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Succinctus

The low global burden of trichinellosis: evidence and implications

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ABSTRACT

Trichinellosis is a cosmopolitan foodborne disease that may result in severe health disorders and even death. Despite international awareness of the public health risk associated with trichinellosis, current data on its public health impact are still lacking. Therefore we assessed, for the first known time, the global burden of trichinellosis using the Disability-Adjusted Life Year metric. The global number of Disability-Adjusted Life Years due to trichinellosis was estimated to be 76 per billion persons per year (95% credible interval: 38–129). The World Health Organization European Region was the main contributor to this global burden, followed by the WHO region of the Americas and the World Health Organization Western Pacific region. The global burden of trichinellosis is much lower than that of other foodborne parasitic diseases and is in sharp contrast to the high budget allocated to prevent the disease in many industrialised countries. To decrease the uncertainty around the current estimates, more knowledge is needed on the level of underreporting of clinical trichinellosis in different parts of the world.

1. Introduction

Trichinellosis is a foodborne helminth disease caused by 12 taxa of the genus *Trichinella* (Pozio and Zarlenga, 2013). Infection occurs when humans consume raw or undercooked meat of different animal origins, e.g. pork, horse or game, containing muscle larvae (Gottstein et al., 2009). The diverse clinical signs of trichinellosis are not pathognomonic. This complicates the diagnosis and leads to medical misclassification and underreporting. In the acute phase of the disease, infected individuals may present with gastrointestinal disorders such as diarrhoea, but also with myalgia, fever, headache and facial oedema (Pozio et al., 2003). Whether or not a chronic form of trichinellosis exists is still under debate. The few case series that included follow-up over a longer time span indicated that myalgia and fatigue can persist for 4 months and in certain cases for up to 2 years (Nemet et al., 2009).

The pathogenicity for humans of *Trichinella* worms was discovered in 1860 by Zenker (Campbell, 1983). The introduction of controls for this parasite was therefore one of the first veterinary public health programmes (Blancou, 2001). Despite the reduction in risk due to the improvement of pig farming practices and the banned use of raw pork scraps to feed pigs since the 1940s (Steele, 1970), many industrialised countries are still implementing strict and costly programmes to prevent the disease at the farm and slaughterhouse level. Indeed, each year more than 200 million pigs are tested in the European Union (EU) for *Trichinella* spp. by the artificial digestion method under the Commission Regulation (EC) 2075/2005 (Alban et al., 2011; EFSA and ECDC, 2014). With a mean expense of €1.31 per tested pig, a gross estimate of the annual cost linked to pig testing in the EU amounts to €220 million (Kapel, 2005). Other sources report an annual cost of approximately US$ 570 million in the EU for inspection for *Trichinella* and US$ 1 billion due to swine and human trichinellosis in the United States (US), primarily for health regulatory activities to prevent infection (Murrell and Pozio, 2000). Despite the economic importance of *Trichinella*, the actual public health impact of human trichinellosis has not yet been quantified.

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The aim of the current study is to provide the first known global burden of disease assessment for trichinellosis, based on the Disability-Adjusted Life Year (DALY) metric. This assessment is part of a larger project coordinated by the World Health Organization (WHO) to assess the global burden of all major foodborne diseases (Torgerson et al., 2014).

2. Materials and Methods

The estimation of the global incidence and mortality of trichinellosis presented here is based on the results of a recent systematic review of the worldwide epidemiology and clinical impact of human trichinellosis between 1986 and 2009 (Murrell and Pozio, 2011). Searches of six international databases yielded 494 reports, of which 261 were selected for data extraction after applying strict relevance and reliability criteria. From 1986 through 2009, there were 65,818 cases and 42 deaths reported from 41 countries. The apparent annual incidence of and mortality caused by trichinellosis was calculated by dividing the average number of cases and deaths in this 24 year period by the 1997 mid-year population (WHO, 1998). As in Murrell and Pozio (2011), we stratified our incidence and mortality rates per billion persons per year by WHO region.

Due to the important variability in reporting of the disease, the apparent incidence and mortality rates per billion persons per year were adjusted to account for underreporting of the cases due to under-ascertainment, medical misclassification and/or absence of effective surveillance systems. Recently, Vu Thi et al. (2013) have shown that in a trichinellosis outbreak in Vietnam, six patients had sought health care while another 30 putative trichinellosis cases had not. As the detection of putative trichinellosis cases was based on serology, the estimate of six "true" trichinellosis cases per "apparent" case is likely an overestimation. However, given the scarcity of data on the level of underreporting for trichinellosis, we applied this correction factor to the incidence and mortality rates per billion persons per year in the WHO African region (AFRO), WHO Eastern Mediterranean region (EMRO), WHO South-East Asia region (SEARO) and WHO Western Pacific region (WPRO), in order to obtain a plausible upper bound for the true incidence and mortality rates per billion persons per year. For the WHO European region (EURO) and WHO region of the Americas (AMRO), where surveillance is likely more efficient, we arbitrarily applied, in the absence of any data, a correction factor of two, implying that for every reported case there is assumed to be at most one non-reported case.

