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Estimating the global distribution and disease burden of intestinal nematode infections: Adding up the numbers – A review

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Abstract

Intestinal nematode infections are among the most common infections of humans in developing countries, but precise estimates of the populations at risk of infection, morbidity and mortality are difficult to derive. Careful evaluation of the global distribution and disease burden of nematodes is essential to determine the cost-effectiveness of control and ensure that control programmes are focused appropriately. In turn, understanding the disease burden depends on a summary measure of health as well as reliable data on risks of infection, morbidity and mortality. This review provides an overview of data sources and methods adopted in the Global Burden of Disease study to estimate the burden of intestinal nematodes, including the empirical and modelling challenges in its estimation. Particular attention is paid to efforts to improve our ability to define at-risk populations, based on a Global Atlas of Helminth Infection, and to better estimate attributable morbidity.

Keywords

Intestinal nematodes; Burden of disease; Global distribution; Prevalence; Morbidity; Mortality; Mapping

1. Introduction

It is in the very nature of parasitologists to count things. Little time passes without a publication presenting a revised set of estimates of numbers infected with parasite A or suffering from clinical condition B. For those of us working in helminthology, this heritage of enumeration originates with Norman Stoll when, during his presidential address to the American Society of Parasitologists in Boston in December 1946, he posed the question: "just how much human helminthiasis is there in the world"? His response was based on thoroughly researched work, inspired by his early overseas work in China, Panama and Puerto Rica, and World War II service on Guam. The resultant 1947 paper, entitled This Wormy World (Stoll, 1947), presented the first systematic attempt to measure the worldwide impact of human parasitism by helminths, and probably remains one of the most widely quoted publications in helminthology.

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Of the 341 helminth species found to infect humans (Coombs and Crompton, 1991), Stoll only considered 25 as having sufficient global significance to merit large-scale control programmes (Stoll, 1947). Among these, intestinal nematodes (or soil-transmitted helminths: *Ascaris lumbricoides*, *Trichuris trichiura* and the hookworms, *Necator americanus* and *Ancylostoma duodenale*) were estimated by Stoll to be the most prevalent helminth species worldwide. More recent estimates suggest that intestinal nematodes continue to infect more than one billion people (de Silva et al., 2003; Bethony et al., 2006). Stoll's estimates, in common with all estimates since (Le Riche, 1967; Peters, 1978; Walsh, 1984; Crompton and Tulley, 1987; Crompton, 1988, [1999]; Bundy and Cooper, 1989; Bundy, 1994, 1997; Chan et al., 1994; Brooker et al., 2000), are based on extrapolation from available empirical data. Stoll recognised, however, that among the biggest hurdles to answering his question was the lack of quality data on infection prevalence (Stoll, 1947). Moreover, prevalence indicates little more than presence or absence, and only a fraction of infections will be associated with morbidity. This is because morbidity due to intestinal nematodes is related to the intensity of infection (worm burden) and the most intense infection occurs in a minority of infected individuals (Anderson and May, 1991; Bundy and Medley, 1992).

Again, Stoll posited the pertinent question: “how approach the assignment of a consideration of the problem of helminthic infection as the cause of disability and disease in the tropics?” (Stoll, 1957). Direct estimates of morbidity due to nematode infection would be preferred, but national health statistics are unreliable because signs and symptoms of infection are generally non-specific, chronic and insidious, and hence often go unreported (Bundy et al., 2004). Instead, estimates have been based on approximations from available data on the prevalence of infection (Chan et al., 1994; Chan, 1997; Bundy et al., 2004). This type of analysis is obviously crude, but formed the basis for estimating the disease burden due to intestinal nematodes in the Global Burden of Disease (GBD) study (Murray and Lopez, 1996; Mathers et al., 2007). Since the initial GBD study, there has been considerable debate concerning burden estimates for helminth infection (Chan, 1997; Hotez et al., 2008; King and Bertino, 2008), especially schistosomiasis (King et al., 2005; Jia et al., 2007; Finkelstein et al., 2008; Hotez and Fenwick, 2009). Notably absent, however, is an understanding of how the estimates for intestinal nematode infections were derived.

