Intestinal Nematode Infections

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1. INTRODUCTION

The effective control of the major intestinal nematode infections of humans involves relatively low cost interventions (Savioli, Bundy & Tomkins, 1992). Informed decisions about the need for investment in control programmes, however, also requires useable estimates of the scale of morbidity (Guyatt & Evans, 1992).

Direct estimates of morbidity would be preferred, but the currently available techniques suffer from major limitations. Active case detection can be useful at the local level (Pawlowski & Davis, 1989), but demands a level of resources that makes its widespread use impractical. Passive case detection, which has more appropriate resource demands (Guyatt & Evans, 1992), is unreliable for geohelminthiases because the symptoms are non-specific; in one prospective study of trichuris colitis only 2% of cases observed in the community had self-

presented to the local health services (Cooper, Bundy & Henry, 1986). Furthermore, there is increasing evidence that the most common and potentially important consequences of infection are insidious effects on nutritional status (Tomkins & Watson, 1989; Nesheim, 1989) and on physical and intellectual development (Stephenson, 1987; Cooper *et al* 1990; Nokes *et al* 1992a; 1992b). Such effects are unlikely to result in self-presentation to passive case detection clinics, and will be grossly underestimated by survey procedures based on the active detection of clinical signs. This is especially so, as the infections are ubiquitous and both passive and active detection are usually based on deviations from local norms, which may be greatly influenced by the infections.

There are no direct estimates of the community morbidity caused by intestinal helminths. Instead, most studies have focused on estimating the prevalence of infections, only a fraction of which will be associated with disease. Perhaps the first estimate of the global prevalence of intestinal nematode infections was presented by Norman Stoll in his "Wormy World" article of 1947 (Stoll, 1947). His technique of extrapolation from survey data has proven robust and has been used to derive many of the more recent estimates which suggest that there are some 1000 million infections with *Ascaris lumbricoides* and only slightly fewer infections with hookworm (both *Necator americanus* and *Ancyclostoma duodenale*) and *Trichuris trichiura* (WHO, 1987; Crompton, 1988,1989; Bundy & Cooper, 1989). In the absence of reliable procedures for estimating disease directly, estimates of burden have been based on extrapolation from the infection prevalence data to provide an estimate of the proportion of infections which are likely to be associated with disease (Warren *et al*, 1993; Chan *et al*, 1994). This requires a careful and conservative approach because of the ubiquity of infection; extrapolating from such large numbers has the consequence that even small errors in estimating the disability attributable to individual cases can result in considerable inaccuracy in estimating the total burden. Because of the inherent potential for error in the use of any extrapolation procedure, the major aims of this chapter are to encourage independent scrutiny of the methodology and to highlight areas which particularly warrant further empirical study.

This chapter builds on the studies of Chan *et al.*, 1994, and Warren, *et al.*, 1993, and attempts to provide improved estimates of burden of disease based on extrapolation from observed estimates of prevalence of infection. The size of the population at risk of disability

is estimated using epidemiological methods developed to describe the relationship between prevalence and mean intensity, and between intensity and potential morbidity (Guyatt *et al*, 1990; Lwambo, Bundy & Medley, 1992), but modified to incorporate the heterogeneity between communities and age classes (Chan *et al.*, 1994). The disability per case at risk is estimated using procedures described elsewhere in this volume, and the regional and global burden of disease is obtained by extrapolation from these estimates.

1.1 Basic Biological Characteristics of Intestinal Nematodes

The analyses presented here focus on the four species of intestinal nematode which are of circumglobal distribution and which occur at high prevalence: *Ascaris lumbricoides*, *Trichuris trichiura* and the two major hookworm species, *Necator americanus* and *Ancylostoma duodenale*.

A.lumbricoides is the large roundworm (15 cm) and lies free in the human duodenum where it feeds on lumenal contents (see Crompton *et al.*, 1989, for further details of the biology of this parasite). Like all the other nematodes considered here the worms are dioecious. The female produces some 100,000 eggs per day which pass out in the faeces of the host and embryonate externally at a rate determined by local environmental factors. The eggs hatch on ingestion, releasing a larva which undergoes a tissue migration involving the cardiovascular and pulmonary systems. The larva moults as it migrates and ultimately is coughed up from the lungs, swallowed, and becomes established as the adult in the small intestine. The cycle from egg deposition to female patency has a duration of some 50 days.

T.trichiura, the human whipworm, is a much smaller worm (25 mm) and inhabits the colon (see Bundy and Cooper, 1989). The anterior two thirds of the worm is thin and thread-like and is laced through the mucosal epithelium, upon which the worm is believed to feed, leaving the blunt posterior projecting into the colonic lumen for excretion and oviposition. The female produces some 2000 eggs per day which pass out in the host faeces and embryonate externally. The infectious eggs hatch on ingestion and undergo a specifically local migration, via the Krypts of Lieberkuhen to the mucosal surface. The development cycle takes some 60 days.

The two major hookworm species, which are of similar magnitude to the whipworm, inhabit

the small intestine, where they attach to villi with biting mouthparts (see Schad and Warren, 1990). The worms feed on host blood and move frequently to new sites, leaving multiple, bleeding petechial haemorrhages on the mucosal surface. *A.duodenale* is believed to be more voracious, consuming some 0.14-0.40 ml of blood per day compared with 0.01-0.10 ml by *N. americanus*. The eggs pass out in host faeces and embryonate. Unlike the roundworm and whipworm, the eggs hatch externally releasing a mobile infective larva which actively infects the human host by dermal penetration. *A.duodenale* is also able to infect by the oral route, and there is evidence for vertical transmission of this species either transplacentally or in maternal milk. Having entered the host, the larva undergoes a tissue migration to the lungs and is coughed up and swallowed to moult to the adult in the small intestine. The cycle takes approximately 60 days for both species. *A.duodenale* is apparently able to extend this period by arresting development to the adult stage; a mechanism which may allow avoidance of seasonally hostile external conditions.

1.2 Basic Epidemiological Characteristics

Understanding the epidemiology of helminth infections requires a fundamentally different approach to that required for all other infectious agents. Each worm establishing in a host is the result of a separate infection event, and the number of infective stages shed (the infectiousness of the host) is a function of the number of worms present. In population dynamic terms this implies that the individual worm is the unit of transmission for helminths, while the individual host is the unit for microparasites (Anderson & May, 1982). The size of the worm burden (the intensity of infection) is therefore a central determinant of helminth transmission dynamics, and is also the major determinant of morbidity since the pathology is related to the size of the worm burden, usually in a non-linear fashion (Stephenson, 1987; Cooper & Bundy, 1989). Since the size of the worm burden varies considerably between individuals, and infection implies only that worms are present, a population of "infected" people will exhibit considerable variation in the severity of disease manifestations. The intuitive assumption that all infections are equal may help to explain the historical confusion over the pathogenicity and public health significance of helminth infection (Bundy, 1988; Cooper & Bundy, 1989). From these considerations it is apparent that an understanding of helminth epidemiology centres around an understanding of the patterns of infection intensity.

1.3 Worm Burden Distributions

Worm burdens are neither uniformly nor randomly distributed amongst individuals, but are highly overdispersed such that most individuals have few worms while a few hosts harbour disproportionately large worm burdens (Fig 1). This pattern has been described for *Ascaris lumbricoides* (Croll *et al*, 1982), both species of hookworm (Schad & Anderson, 1985) and *Trichuris trichiura* (Bundy *et al*, 1985). Most studies suggest that approximately 70% of the worm population is harboured by 15% of the host population. These few heavily infected individuals - the "wormy people" described by Croll & Ghadirian (1981) - are simultaneously at highest risk of disease and the major source of environmental contamination.

[figure 1]

Studies of reinfection suggest that individuals are predisposed to a high or low intensity of infection; the size of the worm burden reacquired after successful treatment is positively associated with the intensity of infection before treatment. This association has been shown for all the major geohelminths (Anderson, 1986; Elkins *et al*, 1986; Bundy & Cooper, 1988; Holland *et al*, 1989), and persists over at least two reinfection periods (Chan L. *et al*, 1992). Longitudinal studies of *T. trichiura* (Bundy *et al*, 1988) and *A. lumbricoides* (Forrester *et al*, 1990) confirm that this positive association reflects a direct relation between the rate of reinfection and initial infection status. Thus in an endemic community it appears that there is a consistent trend for an individual to have an above (or below) average intensity of infection. This trend is more apparent in children with *A. lumbricoides* (Haswell-Elkins *et al*, 1987) and *T. trichiura* (Bundy & Cooper, 1988) infection, and more apparent in adults with *Necator americanus* (Bradley & Chandiwana, 1990) infection, perhaps reflecting the different age-intensity patterns of these species. This pattern is also apparent at the family level (Chai *et al*, 1985; Forrester *et al*, 1988,1990; Chan L. *et al*, 1994).

1.4 Worm Burden and Host Age

Overdispersed distributions of infection intensity are observed in the community as a whole and also in individual age-classes. The degree of overdispersion, however, shows some age-dependency. In hookworm infection the distribution becomes more overdispersed in adults (Bradley & Chandiwana, 1990), while in *A. lumbricoides* and *T. trichiura* there is evidence that dispersion increases to a peak in the child age classes (Bundy *et al*, 1987b) and then declines in adults (Chan L. *et al*, 1992). These changes reflect age-specific trends in the proportion infected (the size of the zero class in the frequency distribution) and in the mean

intensity of infection (the mean of the distribution).

The age-dependent pattern of infection prevalence is generally rather similar amongst the major helminth species, exhibiting a rise in childhood to a relatively stable asymptote in adulthood (Fig 2). Maximum prevalence is usually attained before 5 years of age for *A. lumbricoides* and *T. trichiura* and in young adults with hookworm infection. In *A. lumbricoides* there is often a slight decline in prevalence during adulthood, but this is less common with the other major nematode species.

[figure 2]

Prevalence data indicate the proportion of individuals infected, and do not provide a simple indication of the number of worms harboured. Figure 3 shows the relationship between prevalence and worm burden. The marked non-linearity of this relationship is a direct statistical consequence of the overdispersed pattern of intensity. If worm burdens were uniformly (normally) distributed there would be a linear relationship between prevalence and intensity (see Anderson & May, 1985). This is an important relationship since it is central to the method of extrapolation from infection prevalence to infection intensity described in this chapter. It is worth emphasising therefore that the relationships in Figure 3 are firmly based on empirical studies of the major species of intestinal helminths (see Guyatt *et al*, 1990; Lwambo *et al*,1992; Booth, 1994 for detailed discussion of this issue).

[figure 3]

The lack of simple correspondence between prevalence and intensity has the consequence that the observed age-prevalence profiles provide little indication of the underlying profiles of age-intensity. For most helminth species the initial rise in intensity with age closely mirrors that of prevalence but occurs at a slightly slower rate (Fig 4). Maximum intensity occurs at a host age which is parasite species-specific and dependent on parasite longevity, but independent of local transmission rates (Anderson, 1986). For *A. lumbricoides* and *T. trichiura* maximum worm burdens occur in human populations at 5-10 years of age and for hookworms 20-25 years.

[figure 4]

The most important differences in the age-intensity profiles of these species become apparent after peak intensity has been attained. *A. lumbricoides* and *T. trichiura* both exhibit a marked decline in intensity to a low level which then persists throughout adulthood (Fig 4a). Age-

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profiles based on egg density in stool had suggested that there was considerable variation in the patterns seen in hookworm (Behnke, 1987; Bundy 1990), but it now appears, from studies where burdens have been enumerated by anthelmintic expulsion, that the intensity attains a stable asymptote, or rises marginally, in adulthood (Pritchard et al, 1990; Bradley et al, 1992) (Fig. 4b).

Thus, for those species with convex age-intensity profiles, but asymptotic age-prevalence profiles, a similar proportion children and adults are infected but the adults have substantially smaller worm burdens. With hookworm infection, where both prevalence and intensity are asymptotic, more adults are infected and they have larger worm burdens.

2. DEFINITION AND MEASUREMENT

For most helminthiases the relationship between infection and disease is likely to be non-linear and complex. If we accept, for the moment, the simple premise that only heavy worm burdens cause disability, then it is apparent that disability will have an age-dependent distribution, since intensity is age-dependent, and also that disability will have an overdispersed pattern even within the susceptible age-classes. The relationship is further complicated by the non-linear relationship between the severity of disease and the intensity of infection, and by the interaction between symptomatology and the chronicity of infection. Helminthic infection does not inevitably lead to disease: a failure to appreciate this has lead to apparently contradictory results from morbidity studies and may be the major contributor to the under recognition of the public health significance of helminthiasis (Cooper & Bundy, 1988,1989).

An essential pre-requisite, therefore, to assessing the global burden of disease is the estimation of the sub-population of the infected population which has a sufficiently large worm burden to put them at risk of disability. This requires some method of relating prevalence of infection data, which are available from empirical studies in all geographical regions, to intensity of infection data, which are not. In this section we describe procedures for extrapolating intensity from prevalence survey data, and for partitioning the risk of disability.

2.1 Worm Burdens and Morbidity

There is a general acceptance of the simple view that very intense infection results in illness, a view that reflects both clinical experience of overwhelming infection and, perhaps equally importantly, an atavistic repugnance at the insidious invasion of the body by large numbers of worms. Such extremes of infection result in the severe anaemia of necatoriasis and the intestinal obstruction of ascariasis (Stephenson, 1987), and the chronic colitis of classical Trichuris Dysentery Syndrome (Cooper & Bundy, 1988). That helminth morbidity is dependent on infection intensity is, from this perspective, uncontroversial. An understanding of the pattern of the relationship between infection intensity and clinical signs has proven more elusive. This appears to be due to two main factors.

Firstly, intensity and pathogenesis are non-linearly related. Studies of the anaemia associated with hookworm infection indicate that there is a disproportionate reduction in plasma haemoglobin concentration after some threshold worm burden is exceeded. Although profound anaemia is associated with thousands of worms, a clinically important anaemia can be induced by a few hundred worms, the precise threshold depending on host iron status (Lwambo et al, 1992). Note that this occurs despite the constant per capita blood loss due to hookworm feeding (Martinez-Torres et al, 1967) which might intuitively be expected to give a linear relationship between burden and anaemia. Studies of protein-losing enteropathy in trichuriasis also indicate a non-linear relationship with worm burden (Cooper et al, 1990). The rate of gut clearance of α-1-antitrypsin at first rises rapidly with increasing worm burden to a threshold and rises more slowly thereafter (Figure 5). This implies that significant intra-lumenal leakage of protein can occur with T. trichiura burdens of a few hundred worms. The clinical consequences of this loss will be determined by the nutritional and dietary status of the host and by the chronicity of infection (Cooper et al, 1986). In one study, children with the classical Trichuris Dysentery Syndrome had all experienced mucoid dysentery and rectal prolapse for more than 3 years (Cooper & Bundy, 1989).

[figure 5] [figure 6] [figure 7]

The second reason for the lack of understanding of the relationship between intensity and disease is the difficulty of measuring and attributing morbidity. This is in part the classical epidemiological problem of identifying specific morbidity in an endemic population subjected to multiple insults (Walsh, 1984). It is exacerbated for helminth infection, however, by the absence of pathognomonic signs in moderate, but clinically significant, infection. This

problem has been addressed by intervention trials using specific anthelmintic therapy. Such studies have shown, for example, significant improvements in linear growth after treatment of moderately infected and stunted children with hookworm, *A. lumbricoides* or *T. trichiura* infection (Stephenson, 1987; Stephenson *et al*, 1990; Cooper *et al*, 1990) (Figures 6 and 7). Even more subtle consequences of infection are suggested by recent double blind placebo trials which show significant improvement after anthelmintic treatment in the cognitive ability of school children moderately infected with *T. trichiura* (Nokes *et al*, 1991, 1992a) (Figure 8). These results suggest that even moderate helminthic infection may have insidious consequences that are unlikely to be attributed to helminthiasis in public health statistics. In one study of a village population with hyperendemic geohelminthiasis (Cooper *et al*, 1986), only 2% of actual morbidity had been reported to the health authorities.

[figure 8]

Some insights into the relationship between infection and disability can be provided by data analytical procedures (Guyatt *et al*, 1990; Lwambo *et al*.,1992). Empirical studies can provide estimates of the threshold number of worms associated with risk of disability (see above), then using models which describe the empirical relationship between infection intensity and prevalence shown in Figure 3 it is possible to estimate the proportion of individuals which exceed the threshold worm burden (i.e. are likely to suffer disability) at a given prevalence of infection. This relationship between the prevalence of infection and the estimated proportion of the population at risk of disability is shown for a range of thresholds of *A. lumbricoides* in Figure 9. Analysis of the estimated incidence of *Ascaris*-induced intestinal obstruction in relation to the local prevalence of ascariasis (based on empirical data) has in fact shown this type of non-linear relationship (de Silva et al, in press). Non-linear relationships of this form have also been shown in studies of schistosome infections, for which adequate country based morbidity data are available (Jordan & Webbe, 1982). There is a need to obtain similar data for other intestinal nematodes, but this is currently confounded by the difficulties in estimating morbidity directly for these infections. However, one important conclusion of this analysis is that the threshold need not be precisely defined since the form of the relationship between infection and disease is relatively insensitive to the threshold value, provided the value is relatively large (> 20 worms Figure 9).

[figure 9]

These analyses indicate that the proportion at risk of disability increases dramatically as infection prevalence rises. For example, if 25 *A. lumbricoides* worms are associated with

disease, then 20% the population will be at risk at an infection prevalence of 80%, and less than 2% at an infection prevalence of 70%. It is worth noting that both these infection prevalences could reasonably be considered to be high, which may help explain why studies of helminth morbidity in "high" prevalence areas often reach very different conclusions about the public health significance of helminthiasis (see for example Keusch, 1982).

The relationships described here form the basis for the extrapolation procedure developed in this chapter. This procedure involves the use of infection prevalence survey data from individual countries to give an estimate of regional and global prevalence of infection. Then the estimation of the fraction of this infected population which empirical data suggest places the population at risk of disability. The following sections describe this procedure and discuss the validity of its assumptions.

2.2 Estimation of Risk of Disability from Infection Prevalence Data

This estimation is based on the relationship between worm burden and prevalence of infection. The frequency distribution of worm burdens between individuals has been consistently shown to be highly overdispersed (1.3, above). Within a community, the majority of people have few or no worms and a few people have very high worm burdens. Observed distributions can be represented empirically by a negative binomial distribution (Anderson & Medley, 1985; Guyatt et al, 1990; Lwambo et al, 1992; Bundy & Medley, 1992). This theoretical distribution has two parameters, the mean worm burden, μ, and the aggregation parameter, k. General values used in this study are $k=0.54$ for $A.$ $lumbricoides$ (Guyatt et al, 1990), $k=0.23$ for $T.$ $trichiura$ (Booth,1994) and $k=0.34$ for hookworms (Lwambo et al, 1992), and are estimated from empirical data.