The DALY metric has been developed as an alternative method to estimate, compare and rank the burden of diseases by including both fatal and non-fatal health outcomes. DALYs can be interpreted as the number of healthy life years lost due to a disease, and result from the sum of the number of years lived with a disability (YLDs) due to the disease, and the number of years of life lost due to disease-related mortality (YLLs) (Murray, 1994). This concept was first used in the Global Burden of Disease (GBD) study, a comprehensive assessment of the worldwide health impact of more than 100 diseases and risk factors. The calculations of the GBD have been updated several times by both the WHO and the Institute for Health Metrics and Evaluation (Murray and Lopez, 2013).

In a pathogen-based DALY calculation, DALYs are the sum of the YLDs for the non-fatal outcomes of the pathogen and the YLLs for the fatal outcomes (Mangen et al., 2013). The YLDs are calculated as the product of the number of cases, the duration of the outcome until remission or death in years, and a disability weight (DW), expressing the severity of the outcome on a scale from zero to one. The YLLs are calculated as the product of the number of deaths and the standard life expectancy at age of death in years. Instead of absolute numbers, DALYs can also be calculated as rates expressing, for example, the number of healthy life years lost per 100,000 people per year (Devleesschauwer et al., 2014a).

The incidence and mortality rates per billion persons per year were estimated as described below. To account for the uncertainty in the level of underreporting, we let the regional incidence and mortality rates per billion persons per year vary uniformly between their raw and adjusted values. To be able to calculate sex and age stratified DALYs, we further stratified these incidence and mortality rates based on Murrell and Pozio (2011), who found that 51% of cases were male and the majority of cases was between 20 and 50 years of age, with a median of 33.1. A generalised Beta distribution was fitted to the latter estimates to define the full distribution of cases from age 0 to 90 years.

In the absence of data on the probability of occurrence of the major clinical symptoms of acute trichinellosis, we assumed, as a worst case scenario, that all patients would develop diarrhoea, facial oedema, myalgia and fever/headache. Because no specific DW for trichinellosis is available, DWs were derived for each of the outcomes separately. The four clinical symptoms were, respectively, matched to the GBD 2010 health states; diarrhoea: moderate (DW = 0.202), disfigurement: level 2, with itch or pain (DW = 0.187), musculoskeletal problems: generalised, moderate (DW = 0.292), and infectious disease: acute episode, severe (DW = 0.210) (Salomon et al., 2012). These four DWs were then aggregated using the multiplicative method, which defines the aggregated DW as $1 - \Pi_i(1 - DW_i) = 0.637$. This approach avoids aggregated DWs becoming larger than one and thus "worse than death" (Haagsma et al., 2011).

Based on the systematic review, disease duration ranged from 21.5 to 70 days (Murrell and Pozio, 2011). These values were divided by 365 to express the duration in years.

All DALY calculations were performed in a probabilistic framework, using 10,000 Monte Carlo simulations to compute DALY credible intervals (CrI) based on the uncertainty in the various input parameters. The calculations were performed in R 3.0.1 (available at http://www.R-project.org/), based on the functions available in the DALY package version 1.2.0 (available at http://cran.r-project.org/web/packages/DALY/). DALYs were calculated as rates per billion people and, for comparison purposes, as absolute values by applying the DALY rates to the 2010 population (available from http://www.census.gov/ipc/www/idb/worldpop.php). No age weighting or time discounting was applied, in line with the most recent update of the GBD study (Murray et al., 2012).

3. Results

Table 1 summarizes the global and regional *Trichinella* burden estimates. Between 1986 and 2009, an average of 2739 cases and two deaths were reported per year (Murrell and Pozio, 2011). When applying our correction factors, upper limits were obtained of 5751 cases and five deaths per year. These estimates led to a global incidence rate of 469.2 to 985.3 cases per billion persons per year, and a global mortality rate of 0.300 to 0.828 per billion persons per year. The estimated global number of DALYs per billion persons per year was 76 (95% CrI: 38–129; Fig. 1). When applied to the 2010 population, this led to an estimation of 523 DALYs (95% CrI: 263–882). The WHO European region was responsible for 69% (95% CrI: 61%–77%) of this global burden.