Here, I provide a brief review of the methods previously used to estimate the burden of disease due to the intestinal nematodes *A. lumbricoides*, *T. trichiura* and hookworm. I also discuss the empirical, methodological and conceptual limitations of the approach and identify areas requiring further investigation. In particular, I highlight work which has sought to develop a Global Atlas of Helminth Infection in order to provide a better estimate of the global distribution of infection.

2. Measuring the burden of disease

The measurement and comparison of the burden of different diseases necessitates (i) a common metric and (ii) consistent descriptions of key epidemiological parameters, based on the best available information. In the first half of the 20th century, the burden of parasitic diseases was considered from a strictly clinical perspective, focusing on the number of deaths. From the 1960s onwards, researchers began to additionally consider the economic effects of diseases, including studies that investigated the effect of parasitic diseases on worker productivity (Farooq, 1964; Fenwick and Figenschou, 1972; Weisbrod, 1974; Guyatt, 2000). However, estimation procedures based on mortality or productivity fail to sufficiently capture the non-fatal health outcomes of diseases and impact on non-working populations. This omission is especially relevant for intestinal nematodes which are rarely fatal and common among children.

An early attempt to quantify the relative importance of different diseases was the Ghana Health Assessment Project (Ghana Health Assessment Project Team, 1981) which measured the impact of a given disease on a community in terms of the number of healthy days of life lost through illness, disability and death. The measure was derived from a synthesis of information on incidence, case fatality rates and the extent and duration of disability arising. The intention of the researchers was to use this measure to identify priorities for allocation of resources and to estimate the number of health days of life saved by different interventions in relation to the costs of intervention. This approach was later expanded upon in the GBD studies.

The initial GBD study was commissioned by the World Bank in 1992 and sought to provide a comprehensive assessment of disease burden in 1990 (Jamison et al., 1993; Murray et al., 1994; Murray and Lopez, 1996). The study developed a conceptual and methodological framework for the assessment of morbidity and mortality across 107 diseases and injuries and introduced a new metric to quantify disease burden, the Disability-Adjusted Life Year (DALY). This metric combines both years of life lost from premature death (YLLs) and years of life lived with disability (YLDs), translating disabilities into years of healthy life lost by giving each disease state a disability weight ranging from 0 (healthy) to 1 (death). Estimates of disease burden were provided for each sex and among five age groups for different regions of the world, based on empirical estimates of disease incidence, duration of disease, case fatality and mortality. The estimates were calculated on the assumption that each disease condition can only be attributed to a single cause and that can be reliably measured.

The overall goal of the GBD study has been to provide internally consistent, summary measures of disease burden for purposes of cost-effectiveness analysis and priority setting. New estimates for 2001, incorporating methodological developments as well as an analysis of the contribution to disease burden of major risk factors, were published as part of the second revision of the Disease Control Priorities Project (Lopez et al., 2006; Mathers et al., 2006 Lopez et al., 2006). In 2007, a new GBD study was launched with the aim of producing comprehensive and comparable estimates of the burden of 175 diseases and injuries and 43 risk factors in 21 regions of the world for both 1990 and 2005, based on new data and improved techniques (Murray et al., 2007; Anon., 2008). Since its inception, the GBD study has attracted unending debate. Much of this has focused on the methods used to assess the severity and age weightings for disease conditions (Anand and Hanson, 1997; Williams, 1999; Gold et al., 2002), less discussion has focused on the uncertainty of the descriptive epidemiology for some populations, especially in sub-Saharan Africa (Cooper et al., 1998). This latter challenge is particularly relevant for intestinal nematodes – see below.

Estimates from the GBD study incorporate information on four main features of each condition: (i) what is known about disease occurrence – incidence and/or prevalence; (ii) the disability weight assigned to each condition; (iii) the risk and duration of morbidity; and (iv) the risk of mortality. The data sources and approaches to estimating these features for intestinal nematodes are now considered in turn.

3. Estimating prevalence of infection: Towards a Global Atlas

Reliable estimates of the national and sub-national variation in infection risk are essential for burden estimation, especially as there are marked geographical differences in risk (Brooker et al., 2006). Infection is most prevalent among rural communities in warm and humid equatorial regions and where sanitation facilities are inadequate. Infection also occurs in urban areas. Even within areas of low prevalence, small localised areas of high prevalence can exist. Only cold or very hot, arid climates are free of infection. The absence of infection

in temperate areas is probably due to historical improvements in hygiene and sanitation. Over the last two decades, in middle-income countries such as China and Brazil, there have been precipitous declines in prevalence (de Silva et al., 2003), primarily due to urbanisation and economic development (Hotez, 2008). Such poverty reduction, together with a shift to a more urbanised economy, was thought to play an important role in the elimination of hookworm in the American South during the early 20th century (Bleakley, 2007).

