristianovsky, 2015) and 7.3% in Astrakhan (Postnova et al., 2010). Sheep cysts from the Ural region were identified as *E. granulosus* s.s. (Konyaev et al., 2013). In cattle from Orenburg and Sverdlovsk, prevalences of 23–47% (Terentyeva, 2007) and 23.7% were registered (Belimenko and Khristianovsky, 2015).

Further east in Siberia, 0.4% of cattle are infected in Yakutia (Kokolova et al., 2012) and 3.4% of pigs in Tyumen (Yamov and Antropov, 2008).

CE is frequently reported in wild ungulates such as reindeer. In Chukot in the far east of Siberia, CE is present in 6–12% of reindeer (*R. tarandus*) (Government reports) while in Yakutia, prevalences of 17% and 5% have been reported for reindeer and moose, respectively (Kokolova et al., 2012). Older reports give a prevalence of 4.4% in reindeer from Nenets (Sorochenko, 1972).

Infected wild carnivores have been reported in several regions of Russia including the wolves and jackals in the Caucasus (Pliyeva and Uspenskii, 2006): 61% of wolves in Yakutia (Kokolova et al., 2012), 42% of wolves in the Altai region (Pomamarev et al., 2011) and 36% in Nenets (Sorochenko, 1972). *Echinococcus* spp. isolates from wolves, domestic reindeer and wild cervids in the Altai region and Yakutia were identified as genotypes G6, G8 and G10 (Konyaev et al., 2013).

3.5.1.3 Cystic echinococcosis in humans

CE is a notifiable disease in Russia and the Federal Center of Hygiene and Epidemiology reports the total number of cases on an annual basis. Between 2006 and 2010, 2863 CE cases were reported, or 573 per annum. However, when the data from the individual Russian districts and the regional centres are combined with local scientific reports, the annual number of cases can be estimated at about 950 (0.66 cases per 10^5 inhabitants per year), which clearly indicates underreporting to the central public health services. In Orenburg, analysis of hospital records (Korneev et al., 2014) detected 20% more cases than reported by the Government. Likewise, case reports in Dagestan by Abdylazizov (2012) and by Shodmonov and Razikov (2015) are double the numbers reported to the Government.

There is considerable variability in the incidence of CE within Russia. Chukotka has an incidence of six cases per 10^5 inhabitants, but since the population is just 50,000 this only represents three cases reported in 2014 (Rospotrebnadzor, 2016). However, the same report states that there are 90 individuals undergoing treatment with confirmed CE or AE and a further 203 suspect cases. Furthermore, 91 cases of CE were detected during ultrasound surveillance (Malishev and Sobolevskaya, 2002). Thus, in this remote and sparsely populated region, CE appears to be a major health issue. In Yamal-Nenets, another remote region of the Russian north, about five cases per 10^5 inhabitants are seen. Elsewhere in Russia, high human incidences are reported in Dagestan and Karachy-Cherkess in the Caucasus (up to five cases per 10^5 inhabitants per year), Orenburg (up to four cases per 10^5 inhabitants per year) and Saratov (about two cases per 10^5 inhabitants per year). However, cases of human CE have been found in virtually every region of Russia. Even in Moscow, about 50 cases a year are reported, although 80% of these are in migrant workers who originate from elsewhere in Russia or from Central Asian countries such as Kyrgyzstan or Uzbekistan (Rospotrebnadzor, 2016).

There are regional variations in the organs affected by CE. For example, in the Astrakhan region, 69% of cases of CE are hepatic (Postnova et al., 2010). In contrast, in the far north of European Russia, most cases are pulmonary echinococcosis (Bikov et al., 2011; Buzinov et al., 2012). There has been little genotyping undertaken on isolates from humans. In the Altai region and Bashkiria. *Echinococcus granulosus* s.s. cysts have been identified in human CE cases, and the G6 genotype was identified in one patients from Altai (Konyaev et al., 2012a, 2013).

3.5.2 Caucasus and Central Asia: Kazakhstan, Kyrgyzstan, Tadjikistan, Turkmenistan, Uzbekistan, Armenia, Azerbaijan and Georgia

3.5.2.1 Introduction

CE has long been endemic in the five central Asian republics that were previously part of the Soviet Union. This is a large area stretching from the eastern shore of the Caspian Sea across to the western borders of China. Agricultural land in Central Asia is semi arid and mountain pasture resulting in a predominance of pasture-based livestock production. This provides good conditions for the transmission of livestock reservoir of *Echinococcus* species. Since the collapse of the Soviet Union in 1991, CE has emerged as a major zoonosis with substantial increases in incidence in humans. This is due to the privatization of large collective farms, the abandonment of centralized slaughtering and meat processing facilities, and few resources available for veterinary services. There has also been an increase in the dog population and greater availability of infected offal to dogs through unregulated slaughtering of animals (Shaikenov et al., 2003; Torgerson, 2013).

3.5.2.2 Infections in animals

In **Uzbekistan,** the prevalence of CE in sheep has increased from 45% to 62% between 1990 and 2002 (Aminjanov and Aminjanov, 2004). In **Kazakhstan**, prevalences in sheep have also increased in southern Kazakhstan from 14% in the 1980s to 37% by the year 2000 (Torgerson et al., 2002). Generally, prevalences in sheep have been reported between 24% and 48% in southern Kazakhstan with approximately 7% of cattle infected (Torgerson et al., 2003). In western Kazakhstan, prevalences of 18% in sheep and 19% in cattle have been reported (Vaiyeva et al., 2012). In the Kostanay Oblast in the northern part of Kazakhstan, CE was found in 8% of 826 pigs and in 24% of 3823 cattle. Interestingly, in infected pigs, 68% of cysts were found in the lungs, whilst in cattle 73% of cysts were found in the liver (Suleimanova and Shinkina, 2015). This markedly different distribution of organ affinity between the two species might be consistent with different genotypes circulating in different species assemblages.

In the Naryn region of central **Kyrgyzstan** a prevalence of 64% in sheep was reported in 2006 (Torgerson et al., 2009). In **Tadjikistan** prevalence varies with region. Highly endemic areas are located in the north, with over 50% of sheep infected, whereas central and southern districts generally have around 20% prevalence, and only 7% in areas around the Chinese border. Infection varies directly with age in all regions, with prevalence in young animals often less than 10%, and the prevalence in the oldest animals approaching 80% (Muminov et al., 2004).

A number of studies on dogs in the region have revealed widespread infection. In southern areas of **Kazakhstan** – south Kazakhstan, Dzambul and Almaty Oblasts – prevalence in village dogs was 6% while prevalence in farm dogs was 23% (Torgerson, 2013). In the west Kazakhstan Oblast, 15.9% of 176 dogs were infected (Vaiyeva et al., 2012). *Echinococcus granulosus*-like cestodes have also been found in the intestines of two of 51 (4%) of village dogs from Akmola Oblast (Sultanov et al., 2014). In Naryn Oblast in Kyrgyzstan, 19% of 466 dogs were infected (Ziadinov et al., 2008). In Uzbekistan, 531 dogs were investigated using arecoline purgation. Of these, 279 were farm dogs of which 56 were infected (20.1%). Of the remaining 240 village dogs, 19 were infected (7.9%) (Aminjanov and Aminjanov, 2004). In **Tadjikistan**, one study of 120 dogs reported a prevalence of 15.2% (Muminov et al., 2004). In a second study, 23 of 41 dogs were infected with *E. granulosus* at necropsy (Razikov and Adilova, 2011).

A study of wolves in southern **Kazakhstan** revealed eight of 41 (20%) infected with *E. granulosus* (Abdybekova and Torgerson, 2012).

There are relatively few studies on the *Echinococcus* genotypes in animals in central Asia and Caucasus (Table 9). G1 and G6/7 have been isolated from dogs in southern Kazakhstan (Stefanic et al., 2004; Trachsel et al., 2007). In central Kyrgyzstan (Naryn Oblast), G1 and G6/7 have also been isolated from dogs. In addition, G4 (*E. equinus*) has been reported in a single dog in Kyrgyzstan (Ziadinov et al., 2008).

In **Armenia**, studies in the 1970s and 1980s revealed *E. granulosus* in 49.5% of dogs examined and CE in 16.8–46.9% of cattle and in 22.7–47.0% of pigs (Khachatryan, 2015). In the central province of Kotayk, prevalence in sheep can reach 80% (Gevorgyan H.S., personal communication). In a recent molecular survey, all 204 isolates from sheep (89), cattle (72) and humans (43) belonged to *E. granulosus*, while two cysts from pigs belonged to G7 (Ebi, Gevorgyan H.S., personal communication; Gevorgyan et al., 2006; Snabel et al., 2009).

Georgia and **Azerbaijan** have long been considered endemic for *E. granulosus* with pig, sheep and cattle strains reported (Khachatryan, 2015), but there are no data on the prevalence of infection or the genotypes of parasite in the country.

3.5.2.3 Cystic echinococcosis in humans

At the end of the last decade of the 20th century it became apparent that there was an increased incidence of CE in Central Asia (Shaikenov et al., 2003). Official government statistics in **Kazakhstan** documented an increase in cases of CE from about 200 cases per year until 1994, rising rapidly to approximately 1000 cases per year by the beginning of the 21st century (Torgerson et al., 2002). Recent data suggest that the incidence in Kazakhstan has since stabilized at this higher level (Abdybekova et al., 2015). In Kazakhstan, there is a strong association between human incidence and the main sheep rearing areas, with high incidence seen in the southern districts and in West Kazakhstan Oblast (Torgerson et al., 2006).

Likewise there was similar evidence from neighbouring **Kyrgyzstan** with a continuing rise in cases up until 2013 (Raimkylov et al., 2015). In **Tajikistan**, the number of cases increased from 374 in 1992 to 1875 in 2002 (Muminov et al., 2004). Subsequently, data confirmed a similar situation in **Uzbekistan** and **Turkmenistan** (Torgerson et al., 2006). Furthermore, in Uzbekistan, officially reported cases of CE are a substantial underestimate of the numbers of cases being treated (Hong et al., 2013). A detailed case finding study of all hospitals in Uzbekistan uncovered approximately four times the numbers of cases of CE than reported in government statistics (Nazirov et al., 2002).

For **Armenia**, **Georgia** and **Azerbaijan**, relatively high CE incidences have been estimated. In **Armenia**, there were 1470 CE patients reported from 1997 to 2003, representing incidences in urban residents of 4.6 per 10^5 inhabitants and in rural residents of $8.1/10^5$ inhabitants (Khachatryan, 2015). Based on 234 CE cases registered in 2010, an incidence of $7.8/10^5$ was estimated for Armenia (Torgerson, 2017). In Georgia an average of 68 cases has been registered resulting in an incidence of $1.5/10^5$ inhabitants and in Azerbaijan, an annual average of 85 cases (incidence of $0.93/10^5$ inhabitants) was calculated (Torgerson, 2017). More information on human CE is required from the Caucasus.

3.5.3 Middle East: Iran, Iraq, Israel, Jordan, Kuwait, Lebanon, Oman, Palestine, Qatar, Saudi Arabia, Turkey and Yemen

3.5.3.1 Host assemblages and transmission

About 400 million people are living in the Middle East extending from the eastern Mediterranean coast in the west to the Iranian plateau in the east, and from Turkey in the north to Saudi Arabia and Yemen in the south.

Table 10 Genotypes of *Echinococcus* spp. causing cystic echinococcosis in the Middle East (no data found in the missing countries): *Echinococcus granulosus* (G1–3), *Echinococcus equinus* (G4), *Echinococcus ortleppi* (G5), *Echinococcus intermedius* (G6/7) and *Echinococcus canadensis* (G8, G10)

Country	Human	Dog (D), Wild canids (Wc)	Sheep	Camel	Cattle/Buffalo	Goat	Equine
Iran	G1[1,2,3] G2[2,4] G3[1,2,4,5]	D: G1[6] G2[4,6] G3[2,7] G6[7] Wc: G1[8]	G1[9] G3[2,9,10,11]	G1[4,12] G3[2,10,13] G6[1,4,12]	G1[9] G3[2,10,14] G6[9]	G1[12] G6[15] G7[16]	G1/G6/G4[17,18]
Iraq	G1[19]	na			G1[20]		
Jordan		D: G1[21] G4[21]	G1[22]				
Oman			G1[23]	G1[23] G6[23]	G1[23] G6[23]	G1[23]	
Palestine			G1[24] G2[4,24] G3[2,24]				
Turkey	G1[25,26] G3[2,27] G6[27] G7[25]	D: G1[26]	G1[25,26] G3[2,28] G7[25]	G1[26]	G1[26,28,29] G3[2,28,29]	G1[26,28]	G1[30] G4[31,32]
Yemen	G1[33]						

[1] (Zhang et al., 1998); [2] (Rostami et al., 2015); [3] (Kia et al., 2010); [4] (Harandi et al., 2002); [5] (Pezeshki et al., 2013); [6] (Parsa et al., 2012); [7] (Shariatzadeh et al., 2015); [8] (Beiromvand et al., 2011); [9] (Shahnazi et al., 2011); [10] (Hajialilo et al., 2012); [11] (Pezeshki et al., 2013); [12] (Sharbatkhori et al., 2010); [13] (Sharbatkhori et al., 2011); [14] (Pour et al., 2011); [15] (Rajabloo et al., 2012); [16] (Fadakar et al., 2015); [17] (Eslami et al., 2014); [18] (Sarkari et al., 2015); [19] (Hama et al., 2012); [20] (Hama et al., 2015); [21] (Al-Qaoud et al., 2003); [22] (Yanagida et al., 2012); [23] (Al Kitani et al., 2015); [24] (Adwan et al., 2013); [25] (Snabel et al., 2009); [26] (Utuk et al., 2008); [27] (Simsek et al., 2011); [28] (Vural et al., 2008); [29] (Simsek et al., 2010); [30] (Utuk and Simsek, 2013); [31] (Simsek et al., 2015); [32] (Simsek and Cevik, 2014); [33] (Alam-Eldin et al., 2015).

The region has a diverse geography including arid/semiarid tropical regions and humid temperate areas. Precipitation and temperature vary considerably across the ME and even within countries. The Caspian coast of northern Iran receives precipitation of up to 2000 mm per year while the desert areas of eastern/central Iran receive no rain for years.

The Middle East has been one of the hot spots of CE in the world (Cardona and Carmena, 2013; Dakkak, 2010; Dar and Alkarmi, 1997; Sadjjadi, 2006). Sheep and goats are believed to have been domesticated for the first time in the Fertile Crescent of the Middle East around 8500−11,000 years ago, and this was central to CE establishment in livestock/dog assemblages with spillover into people. Therefore the Middle East can be considered as a historically very old human CE-endemic region (Zeder, 2008).