The basis for the estimation of potential disability is that the risk of disability is higher in individuals with higher worm burdens and that there is some threshold worm burden above which disability is more likely to occur (Table 1). The proportion of the population with worm burdens higher than this threshold can then be estimated from the negative binomial distribution (Guyatt & Bundy, 1995; Lwambo et al, 1992; Medley et al, 1993). This approach is necessarily an approximation, since the effects of a given worm burden on an individual will be modified by the condition of an individual (eg. nutritional status and concurrent infections) and the chronicity of the infection.

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Studies indicate that developmental effects of infection (eg cognitive and growth deficits) occur at lower worm burdens than the more serious clinical consequences. We therefore use two sets of thresholds for each species, where the lower threshold corresponds to a higher estimate of potential disability and vice versa. These thresholds are shown in Table 1. The thresholds for *A.lumbricoides* and *T.trichiura* correspond to those given in Chan *et al*, 1994, except for one change in the *A.lumbricoides* thresholds, as explained below. The thresholds for hookworm have been adjusted downwards. This reflects the recent analyses presented by Crompton and Whitehead, 1993, and the observation that the thresholds reviewed by Lwambo *et al* 1992 apply to adults rather than children, as had been assumed in the previous calculations.

[table 1]

There is a lack of data on the relationship between disability threshold and age. However, since a given worm burden is more likely to cause disability in children than in adults the use of a single, age-independent threshold would tend to considerably over-estimate the potential disability. In order to approximate this age effect, in the absence of empirical data, the same proportional changes with age are used for all worm species. The threshold for children under five was taken as 50% of that for adults (i.e. adults require twice the worm burden of pre-school children before suffering ill effects), for five to ten year old children it was taken as 75% of that for adults, and the adult threshold was used for ten to fifteen year old children (Table 1). For *A. lumbricoides* only, the thresholds for the children under five years was taken as 50% of that for the five to ten year olds, to reflect the empirical observation that the age distribution of *Ascaris*-related complications is such that almost equal numbers of these age groups are affected (de Silva *et al*, in press). These estimates are, we believe, conservative, but not firmly based on empirical observation.

[table 2]

Other age-dependent differences are also incorporated into the model. *A. lumbricoides* and *T. trichiura* infections are usually more prevalent in children whereas hookworm infections are more prevalent in adults (1.4, above). For simplicity, a single age-prevalence relationship (one for each species) was used, based on the typical age-prevalence relationship observed in field studies (Table 2). The age-weights for the under-fives has been adjusted upwards from that given in Chan *et al* 1994, for *A.lumbricoides* and *T.trichiura* only, based on re-analysis of empirical data on age-prevalence in these infections (Ratard *et al*, 1991, Yu *et al*, 1989, Rahman, 1993). The use of different prevalences for different age classes implies that

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a separate negative binomial distribution must be calculated for each age class. In order to ensure that the overall prevalence remains unchanged by this procedure, the observed demographic age distribution of the population must be taken into account. The effect of host age on the aggregation parameter (k) remains undefined and the present framework uses a single (species specific) aggregation parameter for all age groups.

2.3 Incorporating Geographical Heterogeneity

The prevalence of infection is non-linearly related to the mean intensity of infection in a community, such that the proportion of the population potentially suffering morbidity is disproportionately greater at higher levels of prevalence (Guyatt & Bundy 1991). If the average prevalence among communities is used as a basis for estimating intensity (and potential disability) for a geographical region, this will grossly underestimate the actual morbidity. It is therefore necessary to incorporate geographical heterogeneity in prevalence within the estimation procedure (Chan et al, 1994). Spatial heterogeneity in intestinal nematode infection is a relatively neglected area of study (Booth & Bundy, 1992; Bundy *et al*, 1991) but its potential importance has been convincingly demonstrated for microparasitic infections (Anderson, 1982; May & Anderson, 1984).

Heterogeneity is considered at several geographical levels in the extrapolation procedure. The highest level is the eight regions of the world defined for the Global Burden of Disease study. EME and FSE were excluded from the analysis since the prevalences of intestinal nematode infections are very low. The remaining six regions are then divided into "population units", of 20 to 100 million people for which mean prevalence values, based on empirical data, are input into the model. Generally these population units coincide with politically defined countries (which is the unit for which prevalence data are most readily available) but some countries with exceptionally large populations, especially China and India, are subdivided into smaller units based on States or Provinces for prevalence estimates.

[figure 10]

The subdivision of a region into population units captures some geographical heterogeneity, but this does not include the heterogeneity within the population unit (or country). Literature searches yielded suitable data for examining within country variation in all six geographical regions. The level of heterogeneity among communities within the same country was assessed using community level estimates of prevalence from different studies. Variation in prevalence

within countries was estimated for nine countries for *A. lumbricoides,* eight countries for *T. trichiura,* and ten countries for hookworm (Figure 10). The number of prevalence surveys available within each country ranged from 21 to 115. A total of 1600 prevalence surveys were examined in this analysis. The within country distributions differed between worm species and between countries but were not markedly skewed or asymmetrical. Good correspondence is found between the data and the theoretical Normal distribution which was therefore used.

[figure 11]

Highly significant positive correlations between mean and standard deviation were observed for *A. lumbricoides* and *T. trichiura* distributions (figure 11a&b). Therefore an estimate of "typical" geographical heterogeneity within a population unit could be estimated for these species from the regression. Hookworm show a wider range of standard deviations and there was no significant correlation between these and the means (figure 11c). This may reflect the fact that the hookworm data include undifferentiated estimates for two quite different parasite species (*A. duodenale* and *N. americanus*). This additional source of variation was captured by taking the mean of the standard deviations as an estimate of within population unit heterogeneity.

These estimates of the geographical variation in prevalence within a population unit were assumed characteristic of each species and were incorporated in the model for all subsequent calculations.

2.4 Summary of Estimation Procedure Assumptions

The framework for estimation of the population at risk of disability involves a set of assumptions about the patterns of infection observed at both the community and the regional level.

Community Level Assumptions

Worm burden frequency distributions are adequately described by the negative binomial distribution. This probability distribution is the most widely accepted empirical description of observed worm burden distributions (see Anderson & May, 1991). However, it has been shown in some parasite species to underestimate the proportion of very low worm burdens and thus, potentially, overestimate the number of people in the higher worm burden classes. This could lead to an overestimation of the population at risk.

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The frequency distribution of worm burdens is species specific and largely independent of geographical region, infection prevalence or age group. Analyses of the available empirical data suggest that the degree of aggregation, as assessed by the negative binomial parameter, k, is remarkably consistent between studies and largely independent of geographical region for all the nematode species considered here (Guyatt *et al*, 1990; Lwambo *et al*, 1992; Booth, 1994). There is some evidence that k increases slightly with prevalence of *A. lumbricoides* (Guyatt *et al*, 1990) and even more marginally with hookworm prevalence (Lwambo *et al*, 1992). Exclusion of this effect would lead to over-estimation of potential morbidity. There is conflicting and limited evidence for the relationship between worm burden distribution and age, with some studies showing an increase and others a decrease in aggregation with age (Bundy *et al*, 1987b). The current assumption of an age-independent distribution could lead to either over or under-estimation of potential morbidity.

Disability occurs above a worm burden threshold which is higher for adults than children. Thresholds were estimated from empirical data (Table 1). Two sets of thresholds were used for each species. An overestimate of the threshold worm burden would lead to an underestimate of potential morbidity and *vice versa*. No information is available on the variation of the threshold with age.

The age prevalence profile can be generalised between communities. A similar general pattern is seen when age prevalence profiles from different studies of the same species are compared (Anderson & May, 1985). The effect on the estimates of changing the shape of the age-prevalence profile are likely to be complex but in general, the larger the differences in prevalence between different age groups, the higher the estimate of population at risk.

Regional Level Assumptions

Infection prevalences between communities in the same country are Normally distributed. Examination of the actual distributions suggested a Normal approximation would be appropriate (Chan *et al*, 1994). The use of a symmetrical distribution is the most conservative assumption since with a skewed distribution with the same mean (such as the negative binomial distribution), the frequency of very high prevalences will be increased . The current assumption may therefore tend to underestimate the population at risk.

The standard deviations of these Normal distributions increase linearly with the mean prevalence for A. lumbricoides and T. trichiura and are independent of mean prevalence for hookworms. These assumptions are the best available estimates of the effect of spatial heterogeneity on the prevalence distribution, and are based on data presented in Chan *et al*, 1994.

The mean-standard deviation relationship is the same in different geographical regions of the world. The data available suggest a consistent relationship but there are insufficient data to assess this relationship by region. It is not known if there are any regional differences nor whether these might increase or decrease the estimates.

A population unit of 20 to 100 million people is a sufficiently fine-grained spatial stratification to capture geographical variation in a population of 4.1 billion people. The size of this unit is constrained by the availability of empirical data. Larger units would reduce the precision of the estimates of potential morbidity.

2.5 Estimation Procedure

The method used for estimation is essentially an integration of all the processes described in the text and is illustrated as a flow chart in figure 12. Fuller details are given in Chan *et al.*, 1994. In summary, the procedure involved the following steps.

[figure 12]

1. Country (or other population unit) prevalence data are obtained and divided into prevalence classes (vector R in figure 1). Five prevalence classes were defined and an intermediate prevalence value (S) was used for calculation purposes. These classes are shown in table 3.

[table 3]

2. The total populations in each prevalence class are multiplied by the transition matrix (M) to give an estimated community distribution of prevalences for the region (C). The matrix is derived using the following procedure. For each reference prevalence class in the estimation, a Normal distribution for the individual community prevalence class distribution in the countries concerned was calculated. For *A. lumbricoides* and *T. trichiura* a standard deviation that increased with mean was used whereas with hookworms a constant standard deviation given by the average standard deviation of the data sets was used. The regional community distribution of prevalences can then be obtained by multiplying a vector of the country mean

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prevalence distribution with a species specific transition matrix which consists of the calculated Normal distributions:

$$C = R.M \qquad (1)$$

The community prevalence distribution has one zero prevalence class and four non-zero prevalence classes equivalent to the four lower prevalence classes of the country prevalence distribution (table 3). Note that in the previous estimation (Chan *et al* 1994) a fifth prevalence class (>75%) was included. This is now considered to over-emphasise the top end of the prevalence range and thus to overestimate the population at risk, and was therefore not used in the present calculations.

The transition matrices used for each of the species are shown in table 4 a-c.

[table 4]

3. Using regional demographic data, the population is divided into classes of community prevalence and age group and the age-weighted prevalence is calculated for each of these classes. The age weights (*A*) are shown in table 2. Given a community prevalence s_i for prevalence class *i*, the prevalence in adults ($p_{i,15+}$) is given by:

$$p_{i,15.} = \frac{s_i}{\sum_j (a_j d_j)} \qquad (2)$$

where a_j is the age weight for age group *j* and d_j is the proportion of the population in age group *j*. The age specific prevalence in the other age groups are then given by:

$$p_{ij} = p_{i,15.} a_j \qquad (3)$$

4. For each of the classes, using the species specific aggregation parameter (*k*) and age specific morbidity threshold (t_j), the potential morbidity estimate (e_{ij}) is calculated using the negative binomial distribution. This theoretical distribution has two parameters, the mean worm burden, μ, and the aggregation parameter *k*. These are related to the prevalence (*P*) in the following way:

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$$P = 1 - (1 + \frac{\mu}{k})^{-k} \tag{4}$$

The basis for the estimation of the population at risk of disability is that morbidity is mainly confined to the fraction of the population with high worm burdens. A threshold worm burden (T) is defined over which morbidity effects are potentially observed (table 1). The individual terms of the negative binomial, $\pi(x)$, (the proportion of individuals with x worms) are given by:

$$\pi(x) = (1 + \mu/k)^{-k} (\frac{\Gamma(k+x)}{x! \ \Gamma(k)})(\frac{\mu}{\mu+k})^x \tag{5}$$

where Γ represents the gamma function. The proportion of the population with more than (T) worms (the morbidity function $Morb(P,T)$) is therefore given by:

$$Morb(P,T) = 1 - \sum_{x=0}^{x=T} \pi(x) \tag{6}$$

The potential morbidity estimate (e_{ij}) is obtained by multiplying the morbidity function by the population in each class (n_{ij}).

$$e_{ij} = n_{ij} \ Morb(p_{ij}, \ t_j) \tag{7}$$

5. The above estimates are summed to give the age specific population at risk estimates for each region (f_j).

$$f_j = \sum_i e_{ij} \tag{8}$$

These procedures were followed for each of the parasitic infections under consideration.

2.6 Estimates of Population Infected and at Risk of Disability

The estimates are shown in tables 5 to 10. For each nematode species, these estimates are given for different age classes and for different geographical regions. Two estimates of

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population at risk are presented for each infection, based on different estimates of worm burden thresholds. Both thresholds are based on empirical data and were chosen to be relatively conservative. The lower estimate of worm burden reflects probable developmental consequences of infection such as impaired growth or fitness while the higher estimate is intended to reflect the likelihood of more serious consequences of infection.

The estimates of population infected are all slightly lower than those presented in Chan *et al*, 1994, due to the exclusion of the highest reference prevalence class from the present extrapolation procedure (see 2.6). This has had an even greater effect on reducing the estimated size of the population at risk of disability from ascariasis and trichuriasis, and on the estimated population above the high threshold for hookworm infection. The estimated population above the lower threshold of hookworm burdens has however increased as a result of the change in threshold (see 2.3).

[tables 5]

The estimates for *A. lumbricoides* are shown in tables 5. The estimated total number of *A. lumbricoides* infections is 1274 million, slightly higher than estimates from other sources (WHO, 1987; Bundy, 1990; Crompton, 1988). The number at risk of morbidity is estimated in the range 12 to 59 million. The overall infection prevalence is 31% in the exposed population while the prevalence of those at risk in the exposed population is between 0.3% and 1.4%.

The model assumes that prevalence of *A. lumbricoides* infection is slightly higher in children of 5 to 15 years old as compared with adults and younger children (Anderson & May, 1985). The results show that this difference is greatly magnified in the estimates of population at risk, such that potential morbidity is significantly higher in school age children than in any other age group. This is due to the non-linear relationship between prevalence of infection and potential morbidity (Guyatt *et al*, 1990).

[tables 6]

The estimates for *T. trichiura* are shown in table 6. The totals show a lower number of infections than for *A. lumbricoides*, there being 902 million infections resulting in a global prevalence of 22%. The total population at risk is also lower for *T. trichiura*; in the range 7 to 26 million.

[tables 7]

The estimates for hookworm infections are shown in table 7. There are an estimated 1278 million hookworm infections and between 35 and 148 million people at risk of disability. The distributions of infection and morbidity, both by age and region, are different from those for A. lumbricoides and T. trichiura. The disability risk due to hookworm infections is much higher in adults. The regional distribution is also different, with the highest prevalence of estimated disability in India.

3. REVIEW OF EMPIRICAL DATABASES BY REGION

In contrast to most other diseases examined in this volume, direct estimates of the community morbidity attributable to intestinal helminthiases are unavailable. Hence the DALY estimates are based on extrapolating the population at risk (intensely infected) from empirical observations of the proportion of the population infected.

The prevalence of infection data used in the current estimation are from a database held at Oxford University, derived from field survey data compiled for a UNESCO report on global prevalence of helminth infection (Bundy & Guyatt, 1990). They are based on an extensive search of the original literature and, as far as possible, represent data collected within the last 20 years, data older than this only being used if no other data were available for a particular country. Additional criteria for data selection include: large sample size and community based studies (i.e not hospital records or institutional data). The number of studies available for each country varied and hence the reliability of the estimate for mean prevalence also varies. For the majority of countries the sample size was at least several thousand individuals. Note that the data presented in Table 8 excludes a substantial number of unpublished surveys used in the actual analysis.

The survey estimates are based on the microscopic detection of parasite eggs in faecal specimens. While A.lumbricoides and T.trichiura eggs can be readily identified, the eggs of the two hookworm species, Ancyclostoma duodenale and Necator americanus, cannot be distinguished by normal diagnostic methods and are recorded here as the combined prevalence of both species. The stool examination procedure also fails to detect light infections, particularly when single examinations are made as in the case of field surveys (Hall, 1982). Furthermore, the procedure will not detect non-fecund infections (eg single worm or single

sex) which may represent a significant minority of infections (Guyatt, 1992; Guyatt & Bundy, 1995). Thus the survey data are conservative and underestimate the true prevalence of infection.

[table 8]

4. ESTIMATION OF DALYs

The analyses to this point have produced estimates of the size of the populations with worm burdens which are likely to result in some form of disability. This section focuses on the estimation of the proportion of the at risk population who are likely to be disabled and the degree of disability, and how this varies with such factors as age and sex. It also attempts to partition the relatively rare mortality attributed to intestinal nematode infection.

The calculation of DALYs is based on the population at risk of disability. It is assumed that there are three sources of DALY loss. Firstly, *contemporaneous* disability of two types: insidious deficits which occur in individuals with worm burdens above the lower threshold in Table 1 and which persists only as long as the individual remains infected (Type A morbidity); and more serious illness which affects those with worm burdens above the higher threshold (Type C morbidity), also during the course of the infection. Secondly, *chronic* disability which occurs in a small proportion of children with worm burdens above the lower threshold and which is life long (Type B morbidity) and finally, life years lost from *mortality*. The sum of these three effects gives the overall DALY estimate.

4.1 Population at Risk of Disability

These populations are estimated in Section 4, above, and shown in Tables 9 to 11. Note that these are not the populations infected but some fraction of these which are at risk of disability because their worm burdens exceed a threshold that has been shown to be associated with some disability. For each species there are two populations considered to be at risk, based on two estimates of threshold burden: a larger population with worm burdens exceeding the lower threshold (associated with insidious, developmental disability which is contemporaneous or permanent, categorised as morbidity Types A and B); and a smaller population with burdens exceeding the higher threshold (associated with more serious,

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contemporaneous disability, categorised as morbidity Type C). The proportion of the population at risk (**not** the prevalence of infection) is given in Tables 9 to 11.

[tables 9 to 11]

These estimates have been recalculated and differ from the original estimates (World Bank, 1993, Chan *et al*, 1994). For *A.lumbricoides* and *T.trichiura* they are substantially lower as a result of removing the highest prevalence reference class from the extrapolation analysis (see 2.6). This change avoids an over emphasis on the highest prevalence classes which contribute disproportionately to the at risk population, and so gives a more conservative estimate. For *A.lumbricoides*, the estimated population of the under-fives at risk of morbidity is much higher than previously because of the increase in the age-prevalence weight and the lowered thresholds. This results in similar estimates of the numbers of under-fives and five- to ten-year olds at risk of morbidity. For *T.trichiura* too, the estimated number of children below the age of five years at risk of morbidity has increased from previous estimates, as a result of the increase in the age-prevalence weight. For the hookworm estimates, there is the same change in procedure in the extrapolation analysis and a change in the worm burden thresholds (see 2.3). The change in threshold was necessary to correctly assign the thresholds to the appropriate age classes in the light of new information. The effects of these changes for hookworm infection are to substantially reduce the estimated size of the population above the higher threshold and to slightly increase the population above the lower threshold.