Until recently, very few countries had conducted national surveys of intestinal nematodes. Perhaps the largest surveys are those conducted in China in 1990 and 2003, where over 300,000 individuals were sampled across the country (Xu et al., 1995; Coordinating Office of the National Survey on the Important Human Parasitic Diseases, 2005). Findings indicate that prevalence of intestinal nematodes fell from 53.6% in 1990 to 19.6% in 2003. National surveys have also recently been conducted in a number of African countries, including Angola, Burkina Faso, Mali, Malawi, Mozambique, Niger, Sierra Leone and Uganda. In countries without comprehensive data, estimates of national prevalence are extrapolated from the available prevalence surveys that have been undertaken. In certain countries, however, very few surveys exist and these have typically been conducted in areas of known high prevalence, potentially over-estimating national prevalence (Brooker et al., 2000).

In an effort to collate available prevalence data into a single resource, a Global Atlas of Helminth Infection was launched with the aim to describe the geographical distribution and prevalence of infection and to highlight areas for which prevalence data are absent (Brooker et al., 2000, 2009). The work involves electronic searches of formal literature and grey literature databases, as well as using personal contacts with researchers and control personnel. Pre-determined inclusion criteria are applied to information identified through searches and data are abstracted into a standardised database and geo-referenced using electronic gazetters. For sub-Saharan Africa alone, the searches have so far identified 9620 spatially independent prevalence surveys of helminth infection undertaken since 1980 (Fig. 1). There is nonetheless wide variation in the coverage of survey data, with some countries including Botswana, Central African Republic, Congo, Democratic Republic of Congo and Zimbabwe having very few or no identified surveys. In an attempt to address this information gap, the included data can be utilised to develop statistical models for the prediction of infection prevalence in areas without suitable data (Brooker et al., 2006). This approach of developing an empirical global database and predictive maps of distribution has many parallels to a similar project developing a global database of malaria, the Malaria Atlas Project (Hay and Snow, 2006; Hay et al., 2009) (<www.map.ox.ac.uk>).

Reliable estimates of prevalence depend crucially on the methods of sampling strategy and diagnosis. As indicated above, the method of sampling may bias estimates in favour of high prevalences among hospital patients and in areas of known transmission. In the Global Atlas, pre-determined inclusion criteria are applied: only cross-sectional prevalence surveys are included and data are excluded if based on hospital or clinic surveys, follow-up surveys of trials, or surveys among sub-populations such as among refugees, prisoner or nomads. The Atlas also includes information on the age class surveyed and diagnostic methods employed. Intestinal nematodes are diagnosed indirectly by microscopic detection of parasites in faecal specimens. However, estimation of prevalence and intensity by routine coprology is subject to systematic errors, due to the complex pattern of worm burden distributions within populations (Bundy et al., 1992) as well as day-to-day fluctuation in egg excretion (Hall, 1981). Delays in processing samples after collection may introduce further bias for detecting hookworm (Dacombe et al., 2007). Paradoxically, estimates of prevalence are least reliable where infection is highest because the relationship between prevalence and intensity is most non-linear when the prevalence is high (Bundy et al., 1992).

Despite these limitations, the Global Atlas represents a significant cartographic resource which is currently being used to define the populations at risk of infection in the ongoing GBD revision. The maps also provide an important planning tool for national control programmes (Brooker et al., 2009). Regular updates of these maps are planned to reflect the changing geographical distribution of helminth infection as control programmes are increasingly being implemented at national scales. To maximise the usefulness of the Global Atlas we have placed the developed country maps of prevalence in the public domain: <www.thiswormyworld.org>.