The parasite circulates primarily among domestic dogs (owned and ownerless stray animals) as definitive hosts and a variety of domestic livestock as intermediate hosts (Dowling et al., 2000; Harandi et al., 2011; Rafiei et al., 2007; Shariatzadeh et al., 2015). However, a wild animal cycle has been documented in Iran and Turkey involving wolf, jackal, hyena and red fox as definitive hosts, and wild sheep (*Ovis orientalis*) and the goitered gazelle (*Gazella subgutturosa*) as intermediate hosts (Dalimi et al., 2002, 2006; Eslami et al., 1981, 2016; Simsek and Eroksuz, 2009).

The stable endemicity of CE in the Middle East is largely due to the diverse number of intermediate host species, with sheep and goats as the principal hosts, followed by camels and cattle. In camels, CE is prevalent with highly fertile and viable cysts (Al Kitani et al., 2015).

As part of the ceremonies related to the annual mass gathering of the Hajj (Muslim pilgrimage to Mecca), millions of livestock (mainly sheep and goats) are imported and sacrificed in Saudi Arabia. This is a defining aspect of CE epidemiology in the Arabian Peninsula.

The following factors are among the major determinants of CE transmission in the region: (1) nomadic/rural lifestyle and traditional livestock husbandry including use of shepherd dogs; (2) food habits including high raw vegetable consumption; (3) unregulated/poor quality abattoirs and widespread practice of home slaughter, particularly in special religious festivals and social events; (4) low awareness of people about transmission and pathogenesis of CE; (5) diverse intermediate host species and high populations of stray dogs.

On the other hand, limiting factors for transmission include mostly arid/semiarid environments with less favourable climate conditions for the survival of *Echinococcus* eggs, avoidance of dogs in Muslim communities and the absence of pig farming due to religious beliefs (Dakkak, 2010; Dar and Alkarmi, 1997; Harandi et al., 2011; Rokni, 2009).

3.5.3.2 Molecular epidemiology

Table 10 summarizes the occurrence of *Echinococcus* species and genotypes causing CE in the Middle East. *Echinococcus granulosus* (G1−3) is the dominant species responsible for most human and animal infections (Harandi et al., 2002; Al-Qaoud et al., 2003; Utuk et al., 2008; Vural et al., 2008; Sharbatkhori et al., 2009), with *E. intermedius* (G6, camel strain) as the second most prevalent species in the region and increasingly recognized in human cases (Rostami et al., 2015; Al Kitani et al., 2015). In addition there have been reports of the occurrence of *E. intermedius* (G7) in Turkey and Iran (Snabel et al., 2009; Eryildiz and Sakru, 2012; Fadakar et al., 2015). In Jordan, most dogs were infected by G1 while a single sample was most similar to *E. equinus* (G4) using RAPD-PCR (Al-Qaoud et al., 2003). More genotype data from the Middle East are required especially from Iraq, Lebanon, Palestine/Israel, Syria and the Persian Gulf countries.

3.5.3.3 Infections in animals

A distinct feature of cystic echinococcosis in the Middle East is the diverse number of intermediate host species involved in transmission; however, sheep and goats are the principal intermediate hosts. *Echinococcus granulosus* (G1−3) has been shown to perpetuate in at least 13 species of mammals in this region [i.e., sheep, goat, cattle, buffalo, one- and two-humped camels, horse, donkey, pig, wild sheep (*Ovis orientalis*), goitered gazelle (*Gazalla subgutturosa* and free-ranging Baboon (*Papio hamadryas*)]. Such a diverse intermediate host system is a fundamental element for the stable endemicity of CE in the Middle East.

No recent data are available on *Echinococcus* infections in dogs from countries in the **Arabian Peninsula**. Older investigations indicated that 15% and 23% of dogs were infected in **Saudi Arabia** and **Kuwait**, respectively (Dar and Alkarmi, 1997; Hassounah and Behbehani, 1976). Several studies from **Saudi Arabia** document CE in sheep, goats, cattle and camel. In the Al-Baha region in western Saudi Arabia, 12.6% of sheep, 6.6% of goats, 8.3% of cattle and 32.9% of camels were infected. Prevalences were significantly higher in the Al-Baha region than in Al-Mekwah and Al-Aqiq, likely due to the more suitable climatic conditions (lower temperature and higher precipitation) in the Al-Baha area (Ibrahim, 2010). In Al-Taif municipal abattoir, 13.5% of sheep and 6.1% of goats were infected, with a higher prevalence in the imported sheep than the local animals (Hayajneh et al., 2014). In

Oman, low prevalence values of CE have been reported from camels (5.3%), cattle (0.6%), sheep (0.07%) and goats (0.03%). Higher fertility was observed in cysts from camels compared to those from sheep and goat (Al Kitani et al., 2015). Prevalence was higher in locally bred livestock than imported animals. In the late 1980s, CE was found in 39.6% of camels in **Kuwait** with higher pulmonary infection (63%) and higher cyst fertility than the hepatic cysts (Abdul-Salam and Farah, 1988). Updated information is required from other countries in the Arabian Peninsula.

In **Palestine** and **Israel**, 18.3% of 93 dogs were positive on copro-PCR in three districts of Al-Khalil (Hebron), Tubas and Jenin (Al-Jawabreh et al., 2015). In three independent studies in northern towns of Yirka and Tamra near the Lebanese border, 7.9%, 14.2% and 10.7% of dogs were found infected based on arecoline purgation (Nahmias et al., 1991; Furth et al., 1994; Hoida et al., 1998). In the latter study, despite 10.7% infection in 56 dogs belonging to Muslim and Druze communities, none of the 150 dogs' excrement from Jewish communities was found infected, underlining the significance of sociocultural parameters and animal husbandry systems in transmission of CE. A recent study from Israel and Palestine reported CE in 9% of sheep slaughtered in abattoirs in Nablus, Jenin and Tubas (El-Ibrahim, 2009). In the northern city of Tamra, 5.9% of 874 sheep and 5.3% of 616 goats were infected (Hoida et al., 1998). In neighbouring Yirka, 75% of sheep and goats were slaughtered at individual households with only 25% at a Yirka abattoir (Nahmias et al., 1991).

In **Lebanon**, 17–32.9% of dogs were historically infected (Araj and Mourad, 2014), but recent infection data are not available. The prevalence of CE has been estimated at 6.6% and >41% in sheep and cattle, respectively (Araj and Mourad, 2014).

Very limited information is available from **Syria** and new investigations are required after the ongoing war. The prevalence of *Echinococcus* infection in dogs was estimated at 9–15%, and prevalences of CE in livestock ranged between 5 and 17%, highest in the northern areas of the country (Dakkak, 2010).

Three major studies have been carried out in **Jordan** since the 1980s indicating *E. granulosus* prevalences in dogs of 14%, 9.4% and 29.5% (Ajlouni et al., 1984; El-Shehabi et al., 1999; Al-Qaoud et al., 2003). Fourteen of twenty-five dogs (56%) were infected around a disposal area of a municipal slaughterhouse, where condemned organs were readily available. In five regions of **Jordan**, CE prevalence was 12.9% in sheep, 12.7% in goats, 0.9% in cattle and 11% in camels (Kamhawi, 1995). CE was found in 44.9% of camels slaughtered in Al-Ramtha abattoir in northern Jordan (Sharrif et al., 1998). In Irbid governate, CE was found in 16.9% of 130 donkeys (Mukbel et al., 2000).

High prevalences have been reported for dogs in **Iraq** in the past. In the 1980s and 1990s, double-digit prevalences have been reported from several provinces in northern, central and southern Iraq, i.e., 20% in Al-Tamim, 38% in Diala, 56% in Theqar and 25% in Baghdad (Molan, 1993; Molan and Baban, 1992; Tarish et al., 1986). The prevalence of *E. granulosus* in dogs decreased from 70.4% in 1991 to 24.3% in 1998 in the northern province of Arbil (Saeed et al., 2000). Different studies in northern **Iraq** reported CE in 2−15% of sheep, 0.5−6.3% of goats, 0.5−10.9% of cattle (Saeed et al., 2000; Jarjees and Al-Bakri, 2012; Meerkhan and Abdullah, 2012) and 20−72% of camels (Molan, 1993).

Several studies on canine echinococcosis in **Turkey** indicated endemicity across the country, ranging from 1% in Aydin (western Turkey) to more than 40% in Kars (northeastern Turkey) (Altintas, 2003; Kuru et al., 2013). In the southern city of Antakya near the Syrian border, 8.9% of owned dogs were positive in a coproantigen test with a highest prevalence of positive dogs in free ranging populations with no deworming history (Guzel et al., 2008). The prevalence of CE in livestock varied from 3.5% to 58.6%, depending on different geographical locations and specimens examined (Altintas, 2008). CE was more prevalent in sheep (46.4%) in Van (Oguz and Deger, 2013) than in cattle (33.9%) in Erzurum (Simsek et al., 2010), goats (22.1%) in Burdur (Umur, 2003) or buffaloes (10.2%) in the central Black Sea Region (Beyhan and Umur, 2011).

In **Iran**, canine echinococcosis has been reported from across the country. The dog population in Iran has been estimated at 3.5−11.5 million animals and more than 70−90% are ownerless stray dogs (Harandi et al., 2011). Using arecoline purgation, 27.2% of 390 farm dogs examined in 13 provinces of Iran were infected with *E. granulosus* (Eslami and Hosseini, 1998). In five western provinces the prevalences ranged between 9% and 31% (Abdi et al., 2013; Dalimi et al., 2002). In the northwestern and northeastern parts of the country, the prevalence of canine echinococcosis is between 17% and 20% (Beiromvand et al., 2011; Shariatzadeh et al., 2015). In Mashhad (largest city in northeast of Iran) 22% of dogs were found infected with *E. granulosus* (Razmi et al., 2006). In central and southern parts of the country, the prevalence ranges from 6.8% in Kerman (in the southeast) to 36.2% in Shiraz (in the south) and 55.7% in Kashan in central Iran (Arbabi and Hooshyar, 2006; Mehrabani et al., 1999; Sharifi and Tasbiti, 1994). While the prevalence of *E. granulosus* in dogs of the northern city of Sari was revealed as 46.7% in 1993, 15 years later, none of 50 dogs examined in the same locality was infected after the establishment of a well-equipped abattoir in the region and improved awareness of the local people about the consequences of home slaughter (Gholami et al., 2011). In **Iran**, CE in livestock constitutes a major economic and public health problem. In a 5-year study of abattoirs in nine districts in the northeastern province of Khorasan, an estimated 52.2% of the livestock viscera condemnations were due to CE (Borji and Parandeh, 2010). The corresponding figure in a similar 5-year study in southwestern province of Khuzestan was 29.2% (Borji et al., 2012a). Several surveys in Iran have indicated CE prevalence in livestock ranging from 1.3 to 74.4% in sheep, 0.4–37.8% in goats, 1.3–40.1% in cattle, 4.3–31.9% in buffaloes, 8.8–35.5% in camels and 2% in donkeys (Ahmadi, 2005; Ahmadi and Meshkehkar, 2011; Eslami et al., 2014; Samavatian et al., 2009). In the northern Caspian coastal provinces, prevalence of CE ranged between 14.6 and 65.2% in sheep, 10.1–37.8% in goats and 12–41% in cattle (Mansoorlakooraj et al., 2011; Ziaei et al., 2011). In northwestern areas of the country, prevalence of CE ranged between 22.2 and 74.4% in sheep, 20–25% in goats and 28.3–38.3% in cattle (Daryani et al., 2007; Mirzaei et al., 2015). In five western provinces of Iran, the prevalence of CE has been reported as 11.1% in sheep, 6.3% in goats and 16.4% in cattle (Dalimi et al., 2002). Lower prevalences have been reported in central and eastern areas of the country where the climate is arid/semiarid with lower precipitation (Ansari-Lari, 2005; Arbabi and Hooshyar, 2006; Fakhar and Sadjjadi, 2007). In a study conducted in the southeastern province of Kerman, the prevalence of CE in sheep and goats was markedly reduced after an extensive dog-culling program (Sharifi et al., 1996).

3.5.3.4 Cystic echinococcosis in humans

Human CE is widespread in the Middle East and is principally considered a disease of rural areas, mainly affecting farmers and livestock herders. However, CE has been increasingly reported in patients living in urban and peri-urban areas (Ok et al., 2007; Dar and Alkarmi, 1997). Most of the data available for human CE in the Middle East are sporadic hospital-based reports as well as seroprevalence studies in different localities. The need for a regional and a national CE registry system as well as regular community-based ultrasound surveys is becoming apparent in the region. Consequently, Turkey, Iran and Palestine have recently joined the European Register of CE (Rossi et al., 2016).

In the Arabian Peninsula, most human infections are reported from **Yemen**, **Saudi Arabia** and **Oman**. In **Oman**, the Salalah region in the southern province of Dhofar is the main endemic focus of CE (Scrimgeour et al., 1999). In central **Saudi Arabia**, 117 CE patients have been described with a male to female ratio of 1.7:1 and a mean age of 40.9 years (Fahim and Al Salamah, 2007). In a retrospective study in a major general hospital in **Qatar**, 32 human CE patients were recorded between 2000 and 2013, but only 3 patients were Qataris. It has been suggested that no local transmission of CE occurs in Qatar, where no stray dogs are present and the abattoirs are under strict veterinary supervision (Al-Ani et al., 2014). In **Yemen**, 796 cases were treated in the five main hospitals in Sana between 2001 and 2008, with a trend for increasing numbers. Females accounted for 61% of cases (Al-Shibani et al., 2012).

In **Palestine** and **Israel**, several studies indicated that CE is endemic in the West Bank, especially towns in the Tamra and Yirka in the north and in Bedouin communities of Negev desert in the south. The incidence of CE has been calculated as 1.2–3.1 per 10^5 inhabitants in the West Bank and $1.0/10^5$ in Gaza (Abu-Hasan et al., 2002; Al-Jawabreh et al., 2015). A significant difference in CE incidence has been documented between Bedouin (2.7%) and Jewish (0.4%) populations in the south, attributed to differences in lifestyle and living conditions as well as socioeconomic status (Ben-Shimol et al., 2016).

CE has been highly endemic in **Lebanon**, with an incidence of $3.8/10^5$ inhabitants and a 2:1 ratio of Christians to Muslims described in the 1950s (Matossian et al., 1977). However, the incidence seems to be decreasing in recent years, although no hard evidence is currently available in the literature (Araj and Mourad, 2014).