4. Discussion

This study provides the first known estimate of the global burden of trichinellosis expressed in DALYs. Given the limited data and knowledge on some key clinical aspects of human

Table 1
Human trichinellosis incidence rates, mortality rates, Disability-Adjusted Life Year (DALY) rates and 2010 DALYs.

WHO region	Incidence rate per billion persons per year (raw; adjusted[a])	Mortality rate per billion persons per year (raw; adjusted[a])	DALY rate per billion persons per year (95% CrI)	2010 DALYs (95% CrI)
AFRO	1.9; 11.4	0.068; 0.408	12 (4–20)	10 (3–17)
AMRO	377.7; 755.4	0.526; 1.052	82 (48–128)	76 (44–119)
EMRO	4.4; 26.4	0.000; 0.000	1 (0–3)	1 (0–2)
EURO	2728.8; 5457.6	1.151; 2.301	405 (202–681)	363 (181–610)
SEARO	6.3; 37.6	0.029; 0.172	6 (2–11)	12 (4–21)
WPRO	34.3; 205.6	0.153; 0.918	34 (12–61)	62 (21–110)
Global	469.2; 985.3	0.300; 0.828	76 (38–129)	523 (263–882)

WHO, World Health Organization; CrI, Credible Interval; AFRO, WHO African Region; AMRO, WHO Region of the Americas; EMRO, WHO Eastern Mediterranean Region; EURO, WHO European Region; SEARO, WHO South-East Asia Region; WPRO, WHO Western Pacific Region.
[a] To adjust for underreporting, a correction factor of 6 was assumed for AFRO, EMRO, SEARO and WPRO, and an adjustment correction factor of 2 for AMRO and EURO.

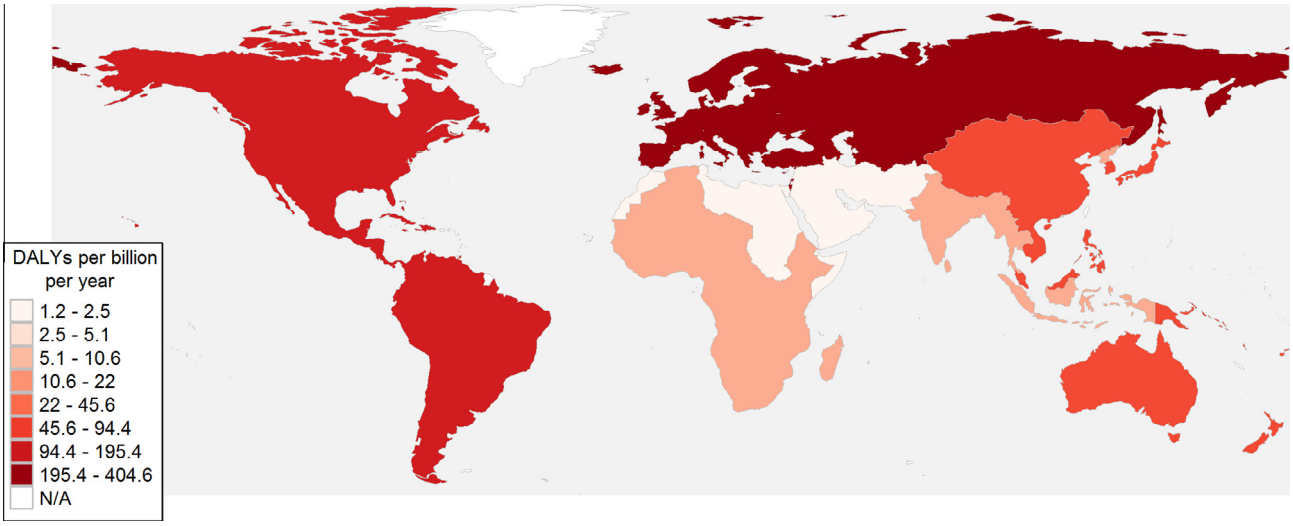

Fig. 1. Global burden of trichinellosis expressed as Disability-Adjusted Life Years (DALYs) per billion persons per year, by World Health Organization region.

trichinellosis, the presented estimates have some limitations. First, due to a lack of knowledge on the occurrence of the different possible clinical outcomes of trichinellosis, we assumed that all cases present with diarrhoea, facial oedema, myalgia and fever/headache. This represents a worst case scenario and may thus overestimate the global burden of trichinellosis. Second, as no DWs are available for facial oedema or myalgia, we had to apply DWs for proxy health outcomes. Third, because the existence of a chronic form of trichinellosis is still questioned, we did not include it in our estimates. More long-term follow-up studies are needed, studying the extent and nature of chronic trichinellosis, and its correlation with severity during the acute stage and the time between infection and treatment. Finally, given the lack of information on the level of underreporting of clinical trichinellosis in most parts of the world, we had to resort to arbitrary correction factors to derive plausible upper bounds of the true incidence and mortality rates. Further studies are needed to generate evidence-based correction factors. Enhanced active and passive surveillance for human trichinellosis would help to validate the current estimates.