4. Morbidity caused by intestinal nematodes: A question of weights

The relationships between intestinal nematodes and morbidity are complex. What is known is that the risk of morbidity is strongly related to the number of worms which an individual harbours (the intensity of infection) and that the presentation of morbidity is related to the chronology of infection, migration and development of parasites in the human host (Brooker and Bundy, 2008). However, defining specific morbidity in endemic settings is problematic since few clinical signs are specific to helminth infection, especially in light and moderate infections, and because of the ubiquity of co-infection and co-morbidity (Bundy et al., 2004).

In ascariasis, migrating *A. lumbricoides* larvae cause symptoms from their actual physical presence and the eosinophic inflammatory responses they elicit. Pulmonary migration induces hypersensitivity, occasionally manifesting as asthma. Female *A. lumbricoides* worms can migrate up the common bile duct into the liver causing bile duct obstruction, which can lead to cholangitis or pancreatitis, liver abscesses and acute upper abdominal pain. The intestinal phase of infection is generally asymptomatic, but heavy infection can cause physiological abnormalities in the small intestine resulting in malabsorption of nutrients and micronutrients, nutritional deficiency and growth failure, especially in children (Hlaing, 1993; O'Lorcain and Holland, 2000). Moderate and heavy infections in children may adversely affect cognitive development (Jukes et al., 2008). Heavy infection can cause serious complications, the most common of which is small bowel obstruction by a bolus of worms, leading to gastrointestinal discomfort, vomiting, and occasionally intussusception and death (de Silva et al., 1997a).

The majority of *T. trichuris* infections are light and asymptomatic, with worms living harmlessly in the caecum and appendix; there is no larval migration through systemic tissue. In heavy infections, worms spread throughout the colon to the rectum, where they cause abdominal pain, haemorrhages, mucopurulent stools and symptoms of dysentery with rectal prolapse (Bundy and Cooper, 1989). The classic picture of trichuriasis is Trichuris dysentery syndrome, thought to be due in part to the acute-phase immune response and an elevation of plasma viscosity. A mild, chronic form, *Trichuris colitis*, can affect children, resulting in growth retardation. In children, even symptomless infections may have subtle and insidious effects on nutritional status, and physical and intellectual growth (Stephenson et al., 2000).

Skin penetration of hookworm larvae can cause an intense itching and burning and result in a pruritic erythematous papulovesicular rash, known as ‘ground itch’. Entry of larva into the gastrointestinal tract frequently results in epigastric pain and non-specific gastrointestinal symptoms. The major clinical manifestation of hookworm infection is intestinal blood loss (Roche and Layrisse, 1966; Stoltzfus et al., 1996). Among individuals with inadequate iron intake and high physiological demands, this blood loss can result in iron deficiency and microcytic and hypochromic anaemia, especially among children and pregnant women. Fortunately, however, the anaemia of hookworm can be effectively reversed by treatment

(Brooker et al., 2008; Smith and Brooker, in press). There is also evidence that hookworm infection has consequences for cognitive function among children (Sakti et al., 1999).

Not all of the above disabling sequelae are included in the GBD study, however. Table 1 presents the disabling sequelae and disability weights assigned to intestinal nematodes in the GBD study. Weights refer to how intrinsically bad a given sequela is for an individual who suffers from it, independent of how many individuals suffer from the sequela or of the society in which that individual lives. Assigning disability weight is difficult due to (i) the lack of standardised information on severity for a particular sequela in comparison with other sequelae and (ii) disability cannot always be measured directly. The 1990 GBD study defined six broad disability classes and then mapped each sequela into the appropriate classes. The 2001 updates included weights based on the person trade-off method, whereby health professionals were asked to make trade-offs between years of healthy life and life extension of individuals suffering 22 indicator disease conditions (Saloman and Murray, 2002). These 22 conditions were then grouped into seven classes and all disability sequelae mapped across these classes. The disability weight is a key component in estimating YLDs for each disability sequelae.

Recent work, employing the EuroQol Group's quality of life questionnaires (<http://www.euroqol.org>), has questioned the disability weight assigned to helminth infection (Jia et al., 2007; Finkelstein et al., 2008), partly because the chronic effects on morbidity are insidious and go undetected (King and Bertino, 2008). It should be appreciated, however, that reaching consensus on appropriate weights for all conditions is inevitably problematic, and increasing the importance of one disease will lead to calls to increase the importance of others. On the other hand, the high global prevalence of intestinal nematodes means that any minor adjustment in disability weight will lead to a large difference in YLD calculations, so getting the weights for intestinal nematodes right is particularly important.