In **Jordan**, according to an investigation in 18 major hospitals, the mean annual surgical incidence of CE has been estimated at $2.9/10^5$ inhabitants (Kamhawi, 1995) and it was estimated that CE surgery constitutes 0.1–1.2% of total surgical operations (Nasrieh et al., 2003). Source of domestic water was described as a significant risk factor for human CE in Jordan (Dowling et al., 2000). It has been suggested that in Muslim countries dog ownership is not a major risk factor for human infection because the major risk in these countries arises from high levels of environmental contamination with dog faeces due to high numbers of ownerless stray dogs (Dowling et al., 2000; Harandi et al., 2011). In the case of **Syria**, current prevalence data regarding human infection are not available and detailed epidemiological studies are required from this country. A single report described more than 20 cases of pulmonary CE undergoing surgery per year in a university hospital in Damascus (Darwish, 2006).

In **Iraq**, CE surgery constitutes about 2% of all surgical operations documented in a retrospective study in two main hospitals in the northern city of Arbil. Between 1990 and 1998 the incidence of CE was estimated at $2.0/10^5$ inhabitants (Saeed et al., 2000). In a 20-year period between 1986 and 2006, 763 patients underwent surgery for pulmonary/thoracic CE in a teaching hospital in Baghdad (Shehatha et al., 2009). In Sulaimani province in the north, a total of 98 cases of CE were hospitalized between 2006 and 2011, indicating an incidence of $2/10^5$ inhabitants (Hama et al., 2014).

In **Turkey**, official reports from the Ministry of Health document more than 52,000 patients undergoing CE-related surgery between 1990 and 2005 (approximately based on US studies 3257 patients per year). The mean annual incidence of CE in Turkey has been estimated at 0.8−2.0 per 10^5 population (Altintas, 2008). However, in some regions, higher incidence rates up to 6.4 per 10^5 have been recorded (Gonlugur et al., 2009). Based on hospital records between 2001 and 2005, most of the human CE patients in Turkey have been reported from central Anatolia (38.6%) and Aegean/Mediterranean regions (33.0%) (Dakkak, 2010). In central Anatolia seroprevalences of 2.7% and 0.9% have been recorded in patients in rural areas around Kayseri using ELISA, IFA and Western blotting, respectively (Yazar et al., 2006). A community-based ultrasound survey of Turkish children in the Aegean province of Manisa indicated 0.3% prevalence of CE while 8.9% and 10.1% seroprevalence was observed in the same individuals using ELISA and IHA, respectively (Kilimcioglu et al., 2006). Other ultrasound-based studies in Elazig and Manisa revealed CE in 0.2% and 0.15% of children (Bakal et al., 2012; Ok et al., 2007). In Aydin, a prevalence of 0.47% based on ultrasound was recorded in all age groups (Ertabaklar et al., 2012).

In **Iran**, recent investigations indicate that CE is present in both rural and urban areas across the country. The number of CE surgeries in Iran has been calculated as 1295 cases per year with a mean annual surgical incidence of $1.6/10^5$ inhabitants (Fasihi Harandi et al., 2012). Surgical incidence of CE ranges from $0.61/10^5$ to $2.6/10^5$ in different geographical areas of the country (Rostami Nejad et al., 2007; Tavakoli et al., 2008; Vejdani et al., 2013).

Asymptomatic CE has been investigated in two community-based ultrasonography surveys as well as seroepidemiological studies. In nomadic populations in the south (Saberi-Firouzi et al., 1998), ultrasound results revealed a prevalence of 1.8% while 13.8% of the individuals were seropositive on ELISA. In rural areas of the southeastern province of Kerman, CE was found in 0.2% of 1140 individuals using ultrasonography, while 7.3% of the samples were seropositive by ELISA (Harandi et al., 2011).

Human and animal CE imposes major public health and economic burdens to Middle Eastern societies. The monetary burden of CE has been estimated at 0.01–0.04% of the gross domestic product of several countries. The cost of animal CE has been estimated at US$ 89.2 million in Turkey (Sariozkan and Yalcin, 2009) and US$ 232.3 million for human and animal CE in Iran (Fasihi Harandi et al., 2012).

3.5.4 South Asia: Afghanistan, Pakistan, India, Bhutan, Nepal, Bangladesh, Sri Lanka, Maldives

3.5.4.1 Host assemblages and transmission

Occurrence of *Echinococcus* spp. causing CE has been documented in South Asia in different regions in the past (Eckert et al., 2001; Schantz et al., 1995). For **Afghanistan**, no transmission data are available; however, CE was described in a US Marine after deployment to Afghanistan (Kronmann et al., 2008) and an immigrant from Afghanistan in the US (Carter et al., 2009); this shows that CE is likely transmitted in this area. Moreover, 77/150 dogs from Kabul (73%) were positive for *E. granulosus,* with one dog infected with 152,700 worms (Le Riche et al., 1988). In **Pakistan**, transmission in the sheep-dog assemblage is important and the lack of abattoirs in rural communities and home slaughter of livestock is common, especially on religious occasions. Lack of public awareness concerning CE transmission, poor hygienic conditions and improper disposal of offal support the access of *Echinococcus* cysts to dogs (Latif et al., 2010).

In **India**, transmission is strongly related to cultural, educational, socio-economical and agricultural factors (Traub et al., 2005). Uncontrolled home slaughter, especially for religious events, is common. Free access of dogs to slaughter waste, improper garbage disposal and presence of stray animals (dogs, cattle) have been identified as risk factors for *Echinococcus* transmission (Singh et al., 2014a). Furthermore, at the local abattoir level, the lack of legislation for meat inspection and safe offal disposal contribute to the maintenance of domestic cycles of transmission (Irshadullah et al., 1989). Buffaloes and cattle are generally considered the most significant intermediate hosts for sustaining the life cycle (Pednekar et al., 2009). Moreover, a wide range of susceptible captive and wild animals may be involved in transmission which has so far not been studied in detail. Despite numerous case reports in humans, especially for India, few epidemiological studies have been performed in southern Asia and so far no large regional or national control programs have been initiated (Traub et al., 2005).

In **Nepal**, CE was first described 1973 in buffaloes, goats, sheep and pigs slaughtered in Kathmandu. A later study by the same first author documented 47 human cases of CE in three hospitals between 1985 and 1990 (Joshi et al., 1997). Stray dogs from areas where livestock are slaughtered (Devleesschauwer et al., 2014) play a major role in the transmission, with cattle and buffalos the most important intermediate hosts. In older studies, 13% of owned dogs were fed with butcher's waste or other raw meats/offal, and 20% of 134 households in a community health survey fed their dogs raw meat and offal (Joshi et al., 1997). Therefore, both stray and owned dogs are important in the transmission of CE in Nepal.

Only preliminary data are available from **Bhutan**, where CE has been documented in cattle and yaks. As home slaughtering is not commonly practised in Buddhist culture and the small sheep population is not used for meat production, CE transmission occurs focally and is probably linked to local risk factors such as sheep production in remote areas and scavenging opportunities by stray dogs with access to meat waste from butcher shops and slaughterhouses (Thapa et al., 2017).

No transmission data are available for **Bangladesh**. An old report describes infection in 62.5% of dogs from Bangladesh, with seasonal variation (Islam, 1980). More recently, active transmission of CE appears to be occurring in Bangladesh due to findings from hospitals in Dhaka, between 2002 and 2011 (Karim et al., 2015). CE has also been reported in cattle (Islam, 1982; Islam and Rahman, 1975). In **Sri Lanka** CE has been reported sporadically in the past.

3.5.4.2 Molecular epidemiology

At least five *Echinococcus* genotypes causing CE are present in South Asia in a variety of hosts (Table 11). *E. granulosus* genotypes (G1 and G3) seem to be the predominant genotypes circulating in sheep and buffaloes and are probably of most zoonotic significance; however, G5 and G6 have been detected in humans.

3.5.4.3 Infections in animals

Prevalence studies, mostly in intermediate hosts, from the last 10 years indicate that CE is endemic in most parts of South Asia (Fig. 9 and Table S9 in the Supplementary Material).

In **Pakistan**, CE in animals is well documented in the literature and older published data show prevalence ranging from 5% to 46% (Iqbal et al., 1989; Khan and Haseeb, 1984; Shafiq et al., 2005). A more recent

Table 11 Genotypes of *Echinococcus* spp. causing cystic echinococcosis in South Asia (no data found in the missing countries): *Echinococcus granulosus* (G1−3), *Echinococcus equinus* (G4), *Echinococcus ortleppi* (G5), *Echinococcus intermedius* (G6/7) and *Echinococcus canadensis* (G8, G10)

Country	Human	Canids	Sheep/ Goat	Camel	Pig	Yak	Cattle/ Buffaloes
India	G1, G3, G5, G6[1]	G1[2]	G1[3,4,5] G2[6] G3[3,4]		G3[3,4] G5[4]		G1−3[3,4,5] G5[4,5] G2[6]
Nepal	G1−3[7,8]	G1	G1, G5[8]		G1−3		G1, G5[8]
Bhutan	G1−3[12]	G1−3[12]				G1−3[9]	G1−3, G5[9]
Pakistan	G1[10,11]		G1, G3[10,11]	G1[10,11]			G1, G3[10,11]
Afghanistan	G6[10]						

[1] (Sharma et al., 2013); [2] (Singh et al., 2014b); [3] (Singh, 2011); [4] (Pednekar et al., 2009); [5] (Gudewar et al., 2009); [6] (Bhattacharya et al., 2007); [7] (Devleesschauwer et al., 2014); [8] (Zhang et al., 2000); [9] (Thapa et al., 2017); [10] (Alvarez Rojas et al., 2014); [11] (Latif et al., 2010); [12] Thapa N.K. and Deplazes P., unpublished data.

study in Punjab documents a reduction of the prevalence, with the following values: camels (17.3%; 95% fertile cysts), sheep (7.5%, 86.4% fertile cysts), buffaloes (7.2%; 84.3% fertile cysts), goats (5.5%; 79.1% fertile cysts) and cattle (5.2%; 75.3% fertile cysts) (Latif et al., 2010). Both G1 and G3 were detected in goats, camels and cattle in Punjab (Latif et al., 2010).

In **India**, the prevalence of intestinal *E. granulosus* in ownerless stray dog populations varies from 3.5% in villages to 33% in towns. Prevalence was higher in stray dogs near slaughterhouses compared to stray dogs of other areas. In Kashmir, dogs in seminomadic pastoral communities in hilly areas had a higher prevalence of *E. granulosus* (35%) than that corresponded to stray dogs in urban areas with access to slaughterhouses (11−17%) [for citations see Traub et al. (2005)]. The role of wolves, foxes and jackals as definitive hosts of *E. granulosus* has not been well documented. In India, the prevalence of CE in intermediate hosts varies considerably with age of the animals and region; however, there is a tendency for decreasing prevalence over the last three decades, especially in urban areas (Pednekar et al., 2009; Singh, 2011; Singh et al., 2014a). CE has been diagnosed in livestock (sheep, goats, cattle and buffaloes) throughout the country, and camels in Aligarh (Irshadullah et al., 1989). High prevalence and high rates of fertility of the cysts in cattle and buffaloes are explained by the older age at which the animals are slaughtered and host-adapted strains (G5, G3) (Pednekar et al., 2009). Moreover, a wide range of susceptible captive and free-ranging wildlife such as deer, wild buffaloes and wild boar may serve as intermediate hosts in a wild animal cycle which has not been studied in detail so far. Total annual median economic losses due to CE in India have been estimated to be US$ 212.35 million, of which 89% was related to cattle and buffalo disease (Singh et al., 2014a).

In **Nepal** (Kathmandu), a study in 17 slaughtering sites revealed CE prevalence in 5% of water buffaloes, 3% of goats, 8% of sheep and 7% of pigs, and further studies in buffaloes in the country revealed CE prevalence of 12–26% (Manandhar et al., 2006). Not surprisingly, several studies have identified taeniid eggs in faeces of stray dogs (for example, 17.6%) (Manandhar et al., 2006), and 15% (3/20) of dogs were infected with *E. granulosus* at necropsy (Joshi et al., 1997).

In **Bhutan**, 10/138 (7.2%) of faecal samples collected in the environment from community dogs in highly populated areas around slaughterhouses or butchers contained eggs of *Echinococcus* species causing CE (Thapa et al., 2017). Furthermore, a survey in Bhutan found CE in 9% of 291 cattle, 26% of yaks and 0% of 167 pigs; most of the cysts isolated were sterile (Thapa N.K., personal communication).

In **Bangladesh**, CE in humans has been reported previously throughout the country (Karim et al., 2015). In abattoirs of the Comilla and Brahmon Baria region CE was diagnosed in 30% of 1460 cattle, 9% of 620 buffaloes, 17% of 460 sheep and 36% of 970 goats (Kabir et al., 2010). A survey in 1975–78 on 611 dogs originating from different parts of the country revealed high variations in prevalence, the highest (76%) being recorded in dogs in and around the slaughterhouses (Islam, 1980).

3.5.4.4 Cystic echinococcosis in humans

Cases of CE in **Pakistan** have been reported in the medical literature and retrospective studies of local hospital records and reports. These reports identified over 470 human CE cases in a 10-year period in Karachi and Punjab [see Latif et al. (2010)]. Despite the predominance of G3 in livestock, the two characterized cysts from humans were G1 (Latif et al., 2010).

In **India** numerous reports of unusual or complicated CE cases document the medical importance of CE in the area. A hospital-based study in north India (Khurana et al., 2007; Singh et al., 2014a) estimated the yearly total number of diagnosed cases without surgery to be 17,075 and the total number of diagnosed cases with surgical/interventional procedure to be 5646. Based on a population of around 1.2 billion, an approximate incidence of 1.878 per 10^5 inhabitants can be estimated. Economic annual median losses for CE in humans have been estimated at approximately

US$ 8.75 million (Singh et al., 2014a). Both the health and economic burden of CE are likely underestimates due to underreporting and underdiagnosis of cases. The burden of CE in India has been estimated as approximately 21,000 DALYs (Budke et al., 2006).

In Nepal, several human case reports document the endemicity of CE in the country (Devleesschauwer et al., 2014). In this study, an annual incidence of 145 CE cases was estimated for Nepal with an annual burden of 251 DALYs.

In **Bhutan**, no published data are available. However, hospital records from the Jigme Dorji Wangchuk National referral Hospital in Thimphu confirmed 53 CE cases that underwent surgery between 2006 and 2013. As for other countries, these data likely underestimate the real incidence; in 2013 alone, six cases of CE were confirmed in the same hospital by histopathological records (Pelden, S., personal communication). Based on these data, an approximate minimal incidence of around one CE case per 10^5 inhabitants can be estimated, but further studies are needed.