Notwithstanding these limitations, even when considering the upper bounds of the DALY CrIs, the global burden of trichinellosis appears very low compared with other foodborne parasitic diseases. Indeed, foodborne trematodoses, alveolar echinococcosis and congenital toxoplasmosis are each responsible for several hundreds of thousands of DALYs worldwide (Torgerson et al., 2010; Furst et al., 2012; Torgerson and Mastroiacovo, 2013). Moreover, the global burden of trichinellosis appears lower than the burden of neurocysticercosis and congenital toxoplasmosis in Nepal alone (Devleesschauwer et al., 2014b).

The global burden of trichinellosis was found to be dominated by the burden in the WHO EURO and AMRO regions. At first glance, this may be due to better surveillance and public health services in these regions ensuring that cases are not missed. However, even when adjusting the observed regional incidence and mortality rates for the presumed levels of underreporting, this discrepancy remained. A more plausible explanation may therefore be the higher meat, and especially pork, consumption in the former WHO regions. This could also explain why the WHO EMRO region, with a high Muslim population, has virtually no trichinellosis. However, in vast parts of Latin America, Africa and Asia, pork is consumed and there is evidence that undercooked pork is consumed because infection with *Taenia solium* is common. Nevertheless, *Trichinella* infection in pigs is rarely reported (Devleesschauwer et al., 2013), indicating that the parasite might not be a common issue in these regions.

The low burden of trichinellosis also contrasts with the high yearly budget allocated to prevent the disease at farm and slaughterhouse level in many industrialised countries (Murrell and Pozio, 2000; Kapel, 2005). The question arises whether the low burden of trichinellosis results from these strong prevention measures or whether the latter are obsolete in industrialised countries where pigs are intensively reared. Both statements are probably true. *Trichinella* meat inspection probably prevented many cases of human infections decades ago when small pig farms with outdoor access were more common. The controlled housing of pig farming systems literally eliminated any possible route of infection, avoiding any contact between pigs and the infected environment, i.e., infected meat from wild or other domestic animals (Thompson,

2013). Within the EU, however, both controlled and non-controlled pig farming systems are still present, the latter especially in central and eastern Europe. Similar differences in housing systems exist between North and South America. Furthermore, organic pig farming allowing free-ranging of the animals is an emerging trend in western European countries and in the US (Burke et al., 2008). Illustrative of the influence of housing systems is the observation that 58% of human cases in the EU and 52% of positive tests in domestic pigs were reported in Romania (EFSA and ECDC, 2014), where over 98% of pig farms raise less than 10 pigs in backyard production systems (available from http://appsso.eurostat.ec.europa.eu/nui/show.do?dataset=ef_lspigaa). Similar differences in human cases exist within the WHO AMRO region (Dupouy-Camet and Murrell, 2007). The impact of housing systems is further illustrated by the increasing number of human trichinellosis cases, and thus of trichinellosis DALYs, attributed to animals other than domestic pigs (Murrell and Pozio, 2011) and to the few million pigs not reared under controlled management conditions (Pozio, 2014).

To address this discrepancy, there is currently an evolution towards more cost-effective risk-based control strategies for *Trichinella*, which will significantly reduce the number of tested domestic pigs in certified herds but increase controls of other pig populations and susceptible wildlife. Indeed, the Codex Alimentarius Commission and the World Animal Health Organisation are developing new guidelines (Codex Alimentarius Commission, 2013; OIE, 2013) and the EU has adopted new provisions that allow exempting officially recognised controlled housing systems in pig farms from *Trichinella* testing as part of meat inspection (EU, 2014). The US Department of Agriculture is reviewing its Trichinae Export Program along these new international guidelines (Gamble, 2011). Certified herds would be subjected to strict regulation and should fulfil specific criteria including physical barriers which prevent contact with other animals, animal carcasses or exposure to meat-containing waste (Kapel, 2005; Murrell, 2013).

5. Conclusion

Globally, trichinellosis is responsible for a minimal human health burden, supporting the need for replacing current *Trichinella* meat inspection regulations with more cost-effective protocols. To provide a full picture of the disease burden and to decrease the uncertainty around the available estimates, there is a need for studies on the level of underreporting of clinical trichinellosis and for prospective epidemiological and clinical studies considering both acute and chronic syndromes.

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