5. Estimating disability due to intestinal nematodes: A review of the approach

This is based on the assumption that disability depends on the number of worms an individual harbours, and that disability occurs above some worm burden threshold (Chan et al., 1994; Bundy et al., 2004). Because estimates of worm burden are unavailable, Chan et al. (1994) developed a mathematical model which uses estimates of prevalence by country to determine the number of people that harbour greater than some species-, age-specific worm burden threshold. This model involves a number of steps. First, the model uses observed patterns of spatial heterogeneity of infection to estimate the geographical variation in prevalence within a country and applies species-specific age weights to estimate prevalence in different age groups.

The next step takes into account the empirical observation that the distribution of worms within communities is highly aggregated, whereby the majority of individuals have few or no worms, and a minority have very high worm burdens. This distribution has the implication that there is a strongly non-linear relationship between (i) the prevalence of infection and the mean worm burden in a community and (ii) prevalence of infection and the proportion of a population who harbour worm burdens above a given threshold (Guyatt et al., 1990; Guyatt and Bundy, 1991; Lwambo et al., 1992). The observed aggregated distribution can be described by the negative binomial distribution (Anderson and May, 1985) and this theoretical distribution is used in the Chan et al. (1994) model to estimate the distribution of worms within populations and hence the numbers of individuals with worm burdens above a given threshold.

Third, estimates of disability were based on the assumption that there is some worm burden threshold above which morbidity is likely to occur (Table 2). Developmental and cognitive effects of intestinal nematodes in childhood were assumed to occur at lower worm burdens, and therefore lower worm burden thresholds were assumed to correspond to disability arising from cognitive and growth deficits (Table 3). It was further assumed that the worm burden threshold associated with disability is 50% of that for adults for children under 5 years of age; 75% for children age 5–9 years; and the adult threshold was used for children aged 10–14 years.

Based on these steps, the model estimates both the size of the population infected and at risk of disability (see Bundy et al., 2004 for estimates by age group and region). This information is combined with estimates on (i) severity weight of the disability, (ii) the duration of the disability and (iii) average age of onset to calculate YLDs. For intestinal nematodes, disability associated with higher worm burden thresholds persists as long as the individual is infected, whilst chronic disability which occurs in children with worm burdens above the lower threshold, is assumed to be life-long (Bundy et al., 2004). The proportion of individuals suffering life-time, irreversible disability and different levels of anaemia and the duration of disability is based on the known pathology of infection (see Table 3).

There are a number of problems in trying to estimate the disease burden due to intestinal nematodes. First, although the selection of the worm burden thresholds was based on the best available evidence, it is apparent that slight differences in the thresholds employed will give rise to significantly different estimates of the population at risk of disability. Thus, there is a need for epidemiological data on observed levels of worm burden and morbidity. Second, estimating the duration of infection is difficult, and it is unclear whether the assumed 1 year is an under-estimate, especially among individuals harbouring light infections. Finally, estimates are crucially dependent on estimates of infection prevalence which, as indicated above, are fraught with their own estimation difficulties.

6. Estimating mortality: An inexact science

Mortality attributable to intestinal nematodes is very hard to define, due to the non-specific consequences of infection and a paucity of reliable data. Estimates have typically been from hospital-based studies, but these undoubtedly will under-estimate mortality because the chronic effects of infection typically go under-reported and the difficulties in attributing cause of death.

For ascariasis, all related deaths are assumed to be due to acute complications, including intestinal obstruction, biliary or pancreatic disease, appendicitis and peritonitis (de Silva et al., 1997a,b). The incidence of *Ascaris*-induced intestinal obstruction has been estimated to be in the range of 0–0.25 cases per year per 1000 in endemic areas, and the case fatality rate is up to 5% (de Silva et al., 1997a). Using a modified approach of Chan et al. (1994) and de Silva et al. (1997b) estimated 10,500 deaths each year are directly attributed to serious complications of ascariasis. Owing to the generalised pathology of *T. trichiura*, coupled with difficulties in differential diagnosis, no reliable estimates of *T. trichiura*-associated mortality exist. For hookworm, anaemia is assumed to be the principal cause of death, with widely differing estimates existing, ranging from 0.1 to 0.5 per 1000 infections per year (Miller, 1979; Pawlowski et al., 1991). In numerical terms, the World Health Organization (WHO) previously estimated that 65,000 deaths per year are attributable to hookworm (WHO, 1992).