In **Bangladesh**, CE has been reported from nearly all geographic areas (Karim et al., 2015). A retrospective hospital-based study in Dhaka between 2002 and 2011 revealed 130 patients (70.8% females), all originating from the northern parts of the country and the majority (76.2%) from rural areas (Karim et al., 2015).

3.5.5 East Asia: China, Mongolia, Korea, Japan

3.5.5.1 Molecular epidemiology and parasite transmission

Occurrence of CE has been documented in East Asia in the past (Eckert et al., 2001; Schantz et al., 1995), and a considerable amount of recent information is available from China (see later).

The G1−3, G6, G7 and G10 genotypes have all been found in China and Mongolia (Table 12). *Echinococcus granulosus* (G1−3) is by far the most commonly isolated and widespread genotype and has been found in humans, sheep, yaks, cattle and dogs, and there are single reports from a camel and from a ground squirrel. *Echinococcus intermedius* (G6) has been found in cattle, camels, humans and dogs in Xinjiang; a human case in Sichuan and goats in Qinghai and in wolves in Mongolia. *Echinococcus intermedius* (G7) has been isolated from four human cases in Heilongjiang in the northeast of China. *Echinococcus canadensis* (G10) has also been isolated from human patients in Heilongjiang and in Mongolia. To date there appears to be no reports of *E. equinus* (G4) or *E. ortleppi* (G5) from East Asia.

Table 12 Genotypes of *Echinococcus* spp. causing cystic echinococcosis in East Asia (no data found in the missing countries): *Echinococcus granulosus* (G1−3), *Echinococcus intermedius* (G6/7) and *Echinococcus canadensis* (G8, G10)

Country	Human ([a])	Dog (D) Wolf (W) ([a])	Sheep (S) Goat (G) ([a])	Cattle (C) Yak (Y) Camel (Cm) ([a])
China: Heilongjiang	G1 (6)[1] G7 (4)[1] G10 (1)[2]			
China: Gansu	G1 (1)[3]		S: G1 (12)[3]	
China: Ningxia	G1 (7)[3]		S: G1 (13)[3]	
China: Sichuan	G1 (45)[4,5,6] G3 (2)[4] G6 (1)[6]		S: G1 (4)[3]	Y: G1 (15): G1[3,4,5]
China: Qinghai	G1 (37)[7]	D: G1 (4)[7] D: G1−3 (4)[8]	S: G1 (102)[3,4,5,6,7,9] G: G6 (2)[9]	C: G1 (13)[3,7] Y: G1 (26)[4,9]
China: Xinjiang	G1 (4)[10] G3 (3)[11,12]	D: G6 (3)[12]	S: G1 (17)[10]	C: G1 (7)[10] C: G6 (2)[10] Cm: G1 (1)[10] Cm: G6 (9)[10,11]
Tibet AR			S: G1 (32)[4,5,6]	Y: G1 (1)[4]
Japan	G1[b]			C: G1−3[b,13]
Mongolia	G1 (46), G6/7 (36), G10 (5)[14,15]	D: G1 (5)[6] W: G10 (3), G6/7 (2)[16]		

[1] (Zheng et al., 2014); [2] (Yang et al., 2015); [3] (Yang et al., 2005); [4] (Yan et al., 2013); [5] (Zhong et al., 2014); [6] (Wang et al., 2015b); [7] (Ma et al., 2008); [8] (Boufana et al., 2015a); [9] (Liu et al., 2013); [10] (Zhang et al., 1998); [11] (Ma et al., 2009); [12] (Bart et al., 2006); [13] (Nakamura et al., 2011); [14] (Ito et al., 2014); [15] (Jabbar et al., 2011); [16] (Ito et al., 2013).
[a]Number of cases.
[b]Imported cases.

3.5.5.2 China

3.5.5.2.1 Infections in animals The distribution of CE in intermediate hosts in China is shown in Fig. 9 (see also Table S9 in the Supplementary Material). CE is highly endemic through much of western China, in Inner Mongolia in the north and further northeast as far as Heilongjiang. In northwestern China, endemic provinces include Gansu, Qinghai, Ningxia and Xinjiang. In southwestern and central China, the western part of Sichuan province and the TAR are endemic. These provinces are also coendemic for AE, although at the local level one or other of the diseases may predominate and CE tends to be more widely distributed with a greater number of cases. The Autonomous Province of **Xinjiang** has some of the most comprehensive data for animals. In 2014, 1801 and 834 sheep of 18,374 examined were infected with hepatic and lung cysts, respectively (Nusilaiti and Yan Hao, 2016). Only in the Changjizhou prefecture was the parasite absent in sheep. Other prefectures had prevalences in sheep ranging from 4.4% (liver cysts) and 1.2% (lung cyst) (n = 9544) in Akesu prefecture to 42.4% (liver cysts) and 34% (lung cysts) (n = 887) in Tacheng Prefecture. Hepatic CE was present in 362 of 3380 cattle and lung cysts were present in 253 of 3380 examined. CE in cattle was absent in Urumqi City, Bozhou, Aletai and Changjizhou Prefectures. Other prefectures had prevalences ranging from 3.3% for hepatic cysts (n = 66, with no lung cysts detected) in Hetian Prefecture to 22.8% (liver cysts) and 14.8% (lung cysts) (n = 189) in Kezhou Prefecture. Of 3842 dogs examined, 378 (9.8%) were positive for taeniid eggs and copro-antigen positive for *Echinococcus*. Canine echinococcosis was not found in Tacheng, Bozhou, Aletai and Yili Prefectures and Urumchi city. Elsewhere, prevalences ranged from 1.1% of 880 dogs in Kashi Prefecture to 25% of 757 dogs in Bazhou Prefecture (Nusilaiti and Yan Hao, 2016).

In **Qinghai**, very high prevalences of CE (78% of 136) have been reported in yaks in Jiuzo county (Yu et al., 2008) and a mean of 48% of 5211 yaks from the Haibi, Haixi Mongol and Yushi, Golog Autonomous Tibetan Prefectures (Cai et al., 2012). High prevalences in sheep are also reported from these districts: 83% of 115 in Jiuzi County (Yu et al., 2008) and 46% of 9468 in the various autonomous Tibetan prefectures (Cai et al., 2012). The prevalence in dogs in these districts was approximately 40% of 1078 (Cai et al., 2012; Yu et al., 2008).

In **Gansu,** in the Gannan Tibetan Autonomous Prefecture, 11% (of 113) sheep, 20% (of 634) yaks and 23% (of 74) dogs were infected (Zhao et al., 2009). In Sunan County, 23% (of 502) sheep were infected (Niu and An, 2012).

In western **Sichuan**, 51% (of 429) yaks were infected (He et al., 2000). More recent reports indicate 21% of 315 yaks and 30% of 210 sheep were infected in the Garze Tibetan Autonomous Prefecture (Guo et al., 2012). Studies of dogs include prevalences of 14.5% (n = 302) (Guo et al., 2012) and 11.1% (n = 365) (Hartnack et al., 2013).

In **Ningxia**, CE was found in 0–9% of sheep in three separate studies (Cleary et al., 2014; Ma et al., 2014; Wu, 2015) and Wang et al. (2008) reported in the same area prevalences of 52% in sheep, 3% in goats, 81% in cattle, 24% in pigs and 19% in camels.

In the **TAR**, CE is common in yak, cattle, sheep and goats (reviewed Feng et al., 2015), and G1 was isolated from sheep and yaks (Table 12). In **Inner Mongolia**, prevalences of CE of 15–48% in sheep and 24–35% in camels have been reported (reviewed by Wang et al., 2008).

3.5.5.2.2 Cystic echinococcosis in humans Cases of human CE have been reported from nearly every province in China (Wang et al., 2010; Table S10) (Fig. 10). However, in eastern China, only few cases are reported and these may be the result of internal migration from the more highly endemic regions further west. The disease is notifiable, and official reports from those seeking hospital treatment are useful in showing the geographical extent of the endemic region, but even hospital treated cases suffer from underreporting. Prevalence studies undertaken using imaging techniques (i.e., ultrasound) give a very different impression of the extent and intensity of disease occurrence compared to hospital reports or official data. Many, if not most, community cases go untreated (and unreported) due to remoteness from medical facilities and poverty. Incidence data based on hospital cases report numbers of cases presenting for treatment over a certain time period. In contrast, community studies using imaging techniques give prevalence data (a snapshot of the proportion of the population suffering from the disease at the time of the study). However, prevalence can be related to incidence (when the prevalence is low and the prevalence and population size is stable) by the relationship: prevalence = incidence × duration (Freeman and Hutchison, 1980).

There are a few data on the likely case fatality ratio of CE in the absence of treatment. If it is relatively low, the duration can be assumed to be the residual life expectancy from the time of diagnosis, which in most studies is between 35 and 40 years, giving a residual life expectancy of 42 years using the latest Chinese life table. This gives an opportunity to compare estimated incidence from the community studies to reported incidence data, giving an indication of the degree of underreporting. Using this methodology, incidence in the populations or districts at risk has been estimated whilst reports based on hospital treated cases are reported alongside as incidence (Fig. 10; Table S10). However, even this approach will underestimate the incidence of new cases as there will be some parasite-induced mortality and ultrasound surveillance will not detect subjects who have pulmonary CE.

In both the nationally reported numbers of cases and those reported at regional or prefecture level, there has been a tendency for an increasing numbers of cases over time. For example, the total number of cases of echinococcosis reported in China was 931 in 2004, increasing to over 5800 in 2008 (Wang et al., 2010), and those in Xinjiang increased from less than 400 in 2005 to 1434 in 2013 (Osman et al., 2014). This is likely because China is rapidly improving the medical and public health programmes and widespread routine surveillance has become a feature of the echinococcosis control programmes now being implemented. Surveillance systems are also continuously improving. This has inevitably resulted in increased numbers of cases being both treated and reported. In Fig. 10 and Table S10 (Supplementary Material) incidence data compiled from officially notified data or from hospital records are given alongside prevalence data from mass ultrasound surveillance, which are then converted to an estimate of incidence per 10^5 inhabitants per year. Where possible, the data are only for CE, with AE data removed. For some incidence data, it was specified only as echinococcosis, although these tended to be in districts where CE is much more common than AE, with the exception of western Sichuan. Data are variably reported at the county, prefecture and province levels.

In **Sichuan** province, most cases of CE originate from the Garze Autonomous Prefecture with perhaps 10% coming from the neighbouring Aba Autonomous Prefecture. Both of these districts are on the Tibetan plateau with a total population of just under 2 million. CE is rare in the rest of Sichuan. Garze Autonomous prefecture is also intensely endemic for AE. Compilation of ultrasound surveillance data from a number of large studies indicated that 334 of 10,186 individuals investigated had lesions of CE (3.2%) with 311 having lesions of AE (3.1%). The mean age of participants was 39 years with a residual mean life expectancy of 42 years. Assuming the life expectancy of AE is just 10 years (Torgerson et al., 2008), the estimated incidences of CE and AE are approximately 78 and 305 cases per 10^5 inhabitants, respectively. The National Infectious Diseases Reporting System reported 9127 cases of echinococcosis between 2007 and 2013, or a mean annual incidence of 173 cases per 10^5 (Wei et al., 2014). These data do not differentiate CE and AE, but indicate that the national reporting system may only be reporting 45% of cases, with the remaining either not seeking treatment, or being under reported by the system.

In the **TAR** CE has been reported from four of seven prefectures, although it is likely that CE is endemic across the entire region. The most intensely endemic district seems to be around Lhasa, where hospital records indicated 526 cases of CE between 2007 and 2013, which translates into an annual incidence of 75 per 10^5 inhabitants (Zheng et al., 2014). A community study found nearly 10% of participants with lesions of CE, which is consistent with the large numbers being treated (Feng et al., 2015). Elsewhere in Nagqu Prefecture, the annual incidence of hospital treated cases has been reported at 27 per 10^5 (Gong et al., 2001), whilst in Chandu over 5% of participants in a community study had CE lesions (Feng et al., 2015).

In **Gansu**, ultrasound surveillance, hospital records and reported data indicate that the incidence of CE is between 2 and 10 cases per 10^5 inhabitants per year.

Qinghai appears to be one of the most intensely endemic provinces for CE, with a large number of cases in each prefecture. Officially notified data reported just 363 cases in 2011 (Li et al., 2013b). However, this is not consistent with large ultrasound screening programmes which have consistently found between 1% and 10% of the population infected with CE and would represent an incidence of 5–10 times that officially reported.

In **Xinjiang**, CE cases are reported from every prefecture, although mostly in the north of the province. Prefecture level incidences range from one to two per 10^5 inhabitants per year in Kashgar and Hotim to just under 20 per 10^5 inhabitants in the Bartal Mongol Autonomous Prefecture [data estimated for 2013, based on the overall trend for Xinjiang (Osman et al., 2014)]. For Xinjiang in total, the surgical incidence was reported at 6.5 cases per 10^5 inhabitants for 2013. As part of the echinococcosis control programme, there have been some large scale ultrasound surveillance programmes. In Emin and Habahe Counties (in Techeng and Altay Prefectures), prevalence of CE was under 1% of over 200,000 subjects, representing over half the total population (Yang et al., 2015). This suggests a lower incidence than the prefecture wide incidence officially reported. In contrast, in a number of counties of the Bortala, Bayingolin Mongol, Kazakh, Altay and Techeng (autonomous) Prefectures, ultrasound prevalences were between 1.5% and 6%, which represents an incidence much higher than official data (Feng, 2012).

In **Ningxia**, officially notified data suggest an annual surgical incidence for the province of 5–7 cases per 10^5 inhabitants per year (Li et al., 2013b; Wang et al., 2010). Hospital records suggest that Xiji, Tongxin and Hiayuan Counties have the highest incidence (Yang et al., 2008).

In **Heilongjiang** and **Inner Mongolia**, only province wide data are available. In both provinces, the anual incidence is approximately 0.5–0.7 per 10^5 inhabitants.

Other provinces sporadically report cases of CE but in very small numbers. In 2013, there were just 162 cases reported from provinces outside the core endemic area of western China, representing an anual incidence of 0.01 cases per 10^5 inhabitants (Li et al., 2013b).

3.5.5.3 Mongolia, Korea, Japan

In Mongolia as in many endemic areas in Asia the lack of confirmation of CE and AE cases and underreporting of human cases have to be considered (Tserennadmid and Enkhjargal, 2000). The documentation of echinococcosis cases goes back to the 1950s in Mongolia; for a recent comprehensive review presenting the historical and current situation of echinococcosis in Mongolia, see Ito and Budke (2015). In **Mongolia**, the life cycle of *E. granulosus* (G1) is typically maintained between dogs and livestock due to the traditional nomadic lifestyle, but the epidemiology of the other genotypes, G10 and G6/7, is not well described so far.