4.2 Contemporaneous Effects of Infection.

Given that people in endemic areas are continuously infected and reinfected throughout life it can be assumed, for present purposes, that incidence is numerically equivalent to prevalence and that infection duration is one year.

With *A. lumbricoides* the most common consequences of infection are insidious effects (Type A morbidity) which are often manifested as effects on development (reviewed by Crompton, Nesheim and Pawlowski, 1989). They are, however, contemporaneous effects in that they can be partially reversed on treatment; that is, they occur only while infection persists. Such effects include reduction in growth rate (height-for-age and weight-for-age), physical fitness and appetite, for school age and younger children (Stephenson *et al*, 1989, 1990, 1993). There is also evidence that this infection has consequences for cognitive ability in school age children.

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Cognitive consequences have yet to be sought in adults, but it would be surprising if adults responded differently from children since the effect is on ability rather than development. We assume here that adults with above threshold worm burdens are affected, although the proportion of adults in this category is very small (0.02%).

The disabling consequences of reduced physical fitness and cognitive ability have yet to be empirically quantified, as is the case for many of the morbid effects for which DALY estimation is attempted. We assume here, by default, that this type of morbidity results in disability at the lowest disability weight (Class 1) and that all those with worm burdens above the lower threshold are at risk.

There are also more serious consequences of infection, largely associated with obstruction of ducts and intestinal lumen by these large worms (Type C morbidity). Systematic data on these acute complications are lacking, but the numerous reports based on inpatient records suggest that ascariasis is an important cause of hospitalisation in endemic areas (reviewed by Pawlowski and Davies, 1989). Ascariasis was the cause of 2.6% of all hospital admissions in Kenya in 1976, and 3% in a children's hospital in Myanmar between 1981 and 1983 (Stephenson et al, 1980; Thein-Hlaing, 1987). Complications due to ascariasis accounted for 0.6% of all admissions to a paediatric surgery department in South Africa in 1987, 5.8% of emergency admissions to a hospital in Mexico in 1975, 10.6% of admissions for acute abdominal emergency to a children's hospital in Myanmar, and between 0.8% and 2.5% of admissions in a survey of hospitals in China (WHO, 1987; Flores and Reynaga, 1978; Thein-Hlaing et al, 1990). The most common abdominal emergencies presenting are intestinal obstruction and biliary ascariasis, the proportions varying geographically, perhaps due to differences in diagnostic procedures (Maki, 1972). In an analysis of nine studies, each consisting of 100 or more patients hospitalised due to ascariasis, intestinal obstruction accounted for 38 - 87% of all complications, with a weighted mean of 72% (de Silva et al, in press). The classical surgical presentation is in patients between 3 and 10 years of age, although adults also may be affected (Davies and Rode, 1982; Chai et al, 1991). Laparotomy due to ascariasis was the second most common cause of all laparotomies in 2-4 year old children in Durban, Lishiu and Sao Paulo, and the fifth or sixth cause in adults in Myanmar, China and Nigeria (WHO, 1987). Analysis of empirical data from 11 studies of patients

hospitalised due to intestinal obstruction in areas endemic for ascariasis (prevalences ranging from 9 to 92%) indicated that the estimated incidence of *Ascaris*-induced intestinal obstruction varied between 0 and 0.25 cases per year per 1000 population in these areas, increasing non-linearly with rising prevalence as indicated in Figure 13 (de Silva *et al*, in press). This is equivalent to about 2% of the number of individuals exceeding the higher threshold. These patients will suffer a severely disabling condition, which may be life threatening (see 4.4 below), but which can be alleviated by appropriate clinical management. If it is assumed that such cases are managed appropriately, then the duration of disability is likely to be of the order of a few weeks. Complicated ascariasis has a reported history of > 10 days followed by 5 days of management, while the management of biliary ascariasis involves 4-6 weeks of observation before opting for surgical intervention (Davies and Rode, 1982).

[figure 13]

In addition to these serious complications which are relatively rare, non-specific symptoms such as intermittent abdominal pain or discomfort, nausea, anorexia and diarrhoea are often seen in patients with ascariasis (Upatham *et al*, 1989), causing them to seek medical attention which may result in hospitalisation for a day or two (Dasmohapatra *et al*, 1971, Thein-Hlaing 1987, Chrungoo *et al*, 1992).

For purposes of the present analyses therefore, all those with worm burdens exceeding the higher threshold are considered to be at risk of disability for a period of approximately two weeks during the course of the infection. The large majority are assumed to suffer illness of a mild-moderate severity (80% in Class 2 and 18% in Class 3 for the 0-4 year olds and 5-10 year olds, 88% in Class 2 and 10% in Class 3 for the older age groups) and a small proportion from more severe disability (2% in Class 4, for all age groups).

With *T.trichiura* there is evidence that moderate intensity infections result in growth deficits that can be reversed by the anthelmintic removal of the worms (Cooper *et al*., 1990; Figure 7), and that these infections result in a protein losing enteropathy and anaemia (Cooper *et al*, 1991; 1992; MacDonald *et al*, 1991; Ramdath *et al*, 1995). In young children there are also effects on development quotient (Griffiths locomotor subscale), anaemia and growth which are at least partially reversible by anthelmintic therapy (Callender *et al* 1994). There is also

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an increasing body of evidence that both cognitive function (Table 12a) and educational achievement are impaired by moderate intensity infections, and that at least some of these effects can be reversed by anthelmintic treatment (Nokes *et al.*, 1992a & b. Simeon *et al*, 1995a; 1995b). As for ascariasis, it is assumed that all those with worm burdens above the lower threshold are at risk of these contemporaneous developmental effects of trichuriasis (Type A morbidity) and result in the lowest disability weight (Class 1) for the duration of the infection.

Particularly large burdens of *T. trichiura* may result in the "classical" dysenteric form of trichuriasis, synonymous with Trichuris Dysentery Syndrome (Ramsey, 1962) and Massive Infantile Trichuriasis (Kouri & Valdes Diaz, 1952). This typically occurs in children between 3 and 10 years of age and is associated with burdens involving at least several hundreds of worms carpeting the colonic mucosa from ileum to rectum. The colon is inflamed, oedematous and friable, and often bleeds freely (Venugopal et al, 1987). Reviews of case histories suggest that the mean duration of disease at the time of presentation is typically in excess of 12 months and that relapse after treatment frequently occurs (Gilman *et al*, 1983; Cooper *et al*, 1990; Callender *et al* 1994). The probability of relapse, and of a child experiencing multiple episodes, is greatly enhanced because a proportion of heavily infected children are predisposed to reacquire heavy infection even after successful treatment (Bundy *et al*, 1987) (see also section 4.3). The typical signs of the syndrome (see Bundy & Cooper, 1989a for a review of 13 studies involving 697 patients) are rectal prolapse, tenesmus, bloody mucoid stools (over months or years), growth stunting, and a profound anaemia which may lead to a secondary anaemia. The complete spectrum of clinical features associated with the syndrome occurs in some 30% of children with intense trichuriasis. Many of the major clinical effects are reversible by appropriate therapy (Cooper, Bundy and Henry, 1986; Gilman *et al* 1983), hence the disability is considered here to be a contemporaneous consequence of infection, and categorized as Type C morbidity. For the present analyses it is assumed that all those with worm burdens above the higher threshold are at risk, that the disability is contemporaneous with infection, has a duration of 12 months, and that severity varies between Class 2 and 4. For affected children (0-15 yrs), it is assumed that 90% are in Disability Class 2, 8% in Class 3 and 2% in Class 4; among adults at risk, 90% are in Class 2, and 10% are in Class 3. Since all those exceeding the higher thresold are also necessarily counted among those exceeding the lower threshold, in order to avoid double counting, the

number in the former category was subtracted from the latter in calculating the proportion at risk of Type A morbidity in trichuriasis.

With hookworm the major consequence of infection is anaemia (see Schad & Banwell, 1984 and Crompton & Stephenson, 1990 for reviews of the extensive literature in this area). Anaemia is associated with: reduced worker productivity; reduced adult and child fitness; reduced fertility in women; reduced IUGR, prematurity and low birth weight; and cognitive deficits (Fleming, 1982; Stephenson et al, 1993; Pollitt et al, 1989; Boivin et al, 1993) (Table 12a, 12b). Since the higher threshold for hookworm infection intensity was selected on the basis of the development of anaemia it is here assumed that 100% of those exceeding this threshold suffer some form of disability equivalent to Type C morbidity in ascariasis and trichuriasis. As discussed elsewhere in this volume and in the original Global Burden of Disease estimates (World Bank, 1993), the consequences of anaemia will be more serious for a subset of the affected population, resulting in Class 2 and Class 3 disability. For the present analyses the Global Burden of Disease disability weight distribution for anaemia was used namely, 70% in Class 2, 24% in Class 3 and 6% in Class 4.

In order to incorporate the fact that children and women of child-bearing age are at higher risk of developing anaemia subsequent to hookworm infection (Holland, 1987), it was assumed that while all children and women of child-bearing age with worm burdens above the higher threshold are at risk of anaemia, only 50% of the adult males and women over 45 years of age are at risk.

For the other two species it is assumed here that the effects are independent of host sex. It is also assumed that the disability weight is age-independent since the method of extrapolating the population at risk incorporates age-weights in both the prevalence of infection and the threshold associated with disability by age.

4.3 Chronic Effects of Infection

In addition to the contemporaneous effects of infection there is evidence that some consequences of infection are irreversible. This is the case for some cognitive deficits (Table 12), some elements of development quotient (Callendar, 1994), and for some growth effects (Stephenson et al, 1993) during childhood. In all studies, some forms of disability in a

proportion of children do not respond to therapy (see for example Figure 6). We estimate that in any annual cohort of heavily infected children some 5% suffer these permanent consequences. Studies of reinfection show that children are predisposed to a particular intensity of infection (Keymer and Pagel, 1990; Hall *et al* 1992), such that some 30% of heavily infected children in an annual cohort would be expected to reacquire heavy infection. Thus each year the proportion of children exceeding the threshold worm burden will consist of some 70% of individuals who have not previously experienced heavy infection, which implies a cumulative increase in the proportion suffering permanent disability. We therefore assume that each year 3% of newly heavily infected children, and children only, suffer life-long consequences of infection.

The disability attributable to these effects, categorized here as morbidity Type B, has yet to be empirically determined. Stunted children may be disadvantaged in education (Moock and Leslie, 1986; Jamison, 1986; Glewwe and Jacoby, 1995), as are children with low development quotients or cognitive impairment (Pollitt, 1990). On the other hand, physical and mental maturation may eventually compensate, to some degree, for initial retardation (Pollitt *et al*, 1986). In a recent study of two years nutritional supplementation of stunted children, locomotor development improved in the first year (as seen with anthelmintic treatment of trichuriasis (Callender et al, 1994)) while other areas of development did not improve until the second year (Grantham-McGregor *et al*, 1991). Given this uncertainty we assume that the permanent consequences of infection result in disability at the lowest weight (Class 1). Thus in calculating the DALYs for all the helminth infections it is assumed here that 3% of children experiencing worm burdens above the lower threshold suffer permanent disability of Class 1. Since the basic population at risk for both morbidity Types A and B in ascariasis and trichuriasis are those individuals with worm burdens exceeding the lower threshold, in order to avoid double counting in calculating DALYs for these two infections, the proportion of children at risk of Type A morbidity is assumed to be 97%.

4.4 Mortality

This is the weakest area of DALY estimation because of the lack of empirical data. Ascariasis is the best documented helminthiasis in terms of mortality. There are numerous studies of case fatality rates in hospitals (reviewed by Pawlowski and Davies, 1989). Analysis of data from six studies each consisting of at least 100 patients hospitalised for

complications of ascariasis, indicated that the case-fatality rate in these cases ranged between 3 and 10%, with a weighted mean of approximately 5% (see Table 13). These studies confirm that death is a not infrequent outcome of complications of ascariasis, but provide little insight into mortality rates in the community. An extrapolation from central hospital data in Myanmar suggests there are 0.008 deaths per 1000 infections per year (Thein-Hliang, 1987), but this is considered to be a considerable underestimate since only a small proportion of children with severe complications is likely to have access to the hospital (Pawlowski and Davies, 1989). Only two population based estimates are available: for the Darmstadt epidemic (0.1 deaths per 1000 infected per year: Krey, 1949) and for Japan prior to national control efforts (0.061 per 1000: Yokogawa, 1976).

[table 13]

For purposes of these analyses, all deaths due to ascariasis were assumed to result from an acute complication of ascariasis. Based on the relationship presented in de Silva *et al* (in press), an estimate was made of the probable number of cases of *Ascaris*-induced intestinal obstruction, which was then assumed to represent 70% of the total number of complicated cases. The number of deaths attributable to ascariasis was then calculated on the assumption of a 5% case-fatality rate in those with complicated ascariasis.

No population based mortality estimates have been published for *T.trichiura* infection. Prior to the advent of safe and effective therapy for *T.trichiura* infection in the late 1970s a number of reports describe paediatric inpatients with Trichuris Dysentery Syndrome who, despite clinical efforts, died as a result of profuse haemorrhage and secondary anaemia (Wong & Tan, 1961, Fisher & Cremin, 1970) or of intussusception (Reeder et al, 1968). Although there continue to be reports of the syndrome (see 4.2, above), a fatal outcome in a clinical setting today would suggest inappropriate management. The picture in the community, however, may be rather different since, in the absence of specific diagnosis, the aetiology of the chronic bloody dysentery may be unrecognised. Nevertheless, mortality is undoubtedly a rare consequence of the 1 billion infections. For present purposes it is assumed there are 10,000 paediatric deaths a year, which are here (Table 10) partitioned by age and region as for *A.lumbricoides*.

The profound anaemia of hookworm infection (see 4.2, above) is life threatening and is

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estimated, although the means of estimation is not described, to result in 65,000 deaths per year (WHO, 1992). Again there is a lack of empirical data, presumably, in this case, because of the difficulty in identifying the aetiology of anaemia-related deaths. This figure is used, by default, in the present analyses and is partitioned to ascribe the highest proportion of mortality to women of childbearing age (15-44 years, 35,000 deaths) and equal numbers in the other adult age groups (10,000 deaths each in women aged 45-60, men aged 15-44 and men aged 45-60). The distribution of deaths between regions is partitioned in the same way as for the other infections.

In including these estimates of mortality we recognise that they are unsupported by vital registration statistics. But it should also be recognised that intense infection is most prevalent in the poorest regions of the poorest countries. In such areas mortality may be most likely because of limited access to appropriate management, while both the diagnosis of cause of death and its registration may be least reliable. There is clear evidence that deaths do occur, what is unclear is the extent of this mortality.

5. DISABILITY

The disability weights and their proportionate distributions are shown in Tables 13a, 13b and 14.

[tables 14 and 15]

Much of the disability associated with helminth infection is insidious and would be unlikely to be brought to clinical attention. As such it is difficult to compare with the more classical clinical signs. On the other hand, cognitive deficits may have profound consequences for educational outcomes and growth stunting is one of the best characterised correlates with underachievement, so these insidious effects may have far reaching societal consequences. Achieving some realistic balance between the clinical consequences for the individual and developmental consequences for society goes beyond the scope of the present exercise, and would require a more sophisticated weighting system, if indeed the effects could be quantified. For present purposes, the very low proportional weighting selected for the chronic effects of infection is influenced by the view that the Class 1 disability weight may be an overestimate of the effects of infection from a clinical perspective.

6. OTHER CONSIDERATIONS IN CALCULATING BURDEN

There are three main reasons why the burden of intestinal helminths may not be adequately captured by the present calculations.

1. There are no direct measures of morbidity against which the extrapolation procedure could be conclusively validated. Although each step in the extrapolation was independently assessed against empirical data as far as possible, there must remain uncertainty until observed data become available.

2. The mortality data are largely unsubstantiated. Mortality has the potential to significantly alter the overall burden estimates. It is therefore unsatisfactory that this central dataset has received so little research attention.

3. There is a particular lack of information on the morbid consequences of infection in young children. It is possible that even very low worm burdens may have disproportionately severe effects on developing physiologies and organ systems.

4. As discussed in Section 5 above, the societal consequences of growth stunting and educational underachievement may be of substantially greater relevance than the disability in the individual.

7. DISEASE AS RISK FACTORS FOR OTHER DISEASES

Intestinal nematode infection is associated with malabsorption and is a potentially important predisposing factor for malnutrition in communities on marginal diets. These effects may relate broadly to PEM, or to specific deficiencies . For example, *A. lumbricoides* infection has been associated with malabsorption of Vitamin A.

Hookworm infection and to a lesser extent trichuriasis are associated with iron loss predisposing to anaemia. It is self evident that the risk of anaemia is dependent on iron balance and thus that infection may be an important contributing factor.

The attributable contribution to global malnutrition is potentially considerable given the ubiquity of infection and its specifically high prevalence in the poorest societies with the least adequate diets.

8. BURDEN AND INTERVENTION

The major intestinal helminth infections can be effectively treated simultaneously with single dose oral therapy. The treatment is widely available, safe, simple and cheap. Prevention of reinfection requires reduction in transmission, which can be achieved by synchronised treatment programmes and by improvements in sanitation.

In the absence of currently financed health interventions there would be some increase in the current burden. For example, there would be a greater number of deaths from intestinal obstruction in the absence of operative procedures, and from severe anaemia or malnutrition in the absence of rehabilitation therapy. However, with some important exceptions such as Japan and Korea, control of intestinal helminth infections is only rarely a component of national public health programmes.

It could be argued that the entire burden could eventually be avoided by appropriate application of currently available interventions. For example, evidence from Korea and Japan indicates that reduction in the prevalence of *A.lumbricoides* infection at the national level results in a significant decline in acute complications of ascariasis requiring hospitalisation (Chai *et al*, 1991) and in ascariasis related mortality (Yokogawa, 1976). Curative treatment would mitigate the contemporaneous or acute effects of infection, while measures to control transmission would avoid chronic developmental disability, although neither could reverse the deficits that are already present in the population.

Economic analyses suggest that carefully targeted community treatment programmes are exceptionally cost-effective (Warren et al, 1993; Guyatt & Evans, 1992; World Bank, 1993). This arises because the therapy is cheap (US$0.20 or less per dose), is required at infrequent intervals (of the order of one year), can have community wide effects even if targeted at some fraction of the population which makes the greatest contribution to transmission (such as school age children), and can be delivered through existing infrastructures (such as schools or the PHC system).