The GBD study employs a statistical death model to estimate deaths by broad cause group. The use of YLLs due to premature death allowed greater weight to be given to deaths at younger ages. The 2001 GBD study attributed 3000 deaths each due to *A. lumbricoides*, *T.*

trichuria and hookworm (WHO, 2002). For *A. lumbricoides* and *T. trichuria*, these deaths were assumed to occur among 5–14 year olds and the majority of the hookworm-related deaths occurred in sub-Saharan Africa.

The data sources and methods by which these different mortality estimates are derived are not always described adequately, and it remains unclear why such different estimates of mortality exist. Establishing the cause of death in many developing countries is difficult and comparative studies are rare; reliable estimates of mortality due to intestinal nematodes are probably unobtainable.

7. The global burden of intestinal nematodes

The majority of this burden is due to morbidity rather than mortality. According to the 2001 GBD study, 58.1 million people suffered high intensity *A. lumbricoides* infection, 26.6 million with high intensity *T. trichiura* infection, and 59.9 million with high intensity hookworm infection. Only 3000 deaths were attributable to each species. Globally, *A. lumbricoides* was estimated to cause the loss of 1.817 million DALYs, *T. trichiura* 1.006 million DALYs, and hookworm 0.97 million DALYs. The majority of DALYs were lost in Southeast Asia (47%) and sub-Saharan Africa (23%).

The GBD study estimates are not the only ones available, however. Chan (1997) estimated that intestinal nematodes cause the loss of 39 million DALYs: *A. lumbricoides* 10.5 million; *T. trichuria* 6.4 million; and hookworm 22.1 million. The higher estimates for *A. lumbricoides* and *T. trichuria* are due to lower worm burden thresholds for the 0–5 years age class (see de Silva et al., 1997b) and the greater emphasis placed on long-term consequences of infection on malnutrition and cognitive development, especially in children. Those for hookworm reflect the impact of infection as an indirect cause of broader morbidity, such as mild anaemia, whereas the GBD estimates only link anaemia to high intensity infections. The DALY model assumes that each disease condition is a distinct clinical entity with a single cause, and it has been argued that clinical syndromes such as anaemia should be apportioned according to their multiple aetiology (King and Bertino, 2008). However, defining precise attributable risks of hookworm in relation to other causes of anaemia, such as malaria, HIV and under-nutrition, is problematic and requires a more detailed analysis of empirical data. A recent summary of the available evidence on the impact of hookworm on anaemia from randomised controlled trial data and cross-sectional survey data is provided by Smith and Brooker (in press). This work shows that moderate and heavy intensity hookworm infections are associated with lower haemoglobin concentration among children aged 5–16 years, but that even light infections were associated with lower haemoglobin in adults. These findings support revisiting the worm burden thresholds used to define the risk of hookworm-related morbidity.

8. Conclusion

The precise amount of morbidity and mortality caused by intestinal nematodes will never be known. This elusiveness is due to the non-specificity of clinical signs, difficulties in parasitological diagnosis and a paucity of reliable and accurate epidemiological data, compounded by the fact that much of the burden is concentrated among countries with weak disease surveillance systems. As a consequence, estimating the global distribution and disease burden continues to be based on informed approximations, using the best available information. This review has sought to provide insight into these estimation approaches, but also help identify areas requiring further empirical investigation and modelling. It is apparent that the efforts to improve our cartography of helminth infection will help better estimate the public health burden of intestinal nematodes. It is also clear that we require a

better understanding of the burden envelope of intestinal nematodes, including the effects upon anaemia and impaired cognitive ability. Reliably defining the disease burden of intestinal nematodes remains as much as a challenge for today's helminth epidemiologists as it did for Stoll in 1946. As the risks of infection and morbidity change in the face of large-scale control, this challenge will continue into the 21st century.