Even though **Korea** is not an endemic area for CE, imported cases are probably increasing in light of the expanding economy and the fact that a high number of Koreans travel or work abroad. At present, **Japan** is not considered as an endemic area of CE and no transmission of the parasite has been documented (Guo et al., 2011). Interestingly, for decades, CE has been detected in cattle imported from foreign countries and fattened in Japan.

Molecular data: Analyses of human CE cases in Mongolia revealed the genotypes G1, G6/7 and G10 (Jabbar et al., 2011; Ito et al., 2014). In wolves, G10 and G6/7 have been identified, but no data concerning isolates originating from ruminants are available (Table 12).

3.5.5.3.1 Infections in animals In a small study in **Mongolia**, 5 out of 14 necropsied dogs were infected with *E. granulosus* (G1) in Bulgan Province (Wang et al., 2005). Only wolves have been identified as definitive hosts of *E. canadensis* (G6/7 and G10) (Ito et al., 2013). Few data are available concerning CE in livestock in **Mongolia**. In a recent study covering all provinces, seroprevalence was 3.6% in 590 sheep, 5.9% in 779 cattle and 9.2% in 338 goats using recombinant Antigen B (8/1) (rAgB8/1) (Chinchuluun et al., 2014). Camels are an important livestock species in some regions of Mongolia and have been found to be infected with *E. granulosus* [cited in Ito and Budke (2015)].

In **Japan**, a recent abattoir survey was conducted annually in Miyazaki (southeastern coast of Kyushu, Japan) over a period of 5 years on 9500 imported cattle from Australia. Hydatid cysts (G1−3) were detected in about 1.8% of cattle (Guo et al., 2011). CE has rarely been reported in Japan, and all confirmed CE cases during the past two decades were imported (Nakamura et al., 2011).

3.5.5.3.2 Cystic echinococcosis in humans Some hospital-based reports of human echinococcosis managed mainly by surgeons and a few community-based screening studies document the occurrence of CE in

Mongolia (Ito and Budke, 2015). For example, CE was diagnosed in 18% of surgical cases treated at the First Hospital of Ulaanbaatar in 1993 [Cross, 1995; cited in Ito and Budke (2015)]. To date, the majority of surgical echinococcosis cases have been confirmed to be CE, except for five cases of AE. Several serological community surveys revealed seroprevalences of echinococcosis to be 2.1–11.7% (Ito and Budke, 2015). Despite questionable specificities of the tests used for serology, this relatively high prevalence documents a high endemicity of CE/AE throughout the country, and further studies are needed to estimate the actual burden of CE for Mongolia.

In **Korea**, 33 CE cases have been reported in the literature; these patients included 25 Koreans, 7 Uzbeks, and 1 Mongolian (2 Korean patients with unclear origin of infection, 31 considered as imported) (Choi et al., 2014).

3.5.6 South East Asia: Indonesia, Vietnam, the Philippines, Malaysia, Thailand and the Lao People's Democratic Republic

There is no evidence of transmission cycles that maintain the causative agents of CE in Southeast (SE) Asia, encompassing Indonesia, Vietnam, the Philippines, Malaysia, Thailand and the Lao People's Democratic Republic (Lao PDR) (Craig, 2004; Eckert et al., 2001; McManus, 2010; Schantz et al., 1995). If CE does exist, transmission is infrequent and restricted to wild animal hosts which have yet to be identified. In this respect, the recent report from Vietnam of a locally acquired case of *E. ortleppi* in a captive primate, that must have acquired the infection locally, is of particular interest (Plesker et al., 2009).

3.5.6.1 Infections in animals

Interest in the potential endemicity of *E. granulosus* in SE Asia was raised following a report in 1974 of natural infection in a dog from Sulawesi in **Indonesia** (Carney et al., 1974). However, a subsequent survey of 63 dogs from Sulawesi found no evidence of *Echinococcus* infection. Data on CE in livestock is not available so far. The possibility of indigenous wildlife cycle(s) was strengthened by the report of a locally acquired case of CE in a primate, a red-shanked douc langur (*Pygathrix nemaeus*) in northern Vietnam in 2008 (Plesker et al., 2009). The species was *E. ortleppi* and, although locally acquired, it was unexpected, as the nearest region where *E. ortleppi* has been previously recorded is the Indian subcontinent (Thompson and McManus, 2002). It is not known if a transmission cycle of *E. ortleppi* is autochthonous in northern Vietnam, or whether the parasite was introduced from elsewhere; for example, in introduced cattle. However, there is no evidence that domestic dogs in Vietnam play a role in the transmission of *E. ortleppi*.

3.5.6.2 Cystic echinococcosis in humans

Sporadic cases of human CE, either imported or seemingly locally acquired, have been reported from various countries in SE Asia but there is no information on the epidemiology of these infections (Eckert et al., 2001; Schantz et al., 1995; Wiwanitki, 2004). A serological survey undertaken on 903 inhabitants of Sulawesi did not provide evidence of CE (Palmieri et al., 1984).

3.6 Australia and New Zealand

3.6.1 Host assemblages, transmission and molecular epidemiology

The endemicity of *Echinococcus* in Australia and New Zealand (see Fig. 11) is a relatively recent occurrence that demonstrates the importance of

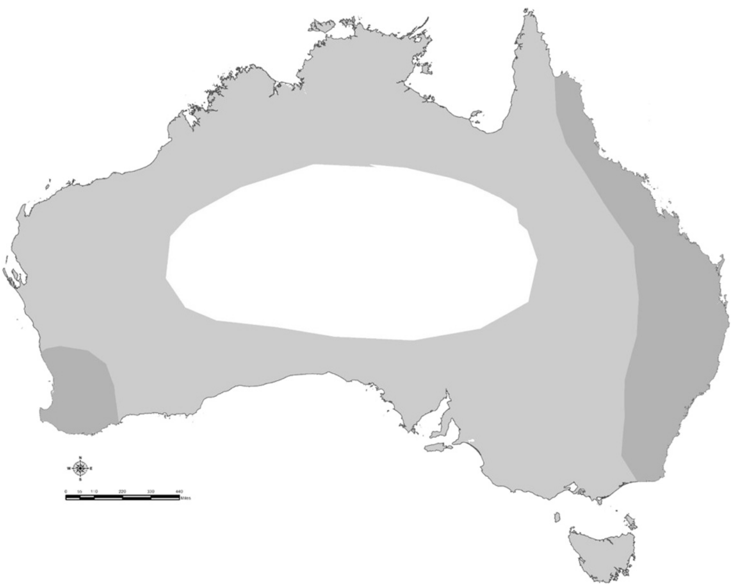

Figure 11 ***Current distribution of Echinococcus spp. causing cystic echinococcosis in domestic intermediate hosts (sheep and cattle) in Australia and in the island state of Tasmania.*** Modified version of the map by (Thompson and Jenkins, 2014) depicting areas of high, low and no transmission of *Echinococcus granulosus* in Australia (dark grey, high transmission; grey, low transmission; white no transmission). For details of the transmission rate in domestic definitive hosts (e.g., dogs) and intermediate hosts (sheep and cattle) in each jurisdiction, see the text.

anthropogenic factors in perpetuating the transmission of the parasite (Thompson, 2013). *Echinococcus* was not present in either country until European settlement when *E. granulosus* was introduced with livestock, principally sheep, by early settlers (Gemmell, 1990). Subsequently, anthropogenic factors were responsible for the transmission of the parasite in a domestic cycle involving sheep and dogs leading to high levels of infection in humans, sheep, and to lesser extent, cattle and dogs, as well as the establishment of a wild animal cycle involving dingoes and macropod marsupials on the mainland of Australia. The control programmes that were instigated were highly successful in both New Zealand and Australia and have been used as models in many other countries where *E. granulosus* is perpetuated in domestic cycles involving dogs and livestock. The historical aspects of establishment, perpetuation and control have been reported in many publications [e.g., Gemmell (1990); Schantz et al. (1995); Beard et al. (2001)] and will not be reiterated here. The current situation in both countries will be summarized.

The Ministry of Agriculture and Forestry declared **New Zealand** provisionally free of CE in 2002 (Anonymous, 2012). It is not clear how long an absence of cases of CE is required before provisional status will change to officially free.

3.6.2 Infections in animals

Fig. 11 reports the current distribution of *E. granulosus* in domestic intermediate hosts (sheep and cattle) in **Australia** and in the island state of Tasmania. Data on the prevalence/incidence of CE in livestock are no longer collected on a routine basis on mainland Australia. *Echinococcus* cysts still occur in sheep on the mainland but prevalence has declined steadily during the last 30 years, and sheep most at risk appear to be those exposed to potential spillover from the wild animal cycle (Jenkins et al., 2014; Thompson and Jenkins, 2014). Recent national surveys in domestic dogs in both urban and rural areas of mainland Australia have demonstrated that the parasite is very uncommon and restricted to rural areas (Palmer et al., 2008; Jenkins et al., 2014). The only routine surveillance of CE undertaken in Australia occurs in Tasmania where provisional elimination of CE was declared in 1996. However, although there are no locally acquired cases of CE in sheep reported, recent reports of *E. granulosus* infections in cattle and dogs suggest transmission is still occurring, albeit at low levels (Jenkins et al., 2014).

A wild animal cycle of transmission is perpetuated on mainland Australia involving dingoes and macropod marsupials. This is confined to eastern and the southwest of Australia (Jenkins and Macpherson, 2003). Because of potential spillover to domestic dogs and sheep, the presence of this cycle will prevent elimination of CE on mainland Australia. The fox, although susceptible to infection, is epidemiologically insignificant in transmission [for details see chapter: Ecology and Life Cycle Patterns of *Echinococcus* Species by Romig et al. (2017)].

3.6.3 Cystic echinococcosis in humans

Notifications of human CE on the mainland of Australia are sporadic and unreliable. New cases continue to be identified but as with the last hospital-based survey (Jenkins and Power, 1996), a significant proportion is in recently arrived immigrants who contracted infection before migrating to Australia (Thompson and Jenkins, 2014). No new human cases have been reported in Tasmania (O'Hern and Cooley, 2013).

3.7 Africa

3.7.1 North Africa: Morocco, Algeria, Tunisia, Libya and Egypt

3.7.1.1 Host assemblages, transmission and molecular epidemiology

For the last two decades, CE has been one of the most important zoonotic diseases affecting North African countries bordering the Mediterranean Sea (Schantz et al., 1995; Ecca et al., 2002; Sadjjadi, 2006; Dakkak, 2010; Hotez et al., 2012; Carmena and Cardona, 2014). The causative agent, *E. granulosus* s.l. has major human health and socioeconomic importance, as well as a significant impact on livestock production (Budke et al., 2006; Torgerson et al., 2014). Annual incidence rates in people usually vary from 5 to 10 cases per 10^5 inhabitants, with minimum and maximum rates of 1 and 25 reported in highly endemic foci, respectively (Torgerson and Macpherson, 2011).

CE is predominantly maintained in these countries by a rural domestic transmission cycle involving dogs as definitive hosts and sheep, cattle, goats, camels, dromedaries and donkeys as intermediate hosts. Clandestine and home-slaughtering (e.g., during weddings and religious feasts) contribute to a secondary suburban and/or urban domestic cycle involving owned and stray dogs that have access to offal of intermediate hosts (Besbes et al., 2003). Wild animals, i.e., golden wolves (*Canis anthus*) as definitive host and wild boars (*S. scrofa*) and antelope (*Addax nasomaculatus*) as intermediate hosts were also infected in the northwest and central regions of Tunisia (Lahmar et al., 2009a). Red fox (*Vulpes v. atlantica*) is a less frequent wild definitive host for *E. granulosus* G1 in Tunisia, with only two cases reported (Lahmar et al., 2009a). The wild animal cycle re-enforces the rural domestic cycle through canid predation of domestic herbivores or environmental contamination of *E. granulosus* eggs in areas inhabited by livestock.

The persistence and spread of CE in **Tunisia** is closely associated with the following epidemiological factors: (1) contact between humans/livestock and infected dogs; (2) large dog to human population ratios (4:1, 6:1 and 12:1 in rural, suburban and urban areas, respectively); (3) transhumant livestock migration to northern areas in spring/summer with guard dogs predominantly fed livestock offal; (4) routine home slaughtering during social or religious observances; (5) inadequate hygiene in the rural areas and (6) insufficient abattoir equipment to destroy infected offal. Similar factors are present in **Morocco**, where the high prevalence of CE in humans and animals is influenced by (1) an abundance of dogs (1.8 dogs per household); (2) poor knowledge of CE (50% of people are aware of the disease) and (3) inadequate abattoir infrastructure and hygiene (El Berbri et al., 2015a).

The main drivers for CE transmission in **Morocco** (Kachani et al., 2003; Azlaf et al., 2007; Dakkak, 2010) have identified the high number of stray dogs and close proximity of un-dewormed owned dogs living with humans and livestock; behaviours and practices of the rural population; poor human hygiene practice; the infected environment (soil, food, drinking water) with *Echinococcus* eggs; animal slaughtering in fields or at home for family and religious occasions; abattoirs lacking appropriate facilities and hygiene to which free-roaming dogs have easily access. In **Algeria**, CE is primarily maintained by a synanthropic cycle involving domestic dogs and livestock (sheep and cattle), where dogs are fed offal discarded from animals slaughtered for human consumption (Kouidri et al., 2012).

The same host assemblage is observed in **Libya**, where livestock are slaughtered in a clandestine and uncontrolled manner, providing dogs with a ready source of infection (Buishi et al., 2005). In this country, *Echinococcus* spp. are transmitted primarily through a rural pastoralist life cycle between dogs and ruminants (sheep, camels, cattle and goats) (Elmajdoub and Rahman, 2015); no reports are found on the wildlife cycle. In **Egypt**, CE is a disease of pastoral communities due to the abundance of stray dogs and common home slaughter/street practices. Various livestock are major reservoirs for the human infection (Omar et al., 2013).

So far, despite attempts to control slaughtering practices and to promulgate health education, no regional or national control programs have been established in North Africa.