9. CONCLUSIONS

The global morbidity due to intestinal nematode infections, although generally accepted to be

large, has proved difficult to quantify. The method presented here provides a framework whereby potential global burden may be estimated in the absence of any direct measures of morbidity. The estimates are intended to give some indication of the potential burden of intestinal helminthiases rather than to provide absolute values. It would of course be possible to seek further refinement of the approach, but our view is that the most pressing need is to obtain reliable community data on the observed levels of morbidity and on the consequences of disability. The present analyses indicate that even low levels of individual disability can sum to a considerable burden with such ubiquitous infections; the important question is what this implies for communities in practice. The analysis has revealed important lacunae in our knowledge of these infections and it is hoped that this might guide future applied research.

The present estimates suggest that the potential morbidity attributable to geohelminthiases is much greater than previously supposed. This reflects the inclusion of both the traditionally recognised clinical effects of helminthiases (see WHO, 1992) and more recently recognised developmental effects, which rarely result in clinical presentation but which may have major consequences for the individual and the community.

Another general implication of the results arises from the similarity of the age and regional distributions for *A. lumbricoides* and *T. trichiura* infection and morbidity. This observation has been made before for prevalence data (Booth & Bundy, 1992), and strong positive correlations between *A. lumbricoides* and *T. trichiura* prevalences in communities have been demonstrated. This suggests that these two infections could be controlled within a single programme. The age distribution of the burden also supports the conclusion that there are particular benefits in targeting control of *A. lumbricoides* and *T. trichiura* infection at school age children (Bundy *et al*, 1985; Savioli *et al*, 1992).

The results suggest that the vast majority of the morbidity due to intestinal nematodes is readily avoidable or reversible using existing and cost-effective approaches, and that the mortality is also a largely avoidable or remedial consequence of acute infection. These observations, and the scale of the burden of current disease, argue for greater public health emphasis on the control of intestinal helminthiases.

ACKNOWLEDGEMENTS

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FIGURE LEGENDS.

Figure 1: Frequency distributions of the major intestinal nematodes of humans. All the distributions are markedly overdispersed (Data from Seo *et al*, 1974; Bundy, 1986; Schad & Anderson, 1985).

Figure 2: Age-prevalence profiles for geohelminths (Data from Hsieh, 1970; Bundy *et al*, 1987a).

Figure 3. Non-linear relationship between infection prevalence and intensity for *Ascaris lumbricoides* based on anthelmintic expulsion as a measure of intensity (redrawn from Guyatt *et al*, 1991), and for hookworm (Lwambo et al, 1992) and *T.trichiura* (Booth *et al.*,1994) based on egg counts in faeces.

Figure 4: Age-intensity profiles for a) *A. lumbricoides* (x7) and *T. trichiura* (Bundy, 1988), b) *Necator americanus* (data from Bradley *et al*, 1992; Pritchard *et al*, 1991).

Figure 5. Profile of the relationship between *T.trichiura* worm burden and clearance of alpha-1 antitrypsin, a measure of gut leakage and protein losing enteropathy (Cooper *et al*, 1991). The relationship is markedly non-linear.

Figure 6. Distribution of growth velocity in a population of school age children with mixed intestinal helminth infections (Stephenson *et al*, 1993). The group receiving treatment shows a significant improvement over the placebo group.

Figure 7. Growth velocity against age for children with moderate to heavy *T.trichiura* infection (Cooper *et al*, 1990). The children exhibit dramatic catch up growth after anthelmintic treatment even though they remain on the same, often marginal, diet.

Figure 8. Double blind trial of one test of cognitive function in school age children (Nokes *et al*,1992). Infected and uninfected children have significant differences in cognitive function prior to intervention. All groups show some improvement on retest, as a result of prior experience of testing. But the treated group of infected children show significantly greater improvement than the placebo group of infected children, and on retest are not significantly different from the group which was uninfected initially.

Figure 9. Non-linear relationship between predicted prevalence of morbidity and prevalence of *Ascaris lumbricoides* infection. Each line represents the theoretical form of the relationship (for k=0.54), assuming different threshold worm burdens (from 5 to 30 worms) at which infection is assumed to be associated with disease (redrawn from Guyatt *et al*, 1991).

Figure 10. Representative examples of frequency distributions of community prevalence measured from different surveys in the same country/population unit. The figure shows frequency distributions for hookworm prevalence in population units in which the average prevalence is between 25% and 45%. The shaded bars show the theoretical Normal distribution with mean of 35% and standard deviation of 20% as used in the model. The lines show actual data from Zambia (+), Kenya (x), Nigeria (*) and Malaysia/ Thailand (▲).

Figure 11. Graph to show relationship between standard deviation and mean of prevalence

data from within country prevalence frequency distributions. Each square represents the mean and standard deviation of the prevalence frequency distribution in a particular country/region and the data points are marked with their country of origin. Figure 7a. *Ascaris lumbricoides*. Data come from the countries/regions of (with abbreviation and number of community prevalence surveys in brackets) Nigeria (NIG, 52), Chile (CHI, 64), North Africa (NAF, 31), East Africa (EAF, 91), India (IND, 115), Ethiopia (ETH, 29), Mexico (MEX, 53), Cameroon (CAM, 53) and Indonesia (INS,37). The line shows the regression fit which gave a correlation coefficient, r^2, of 0.66 which is significant at p=0.01. Figure 7b. *Trichuris trichiura*. Data come from the countries/ regions of North Africa (31), Nigeria (50), East Africa (82), India (100), Chile (77), Mexico (46), Indonesia (37) and Cameroon (53). The line shows the regression fit which gave a correlation coefficient, r^2, of 0.67 which is significant at p=0.01. Figure 7c. Hookworms. Data come from the countries/ regions of Ethiopia (46), Nigeria (55), North Africa (31), Kenya (KEN, 45), Zambia (ZAM, 21), Mexico (48), Tanzania (TAN, 22), Malaysia/ Thailand (M&T, 31), Indonesia (37) and India (115). There was no significant correlation and the average standard deviation is 20.

Figure 12. Flow chart to show method of calculation for morbidity estimates.*Notes:*1. The indices i and j refer to prevalence class and age class respectively; 2. The letters in lower case denote elements of the matrix of the same letter in upper case. e.g. a_j are the elements of the matrix A; 3. $p_{i,15+}$ denotes the prevalence in each class for the over 15 years age group (adults); 4. The function "*Morb*" is the proportion of individuals with more than t_j worms in a population of with prevalence p_{ij} as estimated by a negative binomial distribution of worm burdens with $k=0.543$ *(A lumbricoides)*, $k=0.23$ *(T trichiura)* and $k=0.343$ (hookworms) [see text for more details].

Figure 13. Relationship between the prevalence of infection with *A. lumbricoides* and the estimated number of cases of *Ascaris*-induced intestinal obstruction / year / 1000 population (redrawn from de Silva *et al*, in press). The regression line is of the form $y=b_1x^2 + b_2 x$, where $b_1=0.222889$ (S.E. = 0.068795, p=0.01) and $b_2=0.00001179152$ (S.E. 0.047877).

TABLE LEGENDS

Table 1. The worm burden thresholds selected for use in the model. The lower thresholds are based on empirical observations of worm numbers associated with developmental deficits. The higher thresholds are a more conservative value intended to provide a lower bound to the estimate of morbidity. The thresholds were estimated for children in the 5-10 year age class, and then adjusted for other age classes using the procedure described in the text. The lower threshold estimate for *Ascaris lumbricoides* assumes that 30,000 epg is associated with deficits in growth and fitness (see Stephenson *et al*, 1989, 1990) and that worm fecundity is equivalent to approximately 3000 epg/female worm (Muller, 1975). the higher threshold assumes that morbidity is associated with twice this burden. The *Trichuris trichiura* lower threshold is taken from studies of growth stunting in 5-10 year old children (Cooper *et al*, 1990), while the higher threshold is estimated from studies of clinical colitis (E. S. Cooper, personal communication). The hookworm thresholds are based on upper and lower bound estimates of the relationship between infection intensity and anaemia (Lwambo *et al*, 1992).

Table 2. Age prevalence weights

Table 3. Prevalence reference classes used in the estimation procedure.

Table 4. Transition matrices used in the estimation procedure.

Table 5. to 7 Results for ascaris, trichuris and hookworm: prevalence and at risk.

Table 8. Reported survey data.

Table 9, 10 11 ascaris, trichuris and hookworm data for the calculation of DALYs Proportion at risk and mortality are given as per 100,000 population. Durations are given in years. Incidence is not given since data are not available.

Table 12. Selected studies investigating the effects of parasitic helminth infection on 12a. Mental processing. 12b. Physical fitness.

Definitions for this table:

Intervention	One group receives treatment. Groups tested pre and post-intervention.
Placebo controlled	Infected group randomly assigned to treatment or placebo. Groups tested pre and post-intervention.
Case Control	Infected group compared to an uninfected group. Groups matched for age as a minimum. Infected group receives treatment. Uninfected group receives no treatment.
Pair-matched	Infected group and uninfected group pair matched for confounding variables other than just for age.
Cross-section	Infected group compared against Uninfected group. Neither group receives treatment. Groups tested at baseline only.

Presence	Subjects selected for the study on the basis of the presence of infection and not on the basis of the intensity of infection.
Intensity	Analysis of results takes into consideration the intensity of infection.
Light-Moderate	The intensity of infection of subjects recruited to the study.
Heavy Intensity	

ABBREVIATIONS

T	Infected Group treated with anthelmintic
P	Infected Group treated with anthelmintic Placebo
NoT	Infected Group receiving no intervention ie, no treatment or no placebo.
C	Uninfected Control receiving no treatment or placebo

Infd	Infected with parasite spp
Uninfd	Uninfected with parasite spp

KEY

x	Controlled for confounding variables and infection did not remain significant
*	Controlled for confounding variables and infection remained significant

No mark No attempt to control for confounding variables

Table 13. Case-fatality rates in studies of 100 or more patients hospitalised with any complication of ascariasis.

Table 14. Disability weights for contemporaneous effects

Table 15. Disability weights for permanent effects

Table 1. Worm burden thresholds for morbidity used in model

Species	Age class, years	Higher estimate, lower threshold	Lower estimate, higher threshold
A. lumbricoides	0-5	7	15
	5-10	15	30
	10-15	20	40
	15+	20	40
T. trichiura	0-5	90	250
	5-10	130	375
	10-15	180	500
	15+	180	500
Hookworms	0-5	20	80
	5-10	30	120
	10-15	40	160
	15+	40	160

Table 2. Age weights for prevalences used in model.

Species	age class	age weight
A. lumbricoides	0-5	1
	5-10	1.2
	10-15	1.2
	15+	1
T. trichiura	0-5	1
	5-10	1.2
	10-15	1.2
	15+	1
Hookworms	0-5	0.2
	5-10	0.5
	10-15	0.9
	15+	1

Table 3. Prevalence classes and reference (set) prevalences used in the model

class	prevalence range (%)	reference prevalence (%)
1	<25	10
2	25-45	35
3	45-60	52
4	60-75	67
5	75-100	80
4+5*	60-100	67

* combined classes 4 and 5 used for *community* prevalence distribution

Table 4a.   Transition matrix for *Ascaris lumbricoides*

Reference class

Community prevalence distribution

	0	1	2	3	4+5
1	0.251	0.59	0.149	0.01	0
2	0.081	0.264	0.31	0.186	0.159
3	0.057	0.149	0.214	0.175	0.405
4	0.021	0.081	0.149	0.169	0.58
5	0	0.048	0.097	0.133	0.722

A zero class community distribution denotes a prevalence of 0%

Table 4b   Transition matrix for *Trichuris trichiura*

Reference class

Community prevalence distribution

	0	1	2	3	4+5
1	0.288	0.509	0.177	0.026	0
2	0.097	0.259	0.288	0.18	0.176
3	0.068	0.153	0.2	0.17	0.409
4	0.028	0.087	0.149	0.157	0.579
5	0.011	0.047	0.101	0.125	0.716

A zero class community distribution denotes a prevalence of 0%

Table 4c   Transition matrix for hookworms

Reference class

Community prevalence distribution

	0	1	2	3	4+5
1	0.309	0.464	0.187	0.04	0
2	0.04	0.269	0.382	0.203	0.106
3	0	0.089	0.274	0.292	0.345
4	0	0.018	0.118	0.227	0.637
5	0	0	0.04	0.119	0.841

A zero class community distribution denotes a prevalence of 0%

Table 5.
Estimates of numbers infected and at risk of disability for Ascaris lumbricoides

Region	millions population	millions infections	infections %	millions at risk	at risk %
SSA	510	105	20.59	3.40	0.67
				0.60	0.12
LAC	444	171	38.50	8.80	1.98
				1.70	0.38
MEC	503	96	19.15	3.20	0.64
				0.60	0.12
IND	850	188	22.13	7.20	0.85
				1.40	0.16
CHN	1134	410	36.16	18.10	1.60
				3.50	0.31
OAI	683	303	44.36	18.40	2.69
				3.60	0.53
Total	4124	1273		59.00	
				11.50	

by age

age	millions population	millions infections	infections %	millions at risk	at risk %
0-5	554	158	29	20.80	3.75
				3.90	0.70
5-10	482	167	35	18.90	3.92
				5.20	1.08
10-15	437	154	35	11.20	2.56
				2.20	0.50
15+	2650	795	30	8.20	0.31
				0.20	0.01
total	4124	1274	31	59.00	1.43
				11.50	0.28

Table 6.
Estimates of numbers infected and at risk of disability for Trichuris trichiura

region	population	millions infections	infections %	millions at risk	at risk %
SSA	510	88	17.25	1.80	0.35
				0.50	0.10
LAC	444	147	33.11	5.50	1.24
				1.40	0.32
MEC	503	64	12.64	0.02	0.00
				0.00	0.00
IND	850	134	15.78	2.20	0.26
				0.60	0.07
CHN	1134	220	19.40	4.60	0.41
				1.10	0.10
OAI	683	249	36.46	12.20	1.79
				3.20	0.47
Total	4124	902	21.87	26.30	0.64
				6.80	0.16

by age

low	millions population	millions infections	infections %	millions at risk	at risk %
0-5	554	114	20.58	3.00	0.54
				0.30	0.05
5-10	482	122	25.29	11.40	2.36
				4.10	0.85
10-15	437	111	25.41	8.20	1.88
				2.40	0.55
15+	2650	554	20.91	3.60	0.14
				0.04	0.00
total	4124	902	21.87	26.20	0.64
				6.84	0.17

Table 7.
Estimates of numbers infected and at risk of disabililty for hookworms

region	millions population	millions infections	infections %	millions at risk	at risk %
SSA	510	138	26.93	18	2.46
				8	1.06
LAC	444	130	29.40	15	3.44
				3	0.70
MEC	503	95	18.81	8	1.54
				2	0.47
IND	850	306	36.00	47	5.48
				11	1.32
CHN	1134	367	32.36	26	2.29
				2	0.18
OAI	683	242	37.04	35	5.29
				8	1.29
Total	4124	1277	30.98	148	3.59
				35	0.85

by age

	millions population	millions infections	infections %	millions at risk	at risk %
0-5	554	42	7.58	0	0.00
				0	0.00
5-10	482	90	18.66	0	0.00
				0	0.00
10-15	437	147	33.65	10	2.29
				1	0.16
15+	2650	994	37.51	138	5.21
				33	1.25
total	4124	1273	30.87	148	3.59
				34	0.82

TABLE 8.

Summary of Global Burden of Helminth Infections

Country	Sample size	No: sites	Prev.Est. % Ascaris	Prev.Est. % Trichuris	Prev.Est. % Hw	Source
Sub-Saharan Africa						
Benin	423 135	1 1	60	35	N.a = 19	Pampliglione (1971) Par. 13(1-2): 275-
Burkina F.	913	2	0.5			Fauchet (1984)
Cameroon	27040 5040	530 18	45	53	N.a = 49	Ratard et al. Trans.Roy.Soc.Trop.Med.Hyg.85, 84-88 (1991) Carrie (1982) Med.Afr.N. 29(8-9): 557- Ripert (1982) Bull.Soc.Path.Ex. 75:55-61 Ripert (1978) Bull.Soc.Path.Ex. 71(4-5): 361-369 Ripert Epi.Geo.Hum
Cape Verde	1572		72			de Meira (1947) Barbosa (1956) Nogueira (1950)
C.Afr.Rep	214 126 88	5 3 2	19	17	N.a = 34 A.d = 83	Riciardi (1972) Par. 14(2-3): 9- Brumpt (1972) Bull.Soc.Path.Ex. 65:263-
Ethiopia	32276 1059 5506	290 41 95	40	40	N.a = 20 A.d = 1	Tedla. Ethiop.Med.J.24, 79 (1986) Taitcheff (1981) Eth.Med.J. 19:35-
Gabon	2684	21	39	68	43	Garin (1978) Bull.Soc.Path.Ex. 71:157 Richard-Lenoble (1982) Med.Afr.N. 29(8-9): 581-

Country	Sample size		%			Reference
Gambia	684	3	29			McGregor. Trans.Roy.Soc.Trop.Med.Hyg. 46(4),403-427 (1952) Marsden (1963) aFR.cH.h. 9:52
Ghana	422	4	52	30	17	Annan (1986) Para. 92: 209-217
Liberia	690	8	17	19	60	Sturchler (1980) Tropen.Para.31: 87
Madagascar	217	1	61	20	A.d = 30	Cerf (1981) Arch.Inst.Past.Mad. 48(1): 151
Madeira	3313	2	7	0.5	A.d = 18 N.a = 0.1	Santos (1952) Ann.Inst.Med.Trop. 9: 1155-1174
Malawi	289	10	4	15		Burgess (1973) Trop.Geo.Med. 25: 372-380
Mali	2174 2974 1797	4 5 3	0.5	0.5	N.a. = 58	Rougement (1974) Med.Trop.34: 30- Ranque (1982) Med.Afr.N. 29(8-9): 577-
Nigeria	1266	6	67	46.5	31	Oduntan (1974) Ann.Trop.Med.Para. 68(2): 145-
Renunion	2803	10	49	85	24	Bonnefoy (1978) Bull.Soc.Path.Ex. 71: 70-
Senegal	359	4	36	15	N.a = 9	Juminer (1971) Bull.Soc.Path.Ex. 64: 901-
Somalia	556 319	5 3	13	34	A.d = 8	Bianchini (1981) Para. 23: 122 Ilardi (1980) Para. 22(1-2): 141 Ilardi (1981) Para. 23: 191 Ilardi (1986) Trans.Roy.Soc.Trop.Med.Hyg. 81: 336-338
Sudan						Kuntz (1955)
Tanzania	276	1	2	43	N.a = 62 A.d =7	Sturrock (1964) E.Afr.Med.J. 41(11): 520-