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Fig. 1.
Distribution of the 9620 prevalence surveys identified and geo-referenced for sub-Saharan Africa included in the Global Atlas of Helminth Infection by 12th April 2010. See: <www.thiswormyworld.org>. Note that a few countries have undertaken national prevalence surveys, but the data are yet to be included in the Global Atlas, including Angola, Mozambique, Equatorial Guinea and Sierra Leone.

Table 1

Disabling sequelae and disability weights for intestinal nematodes assumed in the 2004 Global Burden of Disease (GBD) study (adapted from Mathers et al., 2006, 2007).

GBD cause/sequelae	Case definition	Disability weight (range)
Ascariasis		
High-intensity infection	Infection with 20–40 worms or more, depending on age group	0.000
Contemporaneous cognitive deficit	Reduction in cognitive ability in children aged 5–14 years, which occurs only while infection persists	0.006
Cognitive impairment	Delayed psychomotor development and impaired performance on language, motor skills, equivalent to 5–10 point deficit in IQ	0.024
Intestinal obstruction	Blockage of the intestines due to worm mass	0.463
Trichuriasis		
High-intensity infection	Infection with 250–500 worms or more, depending on age group	0.000
Contemporaneous cognitive deficit	Reduction in cognitive ability in children aged 5–14 years, which occurs only while infection persists	0.006
Trichuris dysentery syndrome	Rectal prolapse and/or tenesmus and/or bloody muscoid stools due to intestinal mucosa by worms	0.116 (0.114–0.138)
Cognitive impairment	Delayed psychomotor development and impaired performance on language, motor skills, equivalent to 5–10 point deficit in IQ	0.024
Hookworm disease		
High-intensity infection	Infection with 80–160 worms or more, depending on age group	0.000
Anaemia	Anaemia due to hookworm. Defined as Hb <100 g/L in pregnant women, <110 in children and adult women, and <120 g/L in adult men	0.024
Cognitive impairment	Delayed psychomotor development and impaired performance on language, motor skills, equivalent to 5–10 point deficit in IQ	0.024

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Table 2

Intestinal nematode worm burden thresholds for morbidity assumed in the estimation procedure by Chan and colleagues (Chan et al., 1994; Bundy et al., 2004) for *Ascaris lumbricoides*, *Trichuris trichiura* and hookworms.

Species	Age group (years)	Higher estimate, lower threshold	Lower estimate, higher threshold
A. lumbricoides	0–4	10	20
	5–9	15	30
	10–14	20	40
	15+	20	40
T. trichiura	0–4	90	250
	5–9	130	375
	10–14	180	500
	15+	180	500
Hookworms	0–4	20	80
	5–9	30	120
	10–14	40	160
	15+	40	160

Table 3

Contemporaneous and chronic disabling consequences of intestinal nematodes (adapted from Bundy et al., 2004).

GBD cause and disability class	Disabling consequences	Worm burden threshold
Contemporaneous		
Ascariasis		
Class I	Reversible faltering growth and cognitive deficit in children, and/or reduced fitness in children and adults, which lasts for the duration of infection	Higher
Class II	Clinically overt, acute illness, such as abdominal pain, nausea, diarrhoea, and is of short duration and mild to moderate severity	Higher
Class III	Acute complications, including intestinal obstruction, biliary or pancreatic disease, appendicitis and peritonitis	Higher
Trichuriasis		
Class I	Reversible faltering growth and cognitive deficit in children, and/or reduced fitness in children and adults, which lasts for the duration of infection	Higher
Class II	Classical dysenteric forms of trichuriasis, Trichuris dysentery syndrome and Massive Infantile Trichuriasis. Worms carpet the colonic mucosa and the colon is inflamed, oedatous and friable, and often bleeds freely. Assumed to affect 5% of children under 15 years with burdens above higher threshold	Higher
Hookworm		
Class I	Reduced fitness in children and adults, reduced worker productivity in adults, reduced fertility in women, reduced intrauterine growth	Lower
Class II	Mild anaemia (70% of individuals above worm burden threshold)	Higher
Class III	Moderate anaemia (24% of individuals above worm burden threshold)	Higher
Class III	Severe anaemia (6% of individuals above worm burden threshold)	Higher
Chronic		
All species		
Class II	Permanent growth retardation and cognitive impairment, which is a life-long consequence, occurring only 3% of children with burdens above the lower threshold	Lower

GBD, Global Burden of Disease.