3.7.1.2 Molecular epidemiology

Table 13 summarizes *Echinococcus* genotypes identified in North Africa. In **Tunisia**, three species and four genotypes − *E. granulosus* (G1 and G3), *E. equinus* (G4) and *E. intermedius* (G6) − have been identified. The most prevalent genotype (G1) occurs in a wide range of domestic livestock species as well as in humans; whereas the buffalo strain (G3) occurs only in cattle and humans. Mixed infections, involving more than one genotype in a single host, have been observed in people (G1, G6) (Oudni-M'rad et al., 2016) and donkeys (G1, G4). Other hosts include dromedaries in southern Tunisia, infected by G1 and G6, and wild canids (golden wolf and red fox), infected by G1. In **Morocco**, sheep and cattle are infected by G1, G2 and G3; G1 also infects humans, goats, camels and equids. In **Libya**, the most common genotype, G1 occurs in humans, sheep, cattle, camels and dogs, whereas G6 occurs in cattle and camels. Three genotypes occur in **Algeria**: G1 (prominent in humans, sheep, camels and cattle/buffalo), G2 (humans, sheep and camels), and G6 (camels). In **Egyp**t, five genotypes are reported: G1 (camels, sheep), G6 (buffalo, camels, sheep), G4 (equids), G5 (camels) and G6/G7 (pigs). People in Egypt have been infected by three genotypes (G1, G6 and G7). The molecular epidemiology of *Echinococcus* spp. and genotypes in wildlife is poorly documented.

3.7.1.3 Infections in animals

The current distribution of *E. granulosus* in domestic intermediate hosts (sheep, cattle, goats and camels) in Africa is shown in Fig. 12.

In **Tunisia**, *Echinococcus* infections are widespread in dogs (prevalence above 20%) and domestic ruminants, with prevalence levels of 16.4; 8.56; 2.8; 5.9; 8.4% reported in sheep, cattle, goats, camels and equines, respectively [Fig. 12 and Table S11 and S12 of the Supplementary Material] (Lahmar et al., 2013, 2014b). The rural domestic cycle is primarily maintained by sheep and cattle intermediate hosts in north and central regions and by camels in the south. Ultrasound screening of 1039 sheep in Zaghouan (northeastern region) reported a CE prevalence of 40.4% (Lahmar et al., 2007); other surveys have demonstrated a direct correlation of CE infection to age with prevalence ranging from 9.5% in sheep less than one year of age to 96.3% in sheep greater than 5 years of age (Lahmar et al., 1999). In Benguerden (southwestern region), 10.1% of camels were observed with CE (Lahmar et al., 2004). Among wild hosts, 9.7% of golden wolves (Lahmar et al., 2014a) and 18.8% of wild boars (Lahmar S, unpublished) were found infected.

Table 13 Genotypes of *Echinococcus* spp. causing cystic echinococcosis in North Africa (no data found in the missing countries): *Echinococcus granulosus* (G1–3), *Echinococcus equinus* (G4), *Echinococcus ortleppi* (G5), *Echinococcus intermedius* (G6/7)

Country	Human	Dog (D), Wild canids (Wc)	Sheep	Camel	Cattle/Buffalo	Equine	Goat (G), Antelope (A)	Swine (S), Wild boar (Wb)
Morocco	G1[1]		G1[3] G2[3] G3[3]	G1[2]	G1[2,3] G2[3] G3[3]	G1[2]	G: G1[2]	
Algeria	G1[1,4,5] G2[5]		G1[1,4,5,6] G2[5]	G1[5] G2[5] G6[1,4,5]	G1[1,4,5,6]			
Tunisia	G1[6,7,8,9,10,11,12] G3[9] G6[12]	D: G1[8,14,18,28] Wc: G1[8,14,18,28]	G1[6,7,9,13,14]	G1[14,15] G6[7,14]	G1[6,7,9,13,14]	G1[14,16] G4[14,16]	G: G1[14,16] A: G1[17]	Wb: G1[14]
Libya	G1[19,20]	D: G1[18]	G1[18,19]	G1[19] G6[20]	G1[19,20] G6[20]			
Egypt	G1[21,22] G6[22,25,26,27] G7[27]		G1[4,21,23] G6[23]	G1[21,23] G5[23] G6[22,23,25,27]	G6[23]	G4[24]		S: G6[22,27] S: G7[27]

[1] (Bardonnet et al., 2003); [2] (Azlaf, 2007); [3] (El Berbri et al., 2015b); [4] (Bart et al., 2004); [5] (Maillard et al., 2007); [6] (Boubaker et al., 2013); [7] (M'Rad et al., 2005); [8] (Lahmar et al., 2009b); [9] (M'Rad et al., 2010); [10] (M'Rad et al., 2012); [11] (Schneider et al., 2010); [12] (Oudni-M'rad et al., 2016); [13] (Farjallah et al., 2007); [14] (Boufana et al., 2014); [15] (Lahmar et al., 2004); [16] (Lahmar et al., 2014b); [17] (Boufana et al., 2015c); [18] (Boufana et al., 2015a); [19] (Tashani et al., 2002); [20] (Abushhewa et al., 2010); [21] (Abd El Baki et al., 2009); [22] (Abdel Aaty et al., 2012); [23] (Amer et al., 2015); [24] (Aboelhadid et al., 2013); [25] (Khalifa et al., 2014); [26] (Alvarez Rojas et al., 2014); [27] (Alam-Eldin et al., 2015); [28] (Lahmar et al., 2009a).

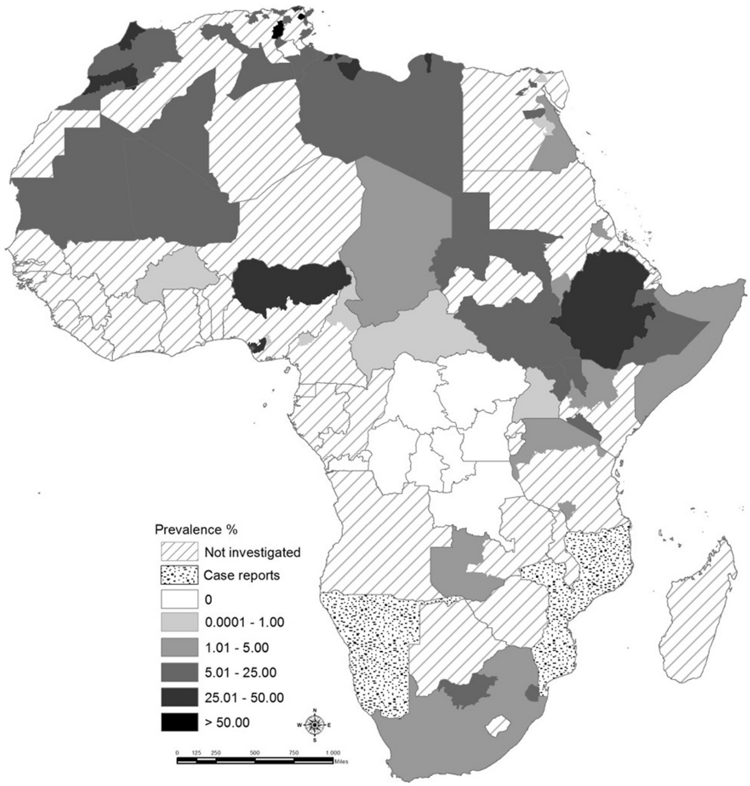

Figure 12 ***Current distribution of Echinococcus spp. causing cystic echinococcosis in domestic intermediate hosts (sheep, cattle, goats and camels) in Africa.*** Areas with case reports of CE in wild intermediate hosts are approximately given if data of domestic intermediate hosts was missing. The detailed information (prevalence data in each jurisdiction) is listed in Tables S11 and S12 of the Supplementary Material.

In **Morocco**, *E. granulosus* is highly endemic in dogs, with prevalence levels as high as 48.4%, 55.4%, and 58.8% in south-central, southern and northwestern areas, respectively. Cattle also experience high levels of CE: 37.6% and 42.9% in northwestern regions (in Loukkos and Sidi Kacem, respectively) (Azlaf and Dakkak, 2006; El Berbri et al., 2015b) and 48.7% in south-central regions (Middle Atlas) (Azlaf and Dakkak, 2006). Sheep are at highest risk of infection in the northwestern areas (Sidi Kacem and Loukkos) (10.9% and 31.65%, respectively) (El Berbri et al., 2015b; Azlaf and Dakkak, 2006). Although cysts from cattle and sheep have similar fertility levels (54.9% and 50.3%, respectively), sheep represent the main source of infection to dogs because they are most commonly slaughtered in the abattoirs of all provinces in Morocco due to their greater population; while cattle are generally slaughtered when they are older than sheep and goats. Control measures targeting CE in both sheep and cattle are appropriate in this context (El Berbri et al., 2015b). A lower disease burden is reported for goats (1.88%), equids (17.8%) in central regions and camels (12%) in the south (Azlaf and Dakkak, 2006).

In **Algeria**, the prevalence of *E. granulosus* in dogs ranges from 15.5% in Batna to 42% in Constantine (Bentounsi et al., 2009). In cattle, CE is considered highly endemic in Tebessa (89.7%), Djelfa (70%) and Tiaret (25.6%), with high levels of cyst fertility reported (Hamrat et al., 2011; Kouidri et al., 2012; Ouchène et al., 2014). Seventy-eight percent of sheep are infected in Tebessa; however, this appears to be an anomaly as sheep experience lower levels of infection than cattle in other regions. This might be explained by differences in age of the slaughtered sheep (young animals) compared to cattle (adult animals). Sheep play an important role in perpetuating and disseminating of CE due to their high infection rates and fertility, while goats do not seem to be very important in transmission dynamics as the majority of cysts were sterile (Kouidri et al., 2013). Camels are also important intermediate hosts, as indicated by the high prevalence (~25%) and fertility (100%) of CE caused by *E. intermedius* (G6) in Ouargla (Bardonnet et al., 2003) and Adrar. Equines (Bardonnet et al., 2003) and wild boars (Ouchène et al., 2014) contribute to parasite transmission in the domestic and wild animal cycles. Domestic dogs are the only known definitive host for *Echinococcus* spp. in Algeria. Golden wolves are a possible wild host, as they have been observed with *E. granulosus* cestodes elsewhere, but the only postmortem study of wild canids did not report the presence of *Echinococcus* species (Jore d'Arces, 1953).

In northwest **Libya** (Tripoli), the infection rate of *Echinococcus* spp. in necropsied stray dogs has been reported as high as 60% (Awan et al., 1990); however, a more recent postmortem study reported prevalences between 26% and 35% (Buishi et al., 2005). Information on canine echinococcosis is not available for other parts of the country. Prevalence of CE in livestock is reported for sheep (55.9%), cattle (28.57%) and goats (40%) (Ekhnefer, 2014), as well as camels (>35%) in eastern (Al-Jabal Al-Akhdar) and northeastern (Benghazi) regions (Ibrahem and Craig, 1998). Livestock CE is lower in north–central regions (Sirte) (Kassem et al., 2013). Hydatid cysts collected from sheep and camels demonstrate high fertility rates (>80%), suggesting that these intermediate hosts are important to the maintenance of *Echinococcus* (Elmajdoub and Rahman, 2015). No information on CE in wild animal hosts in Libya is available.

In **Egypt**, *E. granulosus* is common in stray dogs with prevalence levels of 5% in Dakahlia, 16% in Cairo and 1.8% in Giza (El Shazly et al., 2007; Mazyad et al., 2007; Haridy et al., 2008). Recent studies report a CE prevalence of 18.9% in camels, 12.7% in cattle, 13% in goats, 14.1% in equines and 7.8% in sheep (El-Madawy et al., 2011; Omar et al., 2013; Mahdy et al., 2014). Pigs and buffaloes are less likely to be infected than other intermediate hosts; however, prevalences of 4.46% and 1.4%, respectively, have been reported (Hamdy et al., 1980; Yassien et al., 2013). Fertility of G1 cysts is highest in sheep (72.7%) and camels (79.2%) (El-Madawy et al., 2011; Mahdy et al., 2014).

3.7.1.4 Cystic echinococcosis in humans

Incidence rates of CE are given in Fig. 13 (see also Table S13 of the Supplementary Material). Despite a decrease in mean annual incidence (surgical rate) from 15 to 12.6 cases per 10^5 inhabitants between 1985 and 2005, **Tunisia** remains the highest endemic North African country (Chahed et al., 2015). Annual losses associated with CE in people and animals are estimated at US$ 19 million for this nation (Majorowski et al., 2005). Northwestern and west-central governorates experience the highest burden of CE, which exacerbates issues related to poverty.

CE is a significant public health problem in **Morocco** where a total of 1700 surgical cases of human CE are treated (5.2 cases per 10^5 inhabitants) in the whole country (Budke et al., 2006; El Berbri et al., 2015b). Surgeries are repeated in 3% of cases and a mortality of 3% is reported. Expenses due to CE surgery are estimated to a total cost of US$ 2,550,000.00 (Herrador et al., 2016).

The incidence of human CE in **Algeria** did not change from 1997 to 2008 with approximately 2.1 surgical cases per 10^5 inhabitants, corresponding to 700 cases recorded (Institut National de la Santé Publique Algérien. Relevé épidémiologique annuelle vol. XIII, 2008). The minimum cost for surgical intervention is of US$ 18,200 per case corresponding to a total annual cost of US$ 127,400 (Hamrat et al., 2011). Hydatid disease continues to be a public health concern in Algeria.

Human CE is considered one of the most important parasitic infections in **Libya**. Prevalence ranges from 1.7% in the north (Shambesh et al., 1999) to 9% in the northwest (Nalut) (Mohamed et al., 2014). The highest levels occur in the northeast (Benghazi), where rural residents are disproportionally

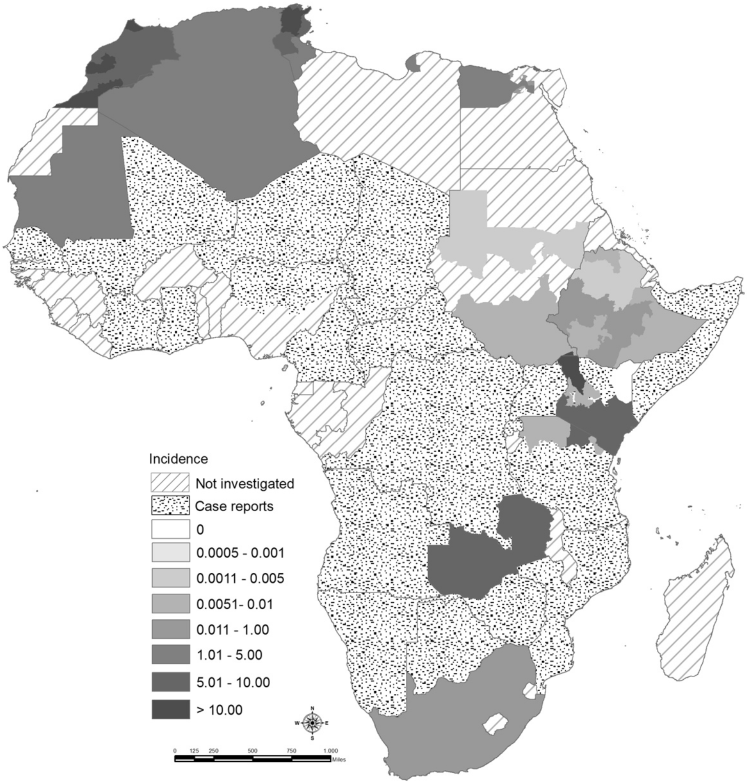

Figure 13 ***Current incidence of human cystic echinococcosis in Africa.*** The detailed information (incidence data in each jurisdiction) is listed in Table S13 of the Supplementary Material. Further prevalence data based on ultrasound surveys in different ethnic groups in eastern Africa are reported in Table 15.

affected compared to their urban counterparts (53.5% versus 46.5%, respectively) (El-Gidaafi and Kassem, 2013). Economic losses due the CE in human and animal populations are not available.