Asc Tri Hw

#	Country						References
21	Togo	93504	6+	7	1	22	All from Lapierre (1982) Med.Afr.N. 29(8-9): 571
22	Uganda	157	3	0	0	38	Sorvillo (1982) Lancet 1(8277): 912
23	Zambia	4920	17		0	0	Wenlock (1977) Trop.Geo.Med. 29: 415-421
24	Zimbabwe	38484		0.5	0.5	10	Goldsmid (1976A) Cen.Afr.J.Med. 22(5): 91
		595					Blackie (1932) Goldsmid (1976B) All from Goldsmid (1976B) Cen.Afr.J.Med. 22: 221-
25	India	23949	59	8	13		Saxena (1971) Ind.Pub.H. 15(1): 31-37
		1270	48		16		Bidinger (1981) Para. 83: 373-380 Arora (1975) J.Com.Dis. 7(4): 264-268 Chowdury (1968) Am.J.Epid. 87(2): 313- Chatterjee (1985) Ind.Pub.H. 29(1): 9- Mukerji (1950) Ind.J.Med.Res. 38(1): 95- Lane (1916) Ind.J.Med.Res. 5: 274 Bagchi (1964) Ind.J.Med.Res. 52(4): 411-417 Sanyal (1972) Ind.J.Med.Res. 60(7): 979
26	China	1477742	2843	47	19	17	Yu 1994
	Other Asia and Islands.						
27	Indonesia	51364	77	71	48	29	Cross (1970) S.E.A.J.Trop.Med.Pub.H. 1(3): 354 Cross (1976) J.Trop.Med. June: 123-131
							Cross (1975) S.E.A.J.Trop.Med.Pub.H. 8(4): 532 Cross (1975) S.E.A.J.Trop.Med.Pub.H. 6(1):52 Cross (1977) S.E.A.J.Trop.Med.Pub.H. 8(3): 390 Clarke (1973) S.E.A.J.Trop.Med.Pub.H. 4(2): 195 Carney (1977) S.E.A.J.Trop.Med.Pub.H. 8(2): 165 Carney (1974) S.E.A.J.Trop.Med.Pub.H. 5(2): 246- Stafford (1980) S.E.A.J.Trop.Med.Pub.H. 11(4): 468 Joseph (1978) S.E.A.J.Trop.Med.Pub.H. 9(2): 264

Country						Reference
Korea	398	1	14	42	0.5	Seo (1983) K.J.Para. 21(1): 95-101
Laos	2493	11	49	50	A.d = 41 N.a = 29	Sornmani (1974) S.E.A.J.Trop.Med.Pub.H. 5(4): 541
Malaysia	96075	30	48	55	49	Kan (1985) Med.J.Malay. 40(3): 202; Kan (1982) Malay. Med.J. 37(2): 180; Russell (1934) Malay.Med.J. 9: 17-22; Russell (1928) Malay.Med.J. 3: 113-123; Dunn (1972) Bull.WHO 46: 99-113; Sinniah (1978) S.E.A.J.Trop.Med.Pub.H. 9(2): 273
PNG	1304 / 1023	33 / 32	24	2	72	Ashford (1981) A.J.Trop.Med.H. 75(3): 269-279; Shield (1986) PNG.Med.J. 29: 317-331
Philippines	1300 / 286	4 / 3	54.8	69	22	Cross (1977) Am.J.Trop.Med.Para. 71(4): 437-; Tatengco (1972) S.E.A.J.Trop.Med.Pub.H. 3(4): 580
Singapore	614	7	45	72	37	Desowitz (1963) Sing.Med.J. 4(8): 30
Taiwan	622	7	91	44	7	Bergner (1964) Am.J.Trop.Med.Hyg. 13: 78-81; Chang (1973) J.Formsoan.Med.Assoc. 72: 297-303
N.B. For Thailand	67300 / 68153	85 / 101	6	5.8	35	Jones (1976) PNG.Med.J. 19(3); Preuksaraj (1981) Epid.APCO. II 54-; Papasarathorn (1975) S.E.A.J.Trop.Med.Pub.H. 6(1): 82; Sadun (1955) Am.J.Hyg. 62: 116-155
Vietnam	409	8	33	14	57	Colwell (1971) S.E.A.J.Trop.Med.Pub.H. 2(1): 25

Latin America and the Caribbean

Country						Reference
Brazil	2511	10	60	36	27	Vinha (1971)
Chile	34799	38	19			Negheme (1983) Rev.Chil.Hyg.Med.Prev. 14:243-257

#	Country					Notes	References
39	Costa Rica	90277	81		26		Negheme (1963) Bol.Chil.Para. 18(3):54-60; Negheme (1952) Bol.Chil.Para. 18(4): 100-103; Schenome (1981) Bol.Chil.Par.36:44-48; Ramirez (1972) Bol.Chil.Par. 27: 116-118; Puga (1980) Rev.Med.Chil. 108: 608
40	Dominica	33161	3	12	28	4	Zamora (1978) Act.Med.Cos.21(3): 271-273; Rojas (1980) Act.Med.Cos. 25(3): 245-251
	Ecuador	1000	2	38	92	N.a = 11	Grell (1981) Ann.Trop.Paed. 1:155-160
		3970	14	50	60	33	Peplow (1982) Bol.San.Panam. 93(3): 233-; Ortiz (1969) Rev.Ecuat.Hig.Med.Trop. 26(2)
		1568	12				
	Guatemala	15383	1	73	1819		Anguila (1981) Bol.Chil.Para. 36:6-9
	Mexico	604	1	62	67		Stoopen (1964) Rev.Med.45: 28-33
	Surinam	854	10	62	45		Asin (1963) Trop.Geo.Med. 15: 257-267
Middle Eastern Crescent							
	Algeria	565	6	41	29	13	Pampiglione (1965) Riv.di Para. 26(4): 243 *(update available)*
4e	Egypt	41476	8	16	17	A.d. = 1	Mohamed. J.Egypt.Soc.Par.15, 2 (1985); Farag (1985) Trop.Geo.Med. 37:29-31; Tadras (1973) J.Egy.Soc.Par. 46:40; Wells (1956) Am.J.Trop.M.H. 5:266-268; Mohamed (1988) J.Egy.Soc.Par. 18(1): 305; Lawless (1956) Am.J.T.M.H. 5:1010-1014; Amal (1986) J.Egy.Soc.Par. 16(2): 601
		39574	5				
47	Iran	1137	7	22	0.5	A.d = 29	Colett (1966) Is.J.Med.Sci. 2(3): 380; Nazari (1980) Bull.Soc.Path.Ex. 73: 108-111
48	Iraq	4000	16			1.3	Niazi (1975) Bull.End.Dis. 16(2): 105-141
49	Marocco	61995	3	1			Cadi-Soussi (1982) Med.Afr.N. 29(8-9): 563-

Parasite	Country	Study design	Sample size	Time between baseline and follow-up - if appropriate	Age of subjects (Years)	Significant effects of helminth infection on mental processing		Investigators
						Baseline differences between infected and uninfected group	Intervention differences	
Trichuris trichiura Moderate - heavy intensity	Jamaica	*Intervention, Placebo controlled* Albendazole	T=62 P=41 C=56	63±8 days	9 - 12	Fluency Digit-span forwards Digit-span backwards Arithmetic Coding Comprehension Matching familiar figures: easy Matching familiar figures: hard Tests in battery = 8	Fluency Digit-span forwards Digit-span backwards	Nokes McGregor Sawyer Cooper Robinson Bundy (1992)
Hookworm Presence	Zaire	*Intervention, Case Control* Levamizole + malaria treatment if Infected only.	T=47 C=50	4 weeks	8.75 ± 1.6	Sequential Processing - incl./ Number Recall Word Order *Mental processing total Tests in battery = 10	Spatial Memory	Boivin Giordani Ndanga Maky Manzeki Ngunu Muamba (1993)
Hookworm + Iron status Presence	Zaire	*Intervention, Placebo controlled* Levamizole. Iron supplements.	T+Iron=17 P+Iron; T only; P only; = 30	4 weeks	Male = 7.7 Fem = 8.0	Not reported	Effect = iron + hookworm trnt Spatial Memory Number Recall Word Order Face Recognition Gestalt Matrix Analogies Mental Processing Total Sequential Total Simultaneous Total	Boivin Giordani (1993)
						Tests in battery = 10		
Trichuris trichiura TDS - very heavy intensity	Jamaica	*Case Control, Intervention, Pair-matched.* Albendazole given to infected children every 4 months.	T=19 C=19	12 months	3 - 6	Griffiths DQ subscales Locomotor Eye hand coordination Hearing and speech Performance	Locomotor	Callender Walker Cooper McGregor (1991)

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Parasite	Country	Study design	Sample size	Time between baseline and follow-up - if appropriate	Age of subjects (Years)	Significant effects of helminth infection on mental processing		Investigators
						Baseline differences between infected and uninfected group	Intervention differences	
Ascaris lumbricoides Presence (Study actually designed to investigate T. trichiura)	Jamaica	Cross-section Matched for class	Infd=196 Uninfd=207 (Infd with T. trichiura= 409)	---	7 - 11	*Reading *Spelling * Arithmetic *School Attendance Tests in battery = 4		Simeon Callender Wong McGregor (1994)
Ascaris lumbricoides Presence	Ecuador	Cross-section	Infd=103 Uninfd C=27	---	9 - 13	* Stroop Words * Peabody raw score * Digit Symbol * Wisconsin Card Sorting Test Interaction with nutrition in Peabody Test *=controlled for nutrition status All sample had high EEG Tests in battery = 13	Not done	Levav Mirsky Schantz Castro Cruz (1995)
Polyparasitism A. lumbricoides, T. trichiura, Hookworm Intensity	Jamaica	Cross-section	Infd = 473 Uninfd = 170	---	9 - 11	Academic stream (children streamed by teachers according to academic ability. Children with least ability more likely to be infected and heavily infected) Only test in battery	Not done	Nokes Cooper Robinson Bundy (1991)
Polyparasitism A. lumbricoides, T. trichiura, hookworm, Schistosome spp. Protozoa Intensity	South Africa	Cross-section All infected with different spp.	Subjects=110	---	10	* Sustained attention (Pathogenicity of parasitic species more important than prevalence/intensity at predicting performance.) Other test = Memory	Not done (Intervention disrupted by flooding)	Kvalsvig Cooppan Connolly (1991)

Parasite	Country	Study design	Sample size	Time between baseline and follow-up - if appropriate	Age of subjects (Years)	Significant effects of helminth infection on mental processing		Investigators
						Baseline differences between infected and uninfected group	Intervention differences	
Trichuris trichiura Low-Moderate & heavy intensity	Italy	*Cross-section*	Uninf=232 Infd=124	---	6 - 10	x Lower school grade correlated with intensity. No relationship when controlled for social and hygienic conditions. Other outcome=promotion.	Not done	de Carneri (1968)
Trichuris trichiura Low-Moderate & heavy intensity	Italy	*Cross-section*	Uninf= 125 Infd=233	---	6 - 11	x Slower promotion, poor grades correlated with intensity. No relationship when controlled for social and hygienic conditions. Other outcome=absenteeism	Not done	de Carneri Carofano Grassi (1967)
Hookworm Intensity	Australia	*Cross-section*	Uninfd=116 Infected Low intensity=65 Infected High intensity=159	---	6.5 - 15.5	Binet-Simon test and Porteus Mazes correlated with intensity of infection.	Not done	Waite Neilson (1919)
Hookworm Presence	USA	*Cross-section*	78	---	6 - 17	* Grade Advancement (deficit of 0.23 grades /year)	Not done	Stiles (1915)

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Table 12b. Selected studies investigating the effects of parasitic helminth infections on physical fitness

Parasite	Country	Study design Measure of activity	Sample size	Time between baseline and follow-up - if appropriate	Age of subjects (Years)	Baseline differences between infected and uninfected group	Intervention differences	Investigators
Polyparasitism T. trichiura A. lumbricoides Hookworm Presence	Kenya	Intervention, Placebo controlled Albendazole. Harvard Step Test	T=18 P=15	7 weeks	6 - 12	Fitness negatively correlated with haemoglobin / iron status.	No change in fitness score & pulse rate in Placebo group. Signif improvement in fitness in Treatment group. Iimprovement sig. related to reduction in hookworm and A. lumbricoides egg counts.	Stephenson Latham Kinoti Kurz Brigham (1990)
Polyparasitism T. trichiura A. lumbricoides Hookworm Presence	Kenya	Intervention, Placebo controlled Albendazole. Harvard Step Test	T=27 P=26	4 months	7 - 13	No difference between infected groups.	No change in fitness score & pulse rate in Placebo group. Signif improvement in fitness in Treatment group. Iimprovement sig. related to reduction in hookworm, weight gain and indreaise in energy intake during the 4 month study period.	Stephenson Latham Adams Kinoti Pertet. (1993)

Data provided by the Partnership for Child Development - Cognition Panel(1994)

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		3 2	Hw Only	2	
	62004 500				
Pakistan	295	3	61	55	49 Kuntz (1960) A.J.Trop.Med.H. 9: 168-172
Saudi	835	1	0.1	0.1	0 El-Rahimy (1986) J.Egy.Para. 16(1): 185-
Tunisia	24047		11		Thiers (1976) Bull.Soc.Path.Ex. 69: 320-329

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Table 9. Data for DALY calculation: Ascariasis

9a

Disease: Ascariasis	Region: Sub Saharan Africa		Sex: Both		Year: 1990			
Age Group	Incidence	Proportion at risk C	A/B	Average age at onset	Duration of risk	Duration of disability A	C	B	Mortality
0-4		259	1546	2	1	1	0.05	81.25	0.3
5-14		265	1181	10	1	1	0.05	71.70	0.3
15-44		2	97	30	1	1	0.05	51.89	0.006
45-49		2	97	50	1	1	0.05	32.49	0.006
60+		2	97	70	1	1	0.05	14.89	0.006

9b

Disease: Ascariasis	Region: Latin America and Car		Sex: Both		Year: 1990			
Age Group	Incidence	Proportion at risk C	A/B	Average age at onset	Duration of risk	Duration of disability A	C	B	Mortality
0-4		1009	5370	2	1	1	0.05	81.25	1
5-14		1083	4506	10	1	1	0.05	71.70	0.9
15-44		11	390	30	1	1	0.05	51.89	0.01
45-49		11	390	50	1	1	0.05	32.49	0.01
60+		11	390	70	1	1	0.05	14.89	0.01

9c

Disease: Ascariasis	Region: Middle Eastern Cresce		Sex: Both		Year: 1990			
Age Group	Incidence	Proportion at risk C	A/B	Average age at onset	Duration of risk	Duration of disability A	C	B	Mortality
0-4		280	1557	2	1	1	0.05	81.25	0.3
5-14		303	1285	10	1	1	0.05	71.70	0.3
15-44		3	113	30	1	1	0.05	51.89	0.005
45-49		3	113	50	1	1	0.05	32.49	0.005
60+		3	113	70	1	1	0.05	14.89	0.005

9d

Disease: Ascariasis	Region: India		Sex: Both		Year: 1990			
Age Group	Incidence	Proportion at risk C	A/B	Average age at onset	Duration of risk	Duration of disability A	C	B	Mortality
0-4		419	2247	2	1	1	0.05	81.25	0.4
5-14		459	1892	10	1	1	0.05	71.70	0.4
15-44		4	163	30	1	1	0.05	51.89	0.006
45-49		4	163	50	1	1	0.05	32.49	0.006
60+		4	163	70	1	1	0.05	14.89	0.006

9e

Disease: Ascariasis	Region: China		Sex: Both		Year: 1990			
Age Group	Incidence	Proportion at risk C	A/B	Average age at onset	Duration of risk	Duration of disability A	C	B	Mortality
0-4		1022	5178	2	1	1	0.05	81.25	1.1
5-14		1184	4546	10	1	1	0.05	71.70	1.1
15-44		13	416	30	1	1	0.05	51.89	0.01
45-49		13	416	50	1	1	0.05	32.49	0.01
60+		13	416	70	1	1	0.05	14.89	0.01

9f

Disease: Ascariasis	Region: Other Asia & Islands		Sex: Both		Year: 1990			
Age Group	Incidence	Proportion at risk C	A/B	Average age at onset	Duration of risk	Duration of disability A	C	B	Mortality
0-4		1403	7399	2	1	1	0.05	81.25	1.2
5-14		1430	6017	10	1	1	0.05	71.70	1
15-44		13	491	30	1	1	0.05	51.89	0.02
45-49		13	491	50	1	1	0.05	32.49	0.02
60+		13	491	70	1	1	0.05	14.89	0.02

Table 10. Data for DALY calculation: Trichuriasis

10a

Disease: Trichuriasis	Region: Sub Saharan Africa		Sex: Both		Year: 1990		
Age Grou	Incidence	Proportion at risk		Average age	Duration	Duration of disability	Mortality
		C	A/B	at onset	of risk	A/C	B	
0-4		19	240	2	1	1	81.25	1
5-14		321	692	10	1	1	71.70	0
15-44		0	56	30	1	1	51.89	0
45-49		0	56	50	1	1	32.49	0
60+		0	56	70	1	1	14.89	0

10b

Disease: Trichuriasis	Region: Latin America & Cari		Sex: Both		Year: 1990		
Age Grou	Incidence	Proportion at risk		Average age	Duration	Duration of disability	Mortality
		C	A/B	at onset	of risk	A/C	B	
0-4		91	994	2	1	1	81.25	1
5-14		1337	2692	10	1	1	71.70	1
15-44		3	250	30	1	1	51.89	0
45-49		3	250	50	1	1	32.49	0
60+		3	250	70	1	1	14.89	0

10c

Disease: Trichuriasis	Region: Middle Eastern Cres		Sex: Both		Year: 1990		
Age Grou	Incidence	Proportion at risk		Average age	Duration	Duration of disability	Mortality
		C	A/B	at onset	of risk	A/C	B	
0-4		0	2	2	1	1	81.25	0
5-14		0	10	10	1	1	71.70	0
15-44		0	1	30	1	1	51.89	0
45-49		0	1	50	1	1	32.49	0
60+		0	1	70	1	1	14.89	0

10d

Disease: Trichuriasis	Region: India		Sex: Both		Year: 1990		
Age Grou	Incidence	Proportion at risk		Average age	Duration	Duration of disability	Mortality
		C	A/B	at onset	of risk	A/C	B	
0-4		19	206	2	1	1	81.25	0
5-14		280	564	10	1	1	71.70	0
15-44		1	52	30	1	1	51.89	0
45-49		1	52	50	1	1	32.49	0
60+		1	52	70	1	1	14.89	0