In **Egypt**, human CE is endemic, but the prevalence is low. The annual incidence rate of surgical intervention ranges from 0.05 to 2.6 cases per 10^5 persons in Cairo and Matrouh, respectively. Surveillance for CE using ultrasound and serology recorded 44 new human CE cases per year during 1997–99 with cases occurring in Alexandria, Cairo, Giza, Nile Delta and North Sinaï, Matrouh (Kandeel et al., 2004). Egypt is surrounded by countries where CE is endemic and highly prevalent, suggesting CE could increase in Egypt if current control measures were relaxed. The socioeconomic impact of CE in Egypt has not been estimated.

3.7.2 Sub-Saharan Africa

3.7.2.1 Introduction and molecular epidemiology

Compared to other continents, sub-Saharan Africa is noted for the largest diversity of *Echinococcus* spp. and genotypes causing CE (Table 14). *Echinococcus granulosus* s.s. is widespread except for the arid northern regions (Sahara and Sahel zones) both in domestic and wild animals [for details on the ecology of species occurring in this endemic area are presented in chapter 'Ecology and Life Cycle Patterns of *Echinococcus* Species' by Romig et al. (2017)]. Areas of high prevalence in animals (Fig. 12) (Tables S11 and S12) usually correlate with high incidence of human CE (Fig. 13) (Table S13 in the Supplementary Material). *Echinococcus felidis* is widespread in eastern and southern Africa, but may be restricted to a wildlife cycle between lions, hyenas and warthogs; to date, there is no indication of any involvement of domestic animals or humans. *Echinococcus equinus* is known from a recently recognized wildlife cycle involving lions, wild canids and zebras, which is probably widespread in southern Africa, but may be absent elsewhere; no infection of domestic animals have been reported so far, and no human cases are known worldwide. *Echinococcus ortleppi* is widespread (from Sudan to South Africa), only seems to be frequent in some countries of southern Africa, where traditional cattle pastoralism is practised; only one human case (from South Africa) has ever been found. *Echinococcus intermedius* (G6/7, pig and camel strain) is dominant in the arid North (Mauritania, Sudan, and probably the countries between including the northern regions of West African countries like Ghana or Nigeria), where transmission appears to be based on camels. However, the camel strain G6 is also found outside the camel raising regions (from southern Kenya to South Africa), where goats may be important for the life cycle, and where the involvement of wildlife is also known.

3.7.2.2 Northern arid zone: Mauritania to Sudan

3.7.2.2.1 Host assemblages and transmission Except for Sudan [where research on CE dates back to the 1950s (Omer et al., 2011)] and Mauritania, data from this vast region are restricted to few reports on human cases in Mali, Niger and Chad and – mostly older – dog and livestock infection data from Mali and Chad. Data from wild carnivores are limited; only one study documents *Echinococcus* infections in African golden wolves (*C. anthus*) (Troncy and Graber, 1969). CE seems to be frequent in camels, but only moderately frequent to rare in other livestock species, while human cases are widespread at moderate to low numbers [see Supplementary

Table 14 Genotypes of *Echinococcus* spp. causing cystic echinococcosis in sub-Saharan Africa: *Echinococcus granulosus* (G1–3), *Echinococcus equinus* (G4), *Echinococcus ortleppi* (G5), *Echinococcus intermedius* (G6/7) and *Echinococcus felidis* (Ef)

Country	Human	Dog (D), Wild carnivores (Wc)	Sheep	Camel	Cattle	Pig (P), Warthog (Wa)	Goat	Wild ruminants (Wr), Wild equines (We)
Mauritania	G6[1,2]			G6[1,2]	G6[1]			
Mali		D: G6[26]						
Ghana	G6[23]							
Sudan	G6[4]		G6[3,4,5]	G5[6] G6[3,4,5]	G5[4,25] G6[3,4,5]		G6[4]	
South Sudan	G1–3[14] G6[4]		G6[4]		G5[3,4] G6/7[4]		G6/7[4]	
Ethiopia			G1–3[1,9]	G1–3[8,9] G6/7[8,9]	G1–3[1,7,8,9] G5[7,8] G6/7[7,9]	P: G1[8] P: G5[8]	G1[8] G6/7[8]	
Somalia				G6[10]				
Kenya	G1–3[3,11,12,13] G6[3,12,13]	D: G1[11] Wc: G1–3[16] Wc: Ef[16]	G1–3[3,11,12,15,17] G5[17]	G1–3[3,11,12,17] G6/7[3,11,12,17]	G1–3[3,11,12,15,17] G5[15,17] G6/7[3,11,12,17]	P: G1[3] P: G5[3] P: G6[3]	G1–3[3,11,12,15,17] G5[17] G6/7[3,11,12,15,17]	Wr: G1–3[16]
Uganda		Wc: Ef[12]				Wa: G1[12] Wa: Ef[12]		
Zambia					G5[18]			
Namibia		Wc: G1–3[21] Wc: G4[19,21] D: G6/7[21] D: Ef[20]			G5[20]	Wa: Ef[21]		Wr: G6/7[21] We: G4[19] We: G5[20]
South Africa	G1–3[24] G5[24] G6/7[24]	Wc: Ef[21,22]						

[1] (Maillard et al., 2007); [2] (Maillard et al., 2009); [3] (Dinkel et al., 2004); [4] (Omer et al., 2010); [5] (Ibrahim et al., 2011); [6] (Ahmed et al., 2013); [7] (Romig et al., 2011); [8] (Tigre et al., 2016); [9] (Hailemariam et al., 2012); [10] (Bowles et al., 1992); [11] (Wachira et al., 1993); [12] (Huttner et al., 2009); [13] (Casulli et al., 2010b); [14] (Romig T., personal communication); [15] (Addy et al., 2012); [16] (Kagendo et al., 2014); [17] (Mbaya et al., 2014); [18] (Banda, personal communication); [19] (Wassermann et al., 2015); [20] (Obwaller et al., 2004); [21] (Aschenborn J., personal communication); [22] (Hüttner et al., 2008); [23] (Schneider et al., 2010); [24] (Mogoye et al., 2013); [25] (Omer R.A., personal communication); [26] (Mauti et al., 2016).

Material Table S11 (cattle, sheep and goats), Table S12 (camels)]. The camel strain (G6) appears to be the dominating CE agent in the entire region, although comprehensive molecular surveys have only been done in Sudan so far (Kamal et al., 2011; Omer et al., 2010). The limited number of human cases in this region (compared to eastern Africa, for example) has been hypothetically linked to a lower infectivity or pathogenicity of that genotype for humans, compared to the genotypes of *E. granulosus* which may be absent or rare in this region.

3.7.2.2.2 Infections in animals In **Mauritania** (Nouakchott), *Echinococcus* was diagnosed in 14% of 120 dogs (Salem et al., 2011). In a recent study in **Mali** (Bamako) 1 of 118 dogs was infected with the camel strain G6 (Mauti et al., 2016). In the central region of **Chad** (Troncy and Graber, 1969), 3.7% of 117 dogs were found positive for *Echinococcus* infections. Two studies documented prevalences of 3% (33 dogs) and 51% (49 dogs) in central **Sudan** (El-Badawi et al., 1979; Saad and Magzoub, 1986).

Prevalence data (of uncharacterized cysts) in Mauritania are high in camels (30.1%), but lower in cattle (5.5%) and sheep (6.5%), based on an unspecified but apparently large sample of slaughtered animals (Salem et al., 2011). This is closely similar to data from Chad, Sudan and the Turkana region of Kenya (Tables S11 and S12). A limited number of isolates from Mauritania, Mali and the overwhelming majority of a large sample from Sudan (98.7% of 532 cysts) were characterized as camel strain G6 (Table 14). The high prevalence in camels might indicate a higher susceptibility of this animal for the prevailing parasite taxon, but data have to be interpreted with care since camels are usually slaughtered at a far older age than other livestock. In cattle-raising areas of eastern Sudan, the White Nile region and South Darfur (Sudan), *E. ortleppi* seems to be of sporadic occurrence in cattle (Omer et al., 2010; Omer R.A., personal communication). In an older survey of wild herbivores in Chad (Graber et al., 1969), in 1 of 14 investigated warthogs (*Phacochoerus africanus*) and 1 of 9 scimitar-horned oryx antelopes (*Oryx dammah*) (now extinct in the wild) CE was diagnosed, but in the same study, 8 elephants (*Loxodonta africana*), 18 lelwel hartebeests (*Alcelaphus lelwel*), 7 korrigum (*Damaliscus korrigum*), 2 common duiker (*Sylvicapra grimmia*), 3 oribi (*Ourebia ourebi*), 4 bohor reedbucks (*Redunca redunca*), 7 kobs (*Kobus kob*), 14 waterbucks (*Kobus ellipsiprymnus defassa*), 36 dorcas gazelles (*Gazella dorcas*), 17 red-fronted gazelles (*Eudorcas rufifrons*), 9 dama gazelles (*Nanger dama*), 9 roan antelopes (*Hippotragus *equinus*), 1 addax (*A. nasomaculatus*), 2 greater kudu (*Strepsiceros cottoni*), and 4 African buffaloes (*Syncerus caffer*) were negative (Table S14C).

3.7.2.2.3 Cystic echinococcosis in humans For **Mauritania**, the surgical incidence was estimated at $1.6/10^5$ inhabitants with indications for a possible increase in recent years (Salem et al., 2011). All genotyped cysts from patients belonged to G6 (Bardonnet et al., 2002). The same is true for three patients in **Sudan**, who originated from the Nuba mountains, Darfur and Khartoum, respectively (Omer et al., 2010). Three ultrasound surveys for human CE have been done in the region, all in Sudan. In Tamboul area of central Sudan, 1 of 300 rural residents (0.33%) was infected (Elmahdi et al., 2004), while in the same area a larger study covering 1055 people resulted in a prevalence of 1.04%. The third survey was done in the Nuba mountains, resulting in 0.32% prevalence among 2182 people (Ahmed et al., 2010). The data from Tamboul area might not be representative for a wider region, since the study area serves as a camel slaughter place, where dogs are known to have extremely high rates of infection (Elmahdi, personal communication). From other countries in the arid zone south of the Sahara, 28 CE patients have been identified from rural areas of **Niger** (Develoux et al., 1991), a total of 12 cases are reported from **Mali** during a 40-year period (Carayon and Robert, 1962; Yena et al., 2002), and there are three published cases from Chad (Sirol and Lefevre, 1971).

3.7.2.3 East Africa: South Sudan, Ethiopia, Eritrea, Somalia, Uganda, Kenya

Host assemblages, transmission and molecular epidemiology: Data on CE in East Africa date back to the 1960s, but most research activities started in the early 1980s. The first surveys centred on the Turkana and Maasai regions of Kenya and Tanzania, which were noted for extremely high incidences of human CE. Today we recognize a hyperendemic region with locally >5% prevalence of human CE that covers northwestern Kenya (Turkana), northeastern Uganda, the southeastern part of South Sudan and adjacent areas of southwestern Ethiopia. A second focus exists in Maasailand at the border of Kenya and Tanzania. All highly endemic areas are inhabited by traditional pastoralists of various ethnic groups that live in contact with large numbers of dogs. However, these hyperendemic foci, although receiving most research attention, are not representative for all of eastern Africa, as CE in humans and/or livestock is apparently far less prevalent, e.g., in central and northeastern Kenya or Somalia. Despite intense research in some foci (see Table S13 in the Supplementary Material), large parts of eastern Africa are practically devoid of CE data, e.g., Rwanda, Burundi and Tanzania south of the Maasai area.

Echinococcus granulosus (G1−3) is the most frequent cause of CE in this region (Table 14), mainly transmitted in a sheep−dog cycle. The camel strain G6 is also widespread, particularly in the more arid parts of northern Kenya and eastern Ethiopia where it affects camels at high prevalences. *Echinococcus ortleppi* is widespread across eastern Africa, but occurs only sporadically in cattle, pigs and goats. *Echinococcus felidis*, as a wildlife parasite, is widespread at least in conservation areas of Kenya and Uganda, apparently without impact on coexisting livestock and humans.

3.7.2.3.1 Infections in animals In sheep, CE is highly prevalent throughout **Ethiopia**, but only moderately frequent in **Kenya** (see Table S11 in the Supplementary Material). *Echinococcus granulosus* is responsible for the majority of infection in sheep in Kenya, and all fertile cysts of sheep in Maasailand (prevalence 16.5%) belonged to this parasite (Addy et al., 2012; Romig et al., 2011). This is probably also true for Ethiopia, although few Ethiopian sheep samples were ever characterized (Hailemariam et al., 2012; Maillard et al., 2007). The spatial heterogeneity of CE prevalence in sheep is therefore difficult to explain and might be linked to environmental factors, as prevalence in small stock of the semiarid Turkana area of Kenya is lower than in the climatically much more favourable Maasailand (Table S11). Sheep sampled in the northern and central parts of **South Sudan** as well as in **Somalia** were rarely infected, and only infertile cysts of *E. intermedius* G6/7 were found; possibly, *E. granulosus* does not occur in the region (Macchioni et al., 1984; Omer et al., 2010). In goats, CE prevalence is generally lower, and the majority of fertile cysts in **Kenya** and **Ethiopia** belonged to *E. intermedius* G6/7 or to *E. ortleppi*. Goats may therefore be a key species to maintain the 'camel strain' in Africa, south of the camel husbandry region, and may be an important additional host for the 'cattle strain'. Prevalence in cattle is highly variable across eastern Africa, peaking at values around 50% in Maasailand and some regions of Ethiopia (Table S11). Cattle are most frequently infected with *E. granulosus* (G1−3), but the majority of cysts are nonfertile. However, fertility rate of *E. granulosus* in cattle seems to differ between regions (Addy et al., 2012; Tigre et al., 2016), which may be related to variants of the parasite, breeds of cattle or age of animals at slaughter [chapter: Ecology and Life Cycle Patterns of *Echinococcus* Species by Romig et al. (2017)]. In contrast, *E. ortleppi* and the camel strain G6 occur far less frequently in cattle, but where they are present, cysts show high fertility (Mbaya et al., 2014; Omer et al., 2010). The sporadic presence of the cattle-adapted *E. ortleppi* in most areas has been tentatively explained by the fact that cattle are often sold alive and slaughtered at abattoirs far from their origin, so that the local dog populations have restricted access to cattle offal (Addy et al., 2012). CE prevalence in camels is extremely high in northwestern Kenya, much less so in northeastern Kenya, eastern Ethiopia and Somalia (Table S12), for reasons unknown. In Kenya, the majority of camel cysts belonged to G6/7, but fertile cysts of *E. granulosus* (G1−3) were also present at lower numbers (Dinkel et al., 2004; Mbaya et al., 2014); the reverse situation was found in eastern Ethiopia (Tigre et al., 2016). There are no prevalence data for pigs in eastern Africa, except for two older studies with negative results from Ethiopia (Table S11). Cysts obtained by opportunistic sampling in western Kenya and Ethiopia belonged to *E. granulosus* (G1-3), *E. ortleppi* and *E. intermedius* G6/7 (Dinkel et al., 2004; Tigre et al., 2016).

A large number of **wild animal** species have been recorded as definitive or intermediate hosts for *Echinococcus* spp. in eastern Africa (Tables S14B and C). Without molecular identification of the parasites it is difficult to appreciate which of these records represent spill overs from domestic lifecycles in areas where livestock and wildlife coexist (e.g., southern Kenya), and which represent transmission systems based on wildlife species. To date, it is clear that *E. felidis* (the former 'lion strain') occurs in most larger national parks and game reserves of **Uganda** and **Kenya** (Queen Elizabeth, Maasai Mara, Nairobi, Samburu, Meru, Tsavo). Lions are frequently infected, although prevalence estimates were only attempted for Queen Elizabeth National Park in Uganda (72%) (Table S14B wild animals). Due to uncertainties in the methodology only a fraction of taeniid eggs from environmental faecal samples could be characterized to species level. In these areas spotted hyenas also seem to be secondary definitive hosts for *E. felidis* (Kagendo et al., 2014). Cysts of this parasite have only been identified from a warthog in Uganda (Huttner et al., 2009). The host range of the parasite may be restricted to wildlife, as no *E. felidis* was identified among 394 cysts of human, sheep, goat, cattle and camel origin from Kenya (Huttner et al., 2009). In contrast, *E. granulosus* (G1−3) is a frequent parasite of livestock and humans in eastern Africa and was also found to be widespread in the lion and spotted hyena populations of four conservation areas of Kenya (Kagendo et al., 2014). Whether this is a spill over from domestic animals is yet unclear. To date, this parasite has only been confirmed in two species of wild herbivores as potential intermediate hosts: cysts were found in 4 of 353 surveyed wildebeest from the Maasai Mara conservation area in southwestern Kenya and in one warthog in Queen Elizabeth National Park in southwestern Uganda (Huttner et al., 2009; Kagendo et al., 2014).

3.7.2.3.2 Cystic echinococcosis in humans The largest number of CE cases in eastern Africa originates from a coherent region covering southeastern **South Sudan**, southwestern **Ethiopia** and northwestern **Kenya** (Romig et al., 2011). As a common feature, the region is inhabited by ethnic groups practising traditional nomadic or seminomadic pastoralism. Older estimates of surgical CE incidences for the Turkana region in Kenya were $40-98/10^5$ inhabitants (Clement et al., 2000) with a peak value of 220 in the northwestern part of the region (French and Nelson, 1982). The public health impact of CE on the Turkana pastoralists is confirmed by older and recent ultrasound surveys giving prevalence estimates of 2.5–3.0% (Table 15). This hyperendemic focus extends to neighbouring ethnic groups in South Sudan (Table 15) and southwestern **Ethiopia**, where clinical prevalences of 4.8% (Fuller and Fuller, 1981) and ultrasound prevalences of 2.9% (Table 15) were reported from the Dassanetch and Nyangatom peoples. Low surgical incidence of $0.18/10^5$ in Central Ethiopia (2008–12) (Assefa et al., 2015) and ultrasound prevalences of 0.0–0.1% (Table 15) in western and northeastern Kenya show that hyperendemicity of CE in East Africa is limited to the region described earlier. The only exception appears to be an additional focus among the Maasai pastoralists in southern Kenya and northern Tanzania, where ultrasound prevalences of 0.5–1.1% and a clinical incidence of $10/10^5$ have been estimated (Table S13; Ernest et al., 2010; Zeyhle, personal communication). In addition to the countries mentioned above, human CE cases have been reported from **Uganda**, **Rwanda** and Somalia (Owor and Bitakaramire, 1975; Babady et al., 2009).

3.7.2.4 West and Central Africa: Nigeria, Burkina Faso, Cameroon, the Central African Republic, Democratic Republic of Congo

3.7.2.4.1 Host assemblages, transmission and molecular epidemiology West and Central Africa are the least known regions of sub-Saharan Africa concerning CE in humans or animals. Our current knowledge is based on few, mostly older, animal surveys and scattered reports of human cases or case series. The abundance of CE appears to be highly unequal, being frequent in livestock of the savanna and semidesert zones of northern West and Central Africa, and being absent or of sporadic occurrence in high-rainfall areas of southern West Africa and the Congo

Table 15 Ultrasound surveys for human cystic echinococcosis in eastern Africa

Country (region)	Ethnic group	Prevalence (%)	Number of humans examined	Reference
South Sudan (southeastern)	Toposa	3.1	378	Macpherson et al. (1989)
South Sudan (southeastern)	Toposa	3.5	1010	Magambo et al. (1998)
South Sudan (southeastern)	Bouya	1.3	996	Magambo et al. (1996)
South Sudan (southeastern)	Dinka	1.2	165	Magambo et al. (1996)
South Sudan (southeastern)	Latuka	0.1	954	Magambo et al. (1996)
South Sudan (southeastern)	Didinga	0.0	1031	Magambo et al. (1996)
South Sudan (southeastern)	Nuer	0.0	210	Magambo et al. (1996)
South Sudan (southern)	Mundari	0.7	610	Barclay et al. (2013)
Ethiopia (southern)	Nyangatom	2.9	1334	Macpherson et al. (1989)
Ethiopia (southern)	Borana	1.8	119	Macpherson et al. (1989)
Ethiopia (southern)	Hamar	0.7	369	Macpherson et al. (1989)
Ethiopia (southern)	Hamar	0.7	990	Klungsoyr et al. (1993)
Ethiopia (southern)	Dassanetch	0	267	Macpherson et al. (1989)
Kenya (northwestern)	Turkana	2.6 (0–5.6)	10,491	Macpherson et al. (1989)
Kenya (northwestern)	Turkana	3.0	10,458	Zeyhle, personal communication (2015)
Kenya (western)	Pokot	0.1	2389	Macpherson et al. (1989)
Kenya (northeastern)	Gabbra	0	38	Macpherson et al. (1989)
Kenya (northeastern)	Somali	0	1252	Macpherson et al. (1989)
Kenya (northeastern)	Samburu	0	368	Macpherson et al. (1989)
Kenya (northeastern)	Rendille	0	710	Macpherson et al. (1989)
Kenya (southern)	Maasai	1.0	2577	Zeyhle, personal communication (2015)
Tanzania (northern)	Maasai	1.1	959	Macpherson et al. (1989)

basin. Nothing is known about the *Echinococcus* spp. in this region, only one human case from Ghana infected with G6 (Schneider et al., 2010) indicates that the predominance of this taxon in the northern arid zone (see Section 4.7.2.2) may extend southwards into western and central Africa.

3.7.2.4.2 Infections in animals In northern **Nigeria**, Dada (1980) found 2.4% of 549 dogs infected with *Echinococcus* and in eastern Nigeria 4.4% of 182 dogs were infected (Okolo, 1986). CE prevalence in northern Nigeria is extremely high in camels (>50%), but moderate to low in sheep, goats and cattle. According to one study (Arene, 1985), there is an additional focus in the **Niger** delta with extremely high prevalence of 31.6%, 24.4%, 42.2%, and 55.9% in groups of 320 cattle, sheep, goats and pigs, respectively. **Burkina Faso**, northern **Cameroon**, the **Central African Republic** and the northeast of the **Democratic Republic of Congo** seem to be little affected by CE, but data are old and limited (Table S11). No information on livestock CE exists from other countries of the region. One extensive wildlife study in Central Africa from the 1960s indicates some involvement of wild mammals (including lions) in CE transmission (Graber and Thal, 1979). No CE was diagnosed in small numbers of potential intermediate hosts examined (Graber et al., 1969), but potential wild host species are now largely eradicated in this region and are unlikely to play any significant role.

3.7.2.4.3 Cystic echinococcosis in humans There are no published surveys on human CE from western and central Africa, but a number of case reports and case series exist from **Senegal** (Hane et al., 1989), **Ivory Coast** (Schmidt et al., 1978), **Ghana** (DeMarais et al., 1992; Schneider et al., 2010), northern **Nigeria** (Afonja et al., 1972; Dada et al., 1980), **Cameroon** (Ankouane et al., 2013), the **Central African Republic** (Develoux et al., 2011) and from what is today the **Democratic Republic of Congo** (De Meulemeester and Dardenne, 1958). These records indicate that CE is widespread. Like CE in livestock, the impact on public health is likely to differ among the different countries, but available data do not allow further conclusions.

3.7.2.5 Southern Africa: Angola, Zambia, Mozambique, Zimbabwe, Namibia and South Africa

3.7.2.5.1 Host assemblages, transmission and molecular epidemiology Large-scale surveys on CE in livestock have been done in South Africa in the 1960s (centering on the studies of Anna Verster), indicating that the parasites are widespread at moderate to low levels across the country. In addition to that, surprisingly few prevalence data are available from southern Africa. Even in the Republic of South Africa, the impact on the human population was only recently estimated, and only isolated case reports indicate the presence of the parasite in other countries of the region. Concerning the *Echinococcus* species involved, extensive taxonomic work based on morphology of adult worms derived from domestic animals and wildlife has been done in South Africa in the 1960s, indicating a high diversity (Verster and Collins, 1966). Recent molecular studies confirmed the presence of the genotypes G1–3, G4, G5, G6 and *E. felidis* in southern Africa (Table 14), making it the most diverse region in sub-Saharan Africa. However, most of these data derive from opportunistic sampling, and the relative impact of the various parasites on livestock, wildlife and humans and their spatial distribution are still far from clear.

3.7.2.5.2 Cystic echinococcosis in animals Comprehensive livestock data from **South Africa** published by Verster and Collins (1966) showed uniformly low to moderate prevalences at that time in sheep (1.0–2.0%), goats (0.8–2.6%), cattle (1.8–8.4%) and pigs (0.4–3.5%) with little geographical variation (Table S11). Older cattle data from **Swaziland** (Mitchell, 1977) and a recent retrospective and prospective study from western **Zambia** (Banda et al., 2013) indicate similar prevalence levels there. There is hardly any information on the impact of different *Echinococcus* spp. on southern African livestock. Opportunistic samples from Zambian and northern **Namibian** cattle were all *E. ortleppi* (Banda F., Aschenborn, personal communication), and earlier morphological studies from South Africa suggest that this agent may be also widespread in the region (Verster and Collins, 1966). One report of *E. ortleppi* from a Namibian zebra suggests a spill over into wild hosts species (Obwaller et al., 2004). A large number of wildlife species had earlier been identified as carriers of *Echinococcus* sp. (Table S14 in the Supplementary Material). *Echinococcus felidis*, described morphologically from South African lions (Ortlepp, 1937), was also characterized molecularly based on specimens from that country (Huttner et al., 2009). A wildlife cycle of *E. equinus* was recently identified involving lions, black-backed jackals and plains zebras in Etosha National Park, Namibia (Wassermann et al., 2015). Older reports on frequent zebra infection in Kruger National Park (South Africa) (Young, 1975) indicate a wide distribution in the latter species. Furthermore, *E. intermedius* G6/7 seems to be widespread in various wild mammal hosts in Namibia (Aschenborn, personal communication).

3.7.2.5.3 Cystic echinococcosis in humans A number of case studies confirms the presence of human CE across southern Africa, including **South Africa**, **Namibia**, **Botswana**, **Angola**, **Zimbabwe** and **Mozambique** (Wahlers et al., 2012; Rossouw et al., 1992; Hajek et al., 2004; WHO, 2010; Bordon et al., 1989; Chopdat et al., 2007). Human CE is generally considered to be rare in the region, although some of the published case series are extensive (e.g., 80 patients over a 3-year period in a treatment centre of Botswana) (Hajek et al., 2004). There is a lack of precise data on the impact of CE on the human population. Clinical data from western Zambia gave an annual incidence of $9/10^5$ inhabitants in the years 2006–10 (Banda, 2013), while a recent retrospective study in South Africa reported 137 new cases per year as a most conservative estimate, which corresponds approximately to a countrywide annual incidence of $0.3/10^5$ (Wahlers et al., 2011). Out of a countrywide sample of 32 human cyst isolates that were genotyped, *E. granulosus* G1–3 was the most frequent cause of human CE in South Africa (81%), followed by *E. intermedius* G6/7 (16%) and *E. ortleppi* (3%). The record of the latter species from a single patient represents the first instance of human CE caused by *E. ortleppi* in Africa (Mogoye et al., 2013).

ACKNOWLEDGEMENTS

Paola Pepe and **Vincenzo Musella** (Department of Veterinary Medicine and Animal Productions, University of Naples Federico II, Italy) for the work on the geographic maps; **Rajnish Sharma** (Department of Veterinary Microbiology, University of Saskatchewan) and **Balbir Dhaliwal** (Guru Angad Dev Veterinary and Animal Sciences University, Ludhiana, India) for epidemiological information concerning India, **Nirmal K. Thapa** (Ministry of Agriculture and Forests, Thimphu, Bhutan) for insider information of Bhutan and surrounding countries and **Valentina Racca** (Institute of Parasitology, University of Zurich, Switzerland) for help with the manuscript preparation.

APPENDIX A. SUPPLEMENTARY DATA

Electronic supplementary material associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/bs.apar.2016.11.001. For authorized users.

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