10e

Disease: Trichuriasis	Region: China		Sex: Both		Year: 1990		
Age Grou	Incidence	Proportion at risk		Average age	Duration	Duration of disability	Mortality
		C	A/B	at onset	of risk	A/C	B	
0-4		47	417	2	1	1	81.25	1
5-14		567	1051	10	1	1	71.70	1
15-44		2	119	30	1	1	51.89	0
45-49		2	119	50	1	1	32.49	0
60+		2	119	70	1	1	14.89	0

10f

Disease: Trichuriasis	Region: Other Asia & Islands		Sex: Both		Year: 1990		
Age Grou	Incidence	Proportion at risk		Average age	Duration	Duration of disability	Mortality
		C	A/B	at onset	of risk	A/C	B	
0-4		127	1459	2	1	1	81.25	2
5-14		1880	3832	10	1	1	71.70	1
15-44		3	325	30	1	1	51.89	0
45-49		3	325	50	1	1	32.49	0
60+		3	325	70	1	1	14.89	0

Table 11. Data for DALY calculation: Hookworm disease

11a

Disease: Hookworm disease	Region: Sub Saharan Africa		Sex: Male		Year: 1990		
Age Group	Incidence	Proportion at risk		Average age at onset	Duration of risk	Duration of disability	Mortality
		C	B			C	B	
0-4		0	0	2	1	1	80.00	0
5-14		180	1260	10	1	1	70.40	0
15-44		2650	5760	30	1	1	50.51	3
45-49		2650	5760	50	1	1	30.99	14
60+		2650	5760	70	1	1	13.58	0

11b

Disease: Hookworm disease	Region: Latin America and C		Sex: Male		Year: 1990		
Age Group	Incidence	Proportion at risk		Average age at onset	Duration of risk	Duration of disability	Mortality
		C	B			C	B	
0-4		0	0	2	1	1	80.00	0
5-14		30	945	10	1	1	70.40	0
15-44		1090	5030	30	1	1	50.51	0
45-49		1090	5030	50	1	1	30.99	2
60+		1090	5030	70	1	1	13.58	0

11c

Disease: Hookworm disease	Region: Middle Eastern Cres		Sex: Male		Year: 1990		
Age Group	Incidence	Proportion at risk		Average age at onset	Duration of risk	Duration of disability	Mortality
		C	B			C	B	
0-4		0	0	2	1	1	80.00	0
5-14		30	480	10	1	1	70.40	0
15-44		770	2400	30	1	1	50.51	1
45-49		770	2400	50	1	1	30.99	3
60+		770	2400	70	1	1	13.58	0

11d

Disease: Hookworm disease	Region: India		Sex: Male		Year: 1990		
Age Group	Incidence	Proportion at risk		Average age at onset	Duration of risk	Duration of disability	Mortality
		C	B			C	B	
0-4		0	0	2	1	1	80.00	0
5-14		70	1575	10	1	1	70.40	0
15-44		2070	8150	30	1	1	50.51	2
45-49		2070	8150	50	1	1	30.99	8
60+		2070	8150	70	1	1	13.58	0

11e

Disease: Hookworm disease	Region: China		Sex: Male		Year: 1990		
Age Group	Incidence	Proportion at risk		Average age at onset	Duration of risk	Duration of disability	Mortality
		C	B			C	B	
0-4		0	0	2	1	1	80.00	0
5-14		2	253	10	1	1	70.40	0
15-44		150	1500	30	1	1	50.51	0
45-49		150	1500	50	1	1	30.99	0
60+		150	1500	70	1	1	13.58	0

11f

Disease: Hookworm disease	Region: Other Asia & Islands		Sex: Male		Year: 1990		
Age Group	Incidence	Proportion at risk		Average age at onset	Duration of risk	Duration of disability	Mortality
		C	B			C	B	
0-4		0	0	2	1	1	80.00	0
5-14		70	1545	10	1	1	70.40	0
15-44		2060	7980	30	1	1	50.51	1
45-49		2060	7980	50	1	1	30.99	6
60+		2060	7980	70	1	1	13.58	0

11g

Disease: Hookworm disease				Region: Sub Saharan Africa		Sex: Female		Year: 1990	
Age Group	Incidence	Proportion at risk C	B	Average age at onset	Duration of risk	Duration of disability C	B	Mortality
0-4		0	0	2	1	1	82.50	0
5-14		180	1260	10	1	1	72.99	0
15-44		2650	5760	30	1	1	53.27	11
45-49		2650	5760	50	1	1	33.99	14
60+		2650	5760	70	1	1	16.20	0

11h

Disease: Hookworm disease				Region: Latin America and C		Sex: Female		Year: 1990	
Age Group	Incidence	Proportion at risk C	B	Average age at onset	Duration of risk	Duration of disability C	B	Mortality
0-4		0	0	2	1	1	82.50	0
5-14		30	945	10	1	1	72.99	0
15-44		1090	5030	30	1	1	53.27	2
45-49		1090	5030	50	1	1	33.99	2
60+		1090	5030	70	1	1	16.20	0

11i

Disease: Hookworm disease				Region: Middle eastern Cres		Sex: Female		Year: 1990	
Age Group	Incidence	Proportion at risk C	B	Average age at onset	Duration of risk	Duration of disability C	B	Mortality
0-4		0	0	2	1	1	82.50	0
5-14		30	480	10	1	1	72.99	0
15-44		770	2400	30	1	1	53.27	2
45-49		770	2400	50	1	1	33.99	3
60+		770	2400	70	1	1	16.20	0

11j

Disease: Hookworm disease				Region: India		Sex: Female		Year: 1990	
Age Group	Incidence	Proportion at risk C	B	Average age at onset	Duration of risk	Duration of disability C	B	Mortality
0-4		0	0	2	1	1	82.50	0
5-14		70	1575	10	1	1	72.99	0
15-44		2070	8150	30	1	1	53.27	6
45-49		2070	8150	50	1	1	33.99	8
60+		2070	8150	70	1	1	16.20	0

Disease: Hookworm disease				Region: China		Sex: Female		Year: 1990	
Age Group	Incidence	Proportion at risk C	B	Average age at onset	Duration of risk	Duration of disability C	B	Mortality
0-4		0	0	2	1	1	82.50	0
5-14		2	253	10	1	1	72.99	0
15-44		150	1500	30	1	1	53.27	0
45-49		150	1500	50	1	1	33.99	0
60+		150	1500	70	1	1	16.20	0

11l

Disease: Hookworm disease				Region: Other Asia & Islands		Sex: Female		Year: 1990	
Age Group	Incidence	Proportion at risk C	B	Average age at onset	Duration of risk	Duration of disability C	B	Mortality
0-4		0	0	2	1	1	82.50	0
5-14		70	1545	10	1	1	72.99	0
15-44		2060	7980	30	1	1	53.27	5
45-49		2060	7980	50	1	1	33.99	6
60+		2060	7980	70	1	1	16.20	0

Table 12a. Selected studies investigating the effects of parasitic helminth infections on mental processing

Parasite	Country	Study design	Sample size	Time between baseline and follow-up - if appropriate	Age of subjects (Years)	Significant effects of helminth infection on mental processing		Investigators
						Baseline differences between infected and uninfected group	Intervention differences	
Trichuris trichiura Moderate intensity	Jamaica	Intervention Placebo controlled Albendazole	T=206 P=201 C=206	26 weeks	7 - 11	* Reading x Spelling * Arithmetic x School Attendance Tests in battery = 4	Treatment interaction effects: Heavily infected & received treatment improved in spelling. Stunted & received treatment improved in school attendance	Simeon, McGregor Callender Wong (1994)
		Intervention Placebo controlled Albendazole	T=96 P=93 C=100	14 weeks	8 - 10	x Fluency x French learning (initial) * Letter search Tests in battery = 6	Treatment interaction effects: Underweight children improved in Fluency	Simeon McGregor Wong (1994)
		Intervention Placebo controlled Albendazole	T=49 P=48 C=48	14 weeks	10 - 11	* Silly sentences x Letter search Tests in battery = 8	None significant	Baddeley, Meeks-Gardner McGregor (1994)
		Intervention Placebo controlled Albendazole	T=67 P=67 C=67	14 weeks	7 - 9	Not done Tests in battery were 2 tests of Intuitive biological thought	None significant	Carey Keil Chang (unpublished)
		Intervention Placebo controlled Albendazole	T=66 P=67 C=63	10 weeks	9 - 11	x Digit-span forwards x Digit-span backwards x Analogical reasoning xPegboard non-dominant hand Tests in battery = 9	None significant	Sternberg Powell McGrane

Table 13

Country and period of study	No. with complicated ascariasis	No. of deaths	Case-fatality rate	Source
USA, 1940's	202	6	2.9 %	Swartzwelder, 1946
S. Africa, '58-'62	100	3	3.0%	Louw, 1966
Brazil, 1970's	454	44	9.7%	Pinus, 1985
Myanmar, '81-'83	641	18	2.8%	Thein-Hlaing, 1987
Myanmar, '84-'86	226	6	2.6%	Thein-Hlaing et al, 1990
India, 1980's	876	38	4.3%	Chrungoo et al, 1992
Total	**2499**	**115**	**4.6%**	

Table 14a. Parameters for contemporaneous disability consequences
Type A morbidity, Ascaris and Trichuris   use lower threshold

| species | age group | proportion disabled | duration years | disability class distribution (disability weights given under class) | | | | | |
				1 0.096	2 0.22	3 0.4	4 0.6	5 0.81	6 0.92
Ascaris	0-4	0.97	1.00	1.000	0.00	0.000	0.00	0.00	0.00
	5-14	0.97	1.00	1.000	0.00	0.000	0.00	0.00	0.00
	15-44	1.00	1.00	1.000	0.00	0.000	0.00	0.00	0.00
	45-59	1.00	1.00	1.000	0.00	0.000	0.00	0.00	0.00
	60+	1.00	1.00	1.000	0.00	0.000	0.00	0.00	0.00
Trichuris	0-4	0.97	1.00	1.00	0.00	0.00	0.00	0.00	0.00
	5-14	0.97	1.00	1.00	0.00	0.00	0.00	0.00	0.00
	15-44	1.00	1.00	1.00	0.00	0.00	0.00	0.00	0.00
	45-59	1.00	1.00	1.00	0.00	0.00	0.00	0.00	0.00
	60+	1.00	1.00	1.00	0.00	0.00	0.00	0.00	0.00

Table 14b. Parameters for contemporaneous disability consequences
Type C morbidity, all species   use higher threshold

species	age group	proportion disabled	duration years	disability class distribution (disability weights given under class)					
				1	2	3	4	5	6
				0.096	0.22	0.4	0.6	0.81	0.92
Ascaris	0-4	1.00	0.05	0.000	0.80	0.180	0.02	0.00	0.00
	5-14	1.00	0.05	0.000	0.80	0.180	0.02	0.00	0.00
	15-44	1.00	0.05	0.000	0.88	0.100	0.02	0.00	0.00
	45-59	1.00	0.05	0.000	0.88	0.100	0.02	0.00	0.00
	60+	1.00	0.05	0.000	0.88	0.100	0.02	0.00	0.00
Trichuris	0-4	1.00	1.00	0.00	0.90	0.08	0.02	0.00	0.00
	5-14	1.00	1.00	0.00	0.90	0.08	0.02	0.00	0.00
	15-44	1.00	1.00	0.00	0.90	0.10	0.00	0.00	0.00
	45-59	1.00	1.00	0.00	0.90	0.10	0.00	0.00	0.00
	60+	1.00	1.00	0.00	0.90	0.10	0.00	0.00	0.00
Hookworms male	0-4	1.00	1.00	0.00	0.70	0.24	0.06	0.00	0.00
	5-14	1.00	1.00	0.00	0.70	0.24	0.06	0.00	0.00
	15-44	0.50	1.00	0.00	0.70	0.24	0.06	0.00	0.00
	45-59	0.50	1.00	0.00	0.70	0.24	0.06	0.00	0.00
	60+	0.50	1.00	0.00	0.70	0.24	0.06	0.00	0.00
Hookworms female	0-4	1.00	1.00	0.00	0.70	0.24	0.06	0.00	0.00
	5-14	1.00	1.00	0.00	0.70	0.24	0.06	0.00	0.00
	15-44	1.00	1.00	0.00	0.70	0.24	0.06	0.00	0.00
	45-59	0.50	1.00	0.00	0.70	0.24	0.06	0.00	0.00
	60+	0.50	1.00	0.00	0.70	0.24	0.06	0.00	0.00

Table 15. Parameters for permanent disability consequences
Type B morbidity, all species   use lower threshold

species	age group	proportion disabled	duration years	disability class distribution (disability weights given under class)					
				1.00	2.00	3.00	4.00	5.00	6.00
				0.10	0.22	0.40	0.60	0.81	0.92
Ascaris	0-4	0.03	81.25	1.00	0.00	0.00	0.00	0.00	0.00
	5-14	0.03	71.70	1.00	0.00	0.00	0.00	0.00	0.00
	15-44	0.00	51.89	1.00	0.00	0.00	0.00	0.00	0.00
	45-59	0.00	32.49	1.00	0.00	0.00	0.00	0.00	0.00
	60+	0.00	14.89	1.00	0.00	0.00	0.00	0.00	0.00
Trichuris	0-4	0.03	81.25	1.00	0.00	0.00	0.00	0.00	0.00
	5-14	0.03	71.70	1.00	0.00	0.00	0.00	0.00	0.00
	15-44	0.00	51.89	1.00	0.00	0.00	0.00	0.00	0.00
	45-59	0.00	32.49	1.00	0.00	0.00	0.00	0.00	0.00
	60+	0.00	14.89	1.00	0.00	0.00	0.00	0.00	0.00
Hookworms male	0-4	0.03	80.00	1.00	0.00	0.00	0.00	0.00	0.00
	5-14	0.03	70.40	1.00	0.00	0.00	0.00	0.00	0.00
	15-44	0.00	50.51	1.00	0.00	0.00	0.00	0.00	0.00
	45-59	0.00	30.99	1.00	0.00	0.00	0.00	0.00	0.00
	60+	0.00	13.58	1.00	0.00	0.00	0.00	0.00	0.00
Hookworms female	0-4	0.03	82.50	1.00	0.00	0.00	0.00	0.00	0.00
	5-14	0.03	72.99	1.00	0.00	0.00	0.00	0.00	0.00
	15-44	0.00	53.27	1.00	0.00	0.00	0.00	0.00	0.00
	45-59	0.00	33.99	1.00	0.00	0.00	0.00	0.00	0.00
	60+	0.00	16.20	1.00	0.00	0.00	0.00	0.00	0.00

FIGURE ①

ASCARIS : KOREA
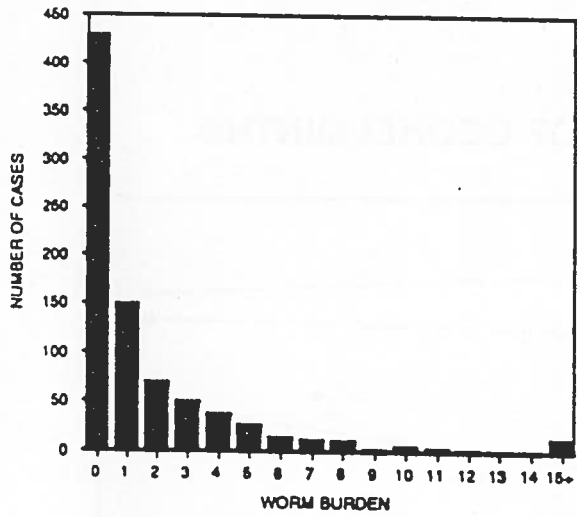
TRICHURIS : ST.LUCIA
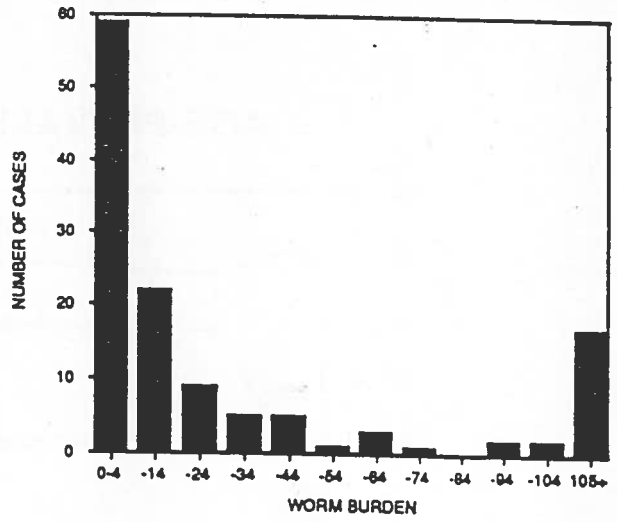
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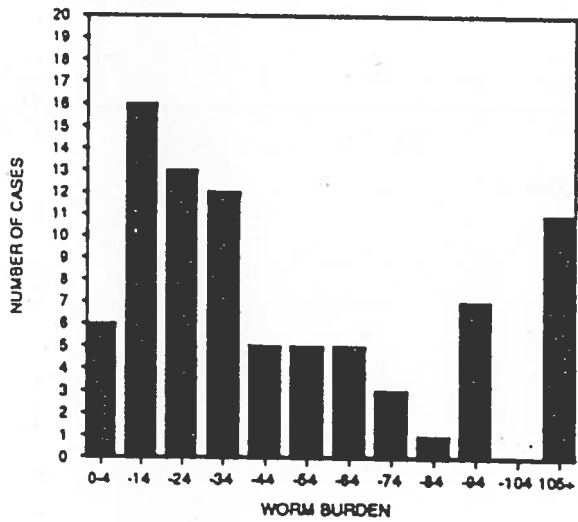
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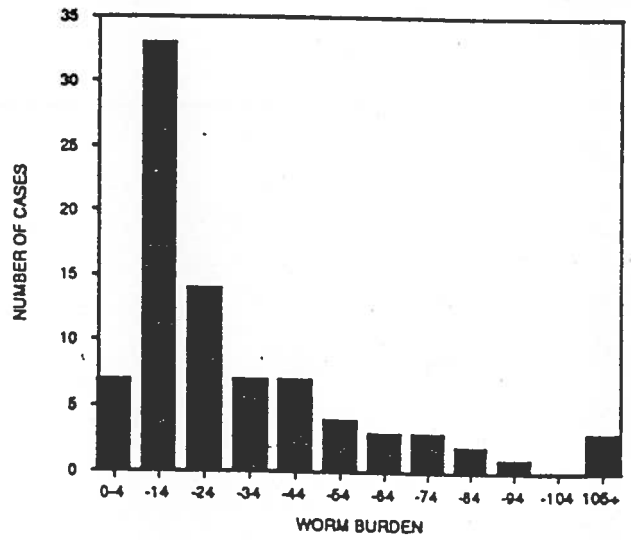
FIGURE ②

AGE-PREVALENCE OF GEOHELMINTHS
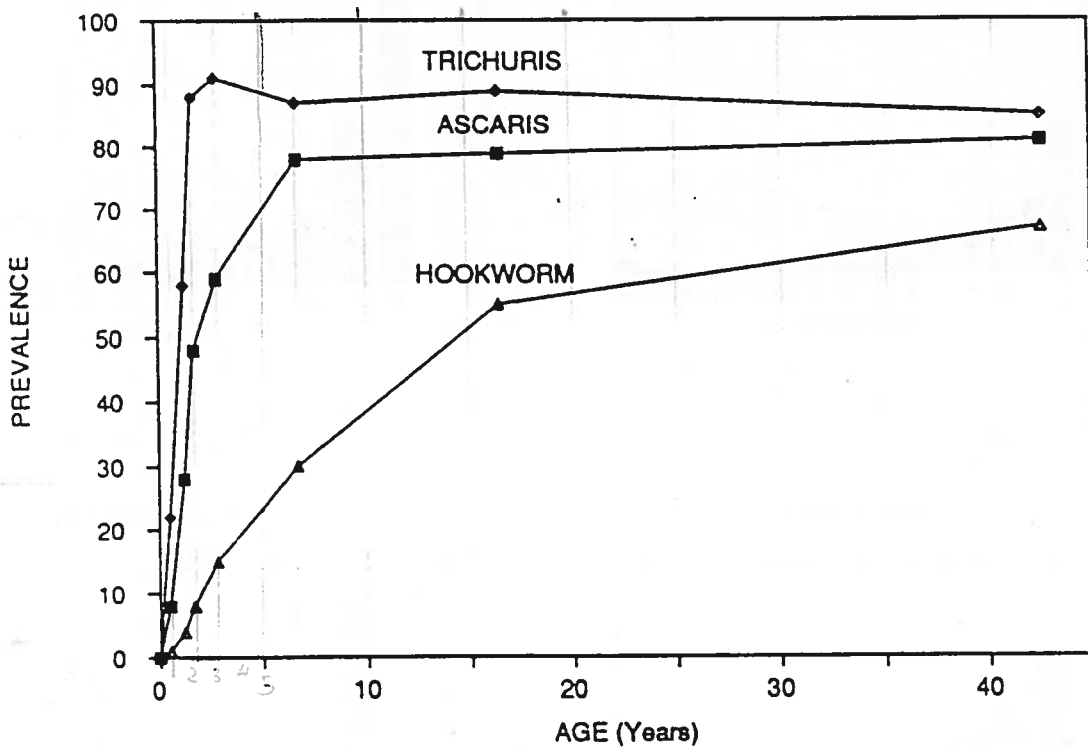
Relationship between prevalence and mean intensity for Ascaris lumbricoides infection (Guyatt et al, 1990)
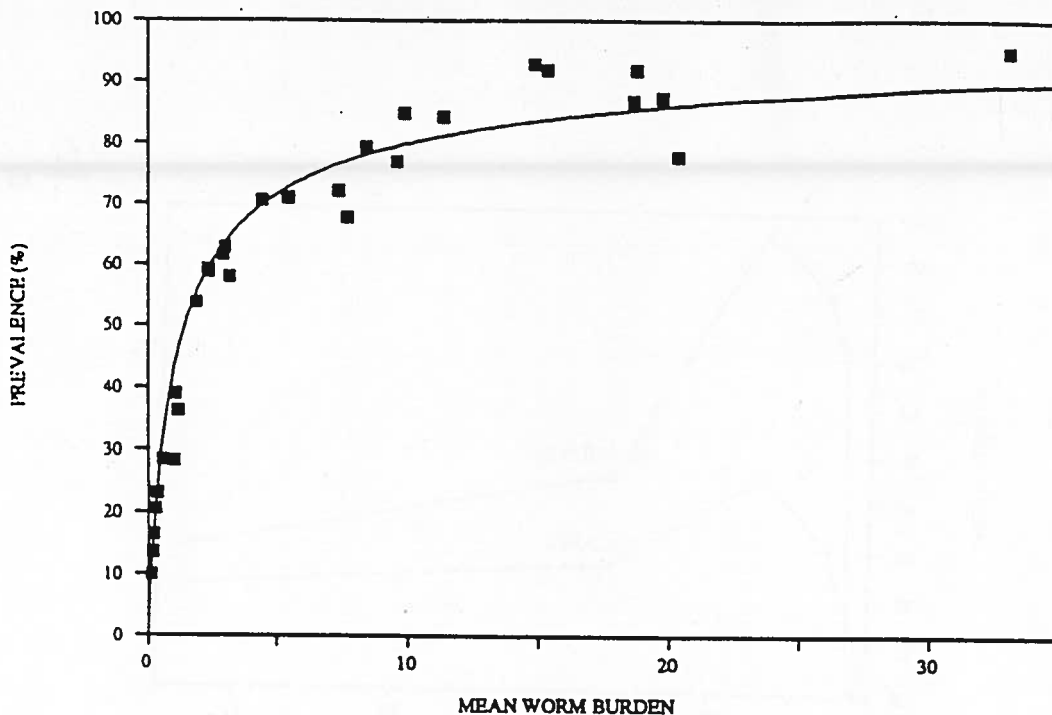
3a
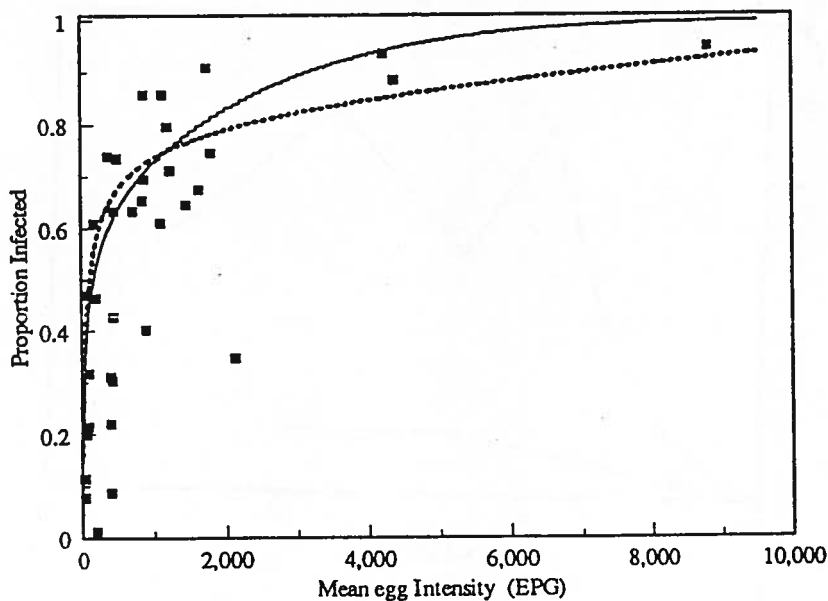
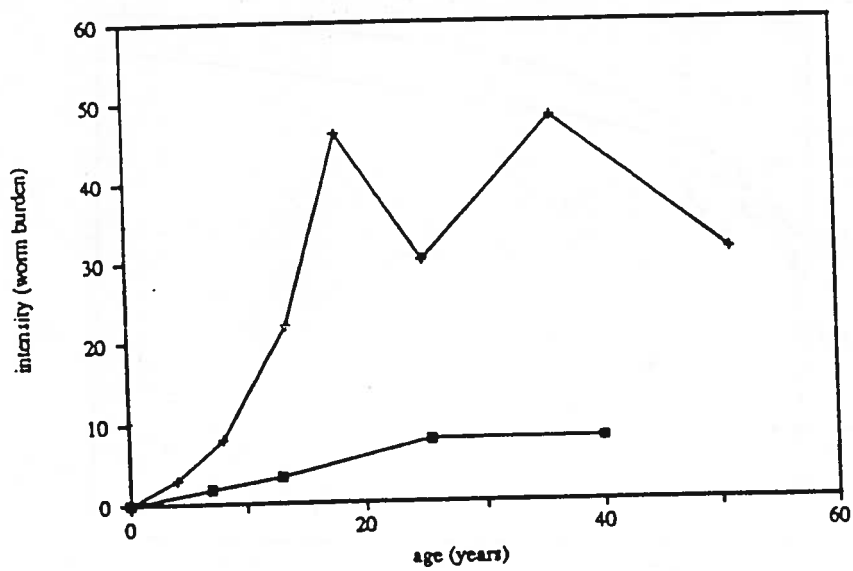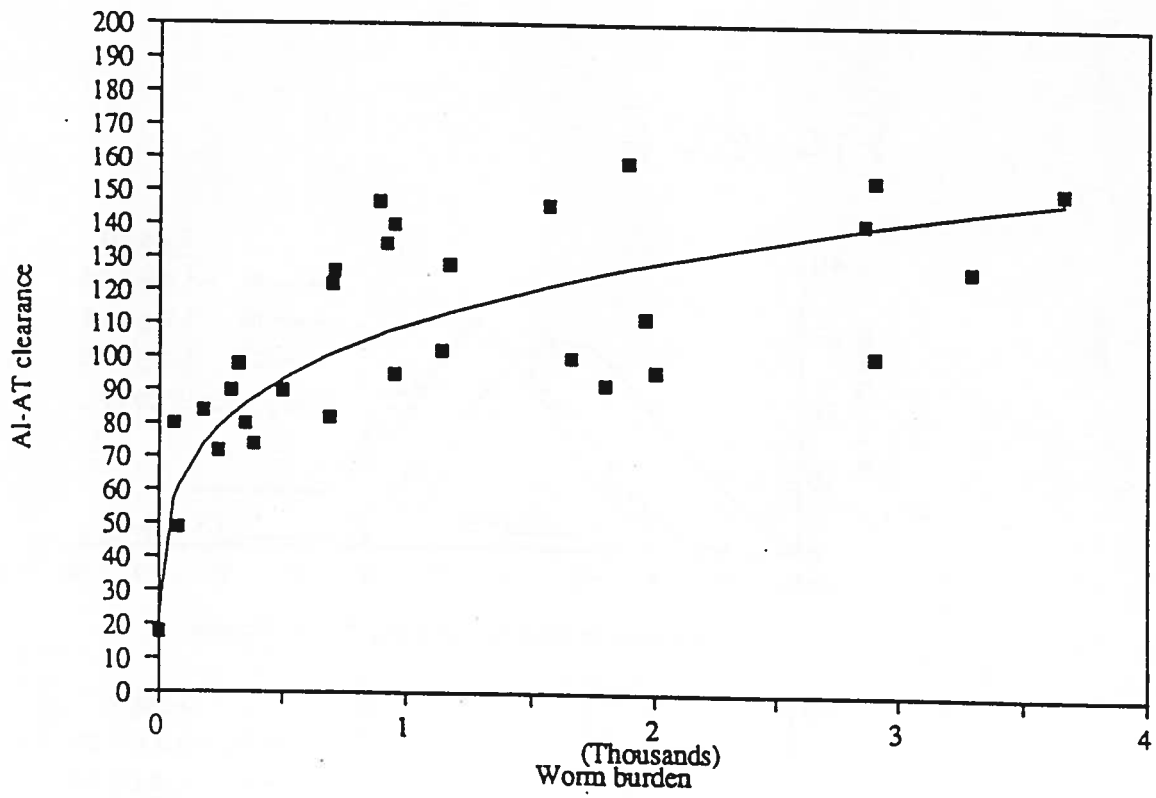Scatter plot from figure 3.3 with model estimates of *T. trichiura* infection egg
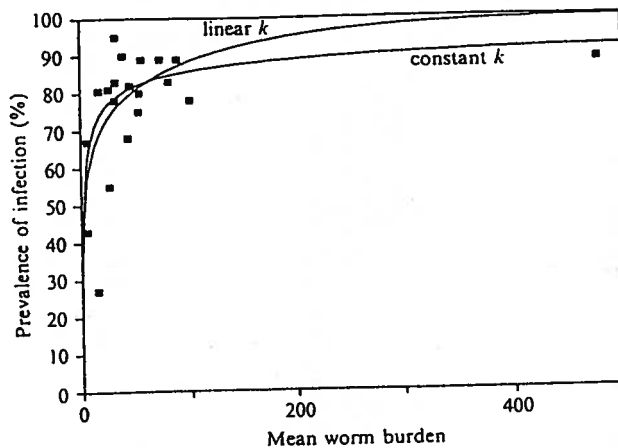
3c

Fig. 1. Relationship between hookworm prevalence of infection and mean worm burden. The curves are the best maximum-likelihood fits for the negative binomial probability distribution with a constant k ($k = 0.343$) and when k is a linear function of mean intensity ($k = a + bM$; $a = 0.2686$; $b = 0.0012$). Log-likelihood function $(l) = -4277.9598$ for constant k and $l = -4256.4384$ for linear k. Hookworm prevalence ... burden show a non-linear association which is adequately

4a

4b

5

Axis labels: Al-AT clearance (vertical), Worm burden (Thousands) (horizontal)

FIGURE 6

Height

FIGURE 7

Rate (cm/year), Age (years)

Reference medians — 97th centiles — 3rd centiles
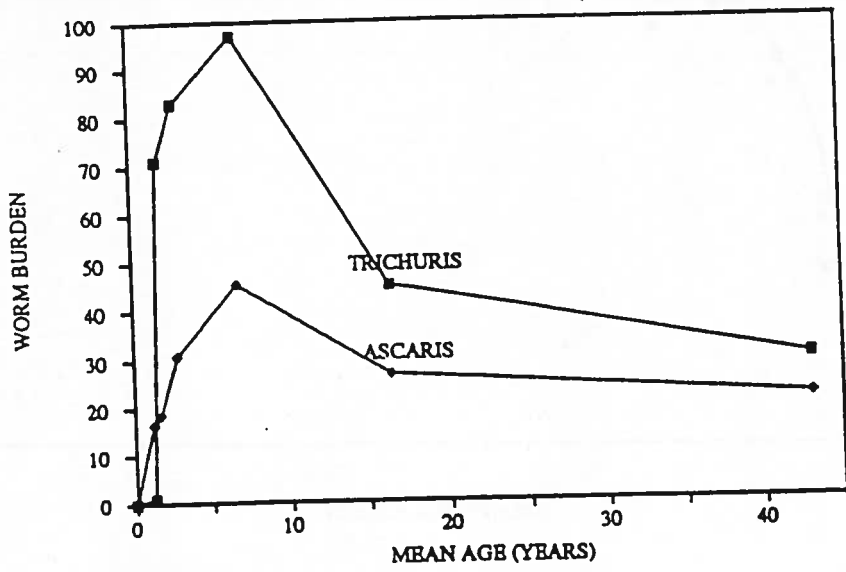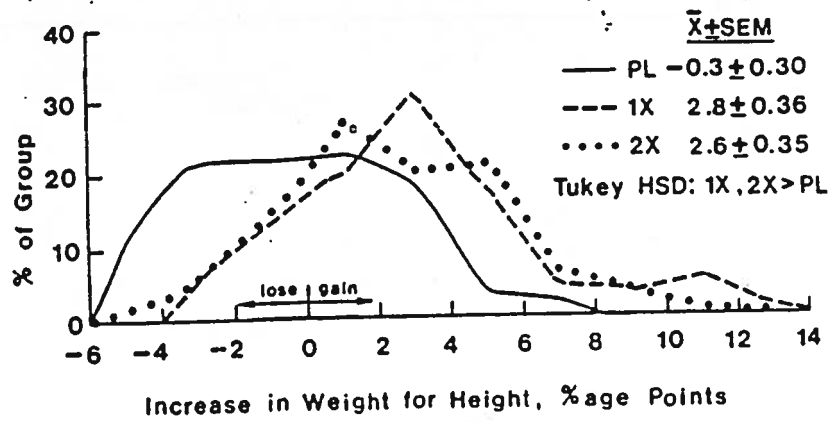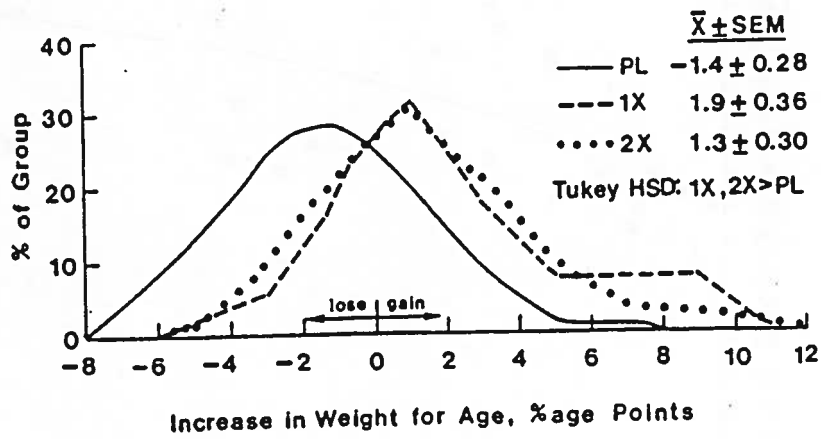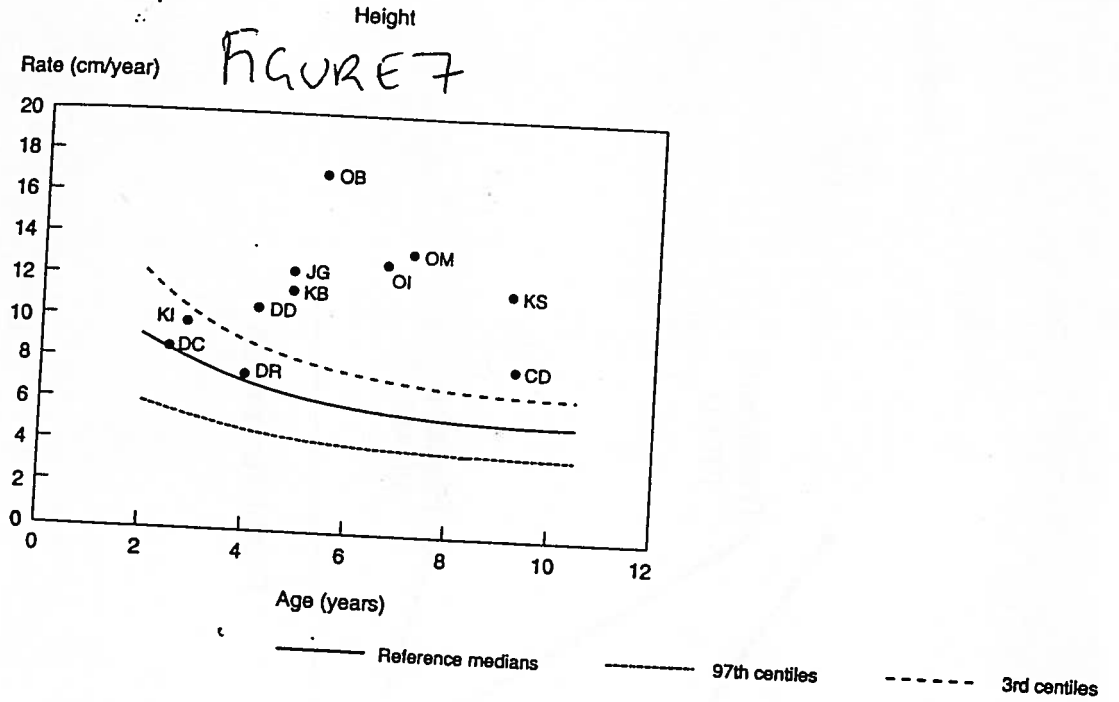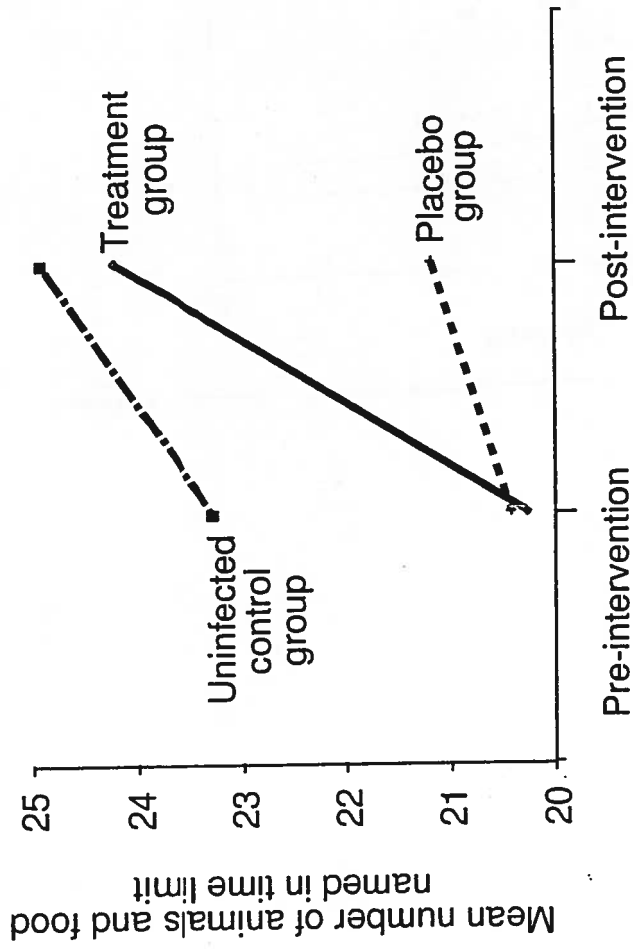
FIGURE 8

FIGURE 9

Relationship between prevalence of Ascaris infection and prevalence of morbidity for different threshold worm burdens (Guyatt & Bundy, in prep)
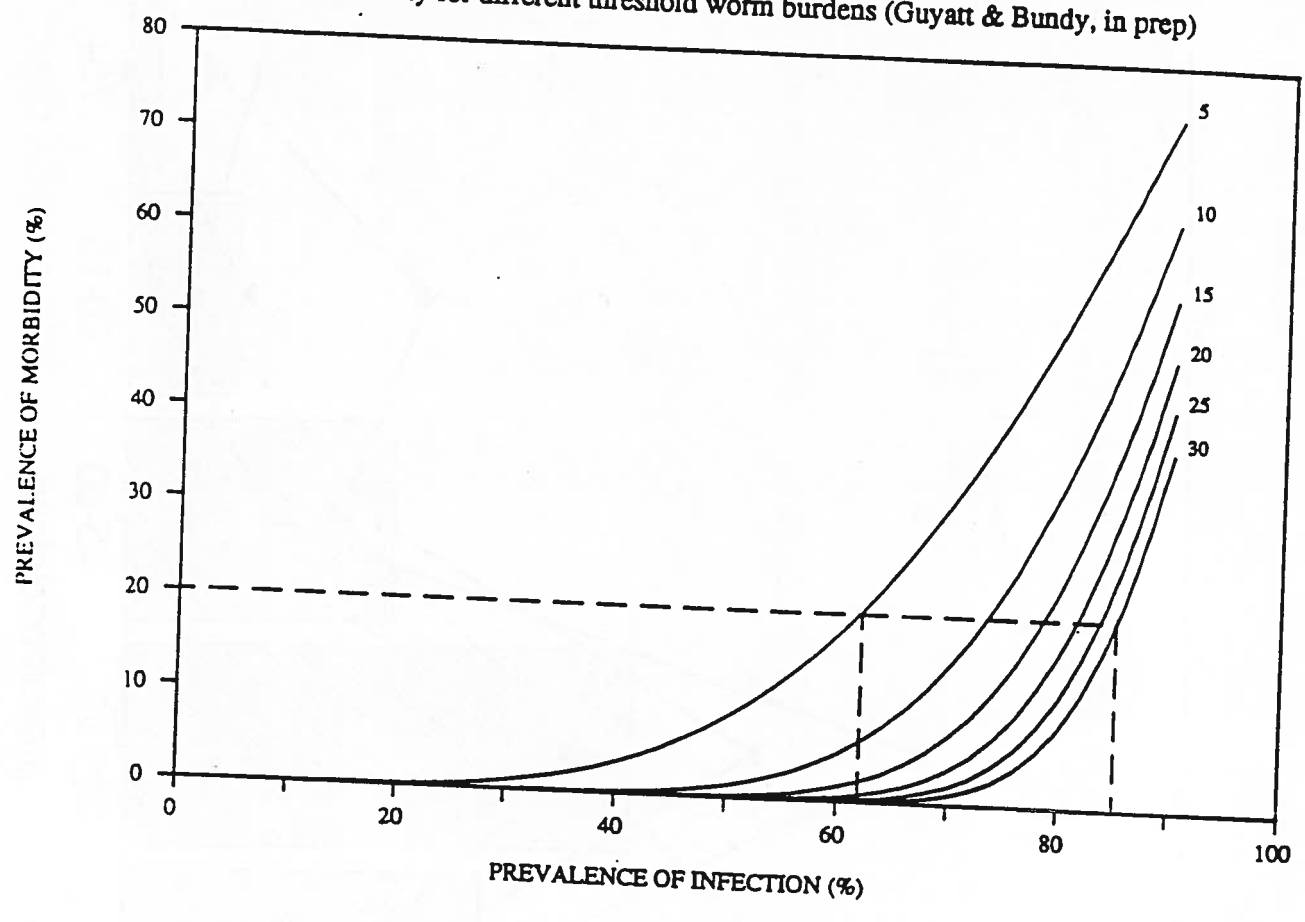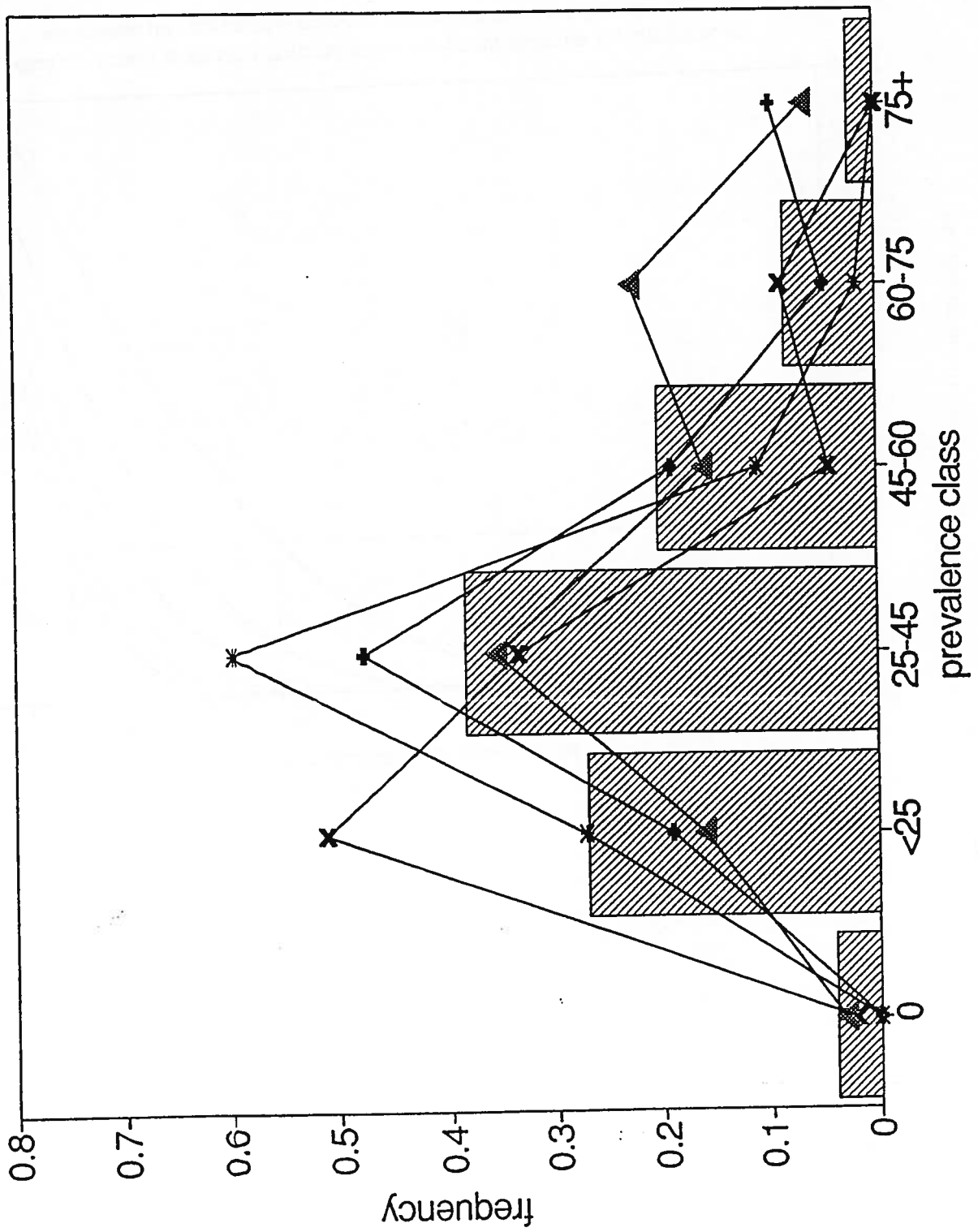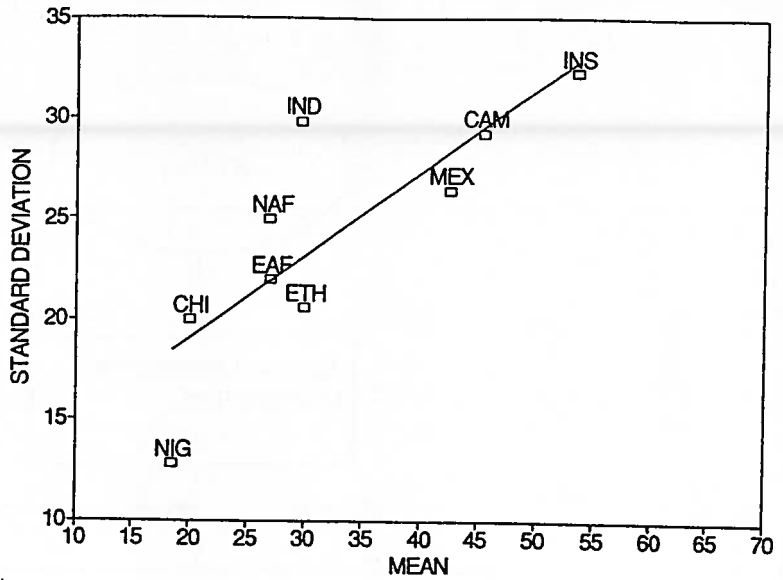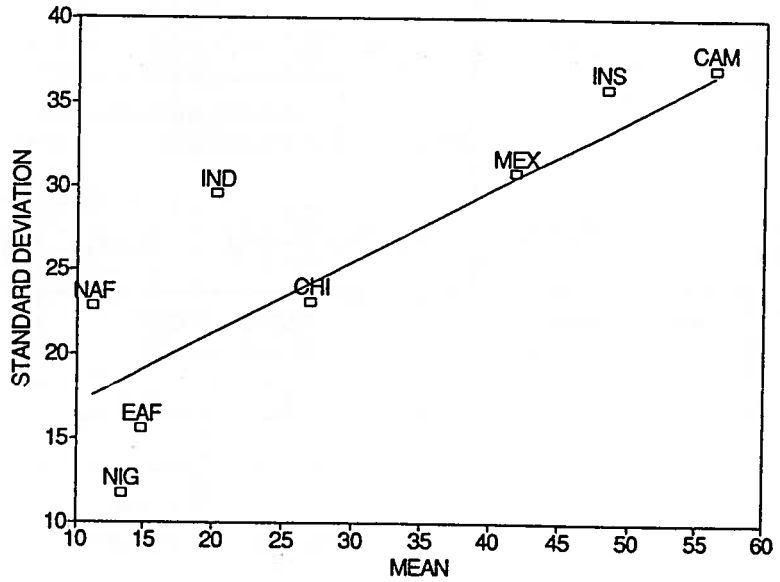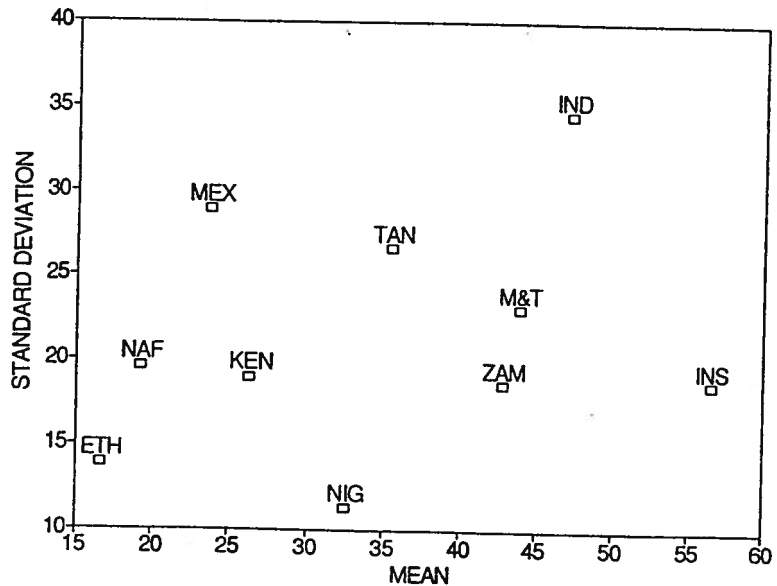
FIGURE 10

FIGURE 11

11a

11b

11c

FIGURE 12.

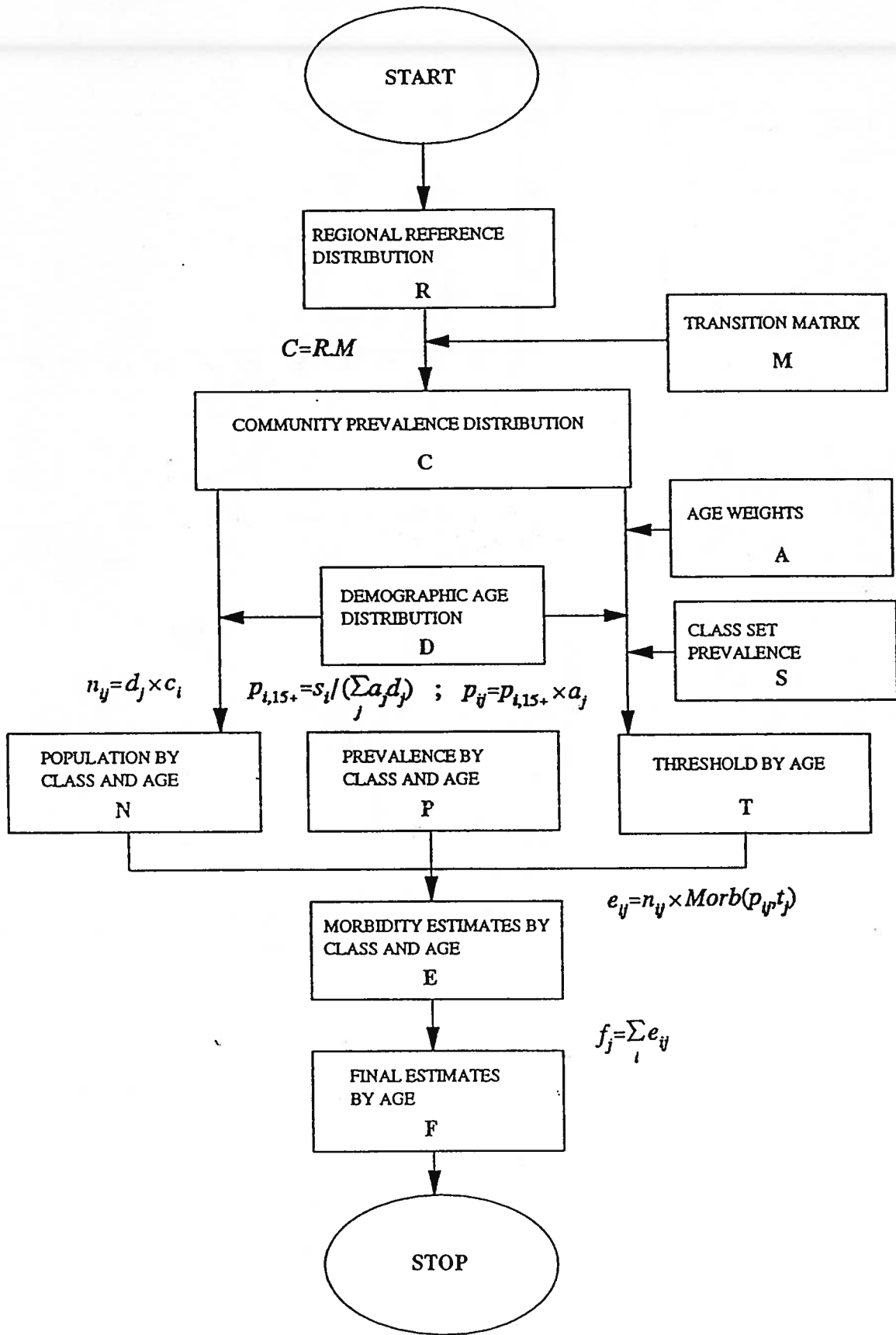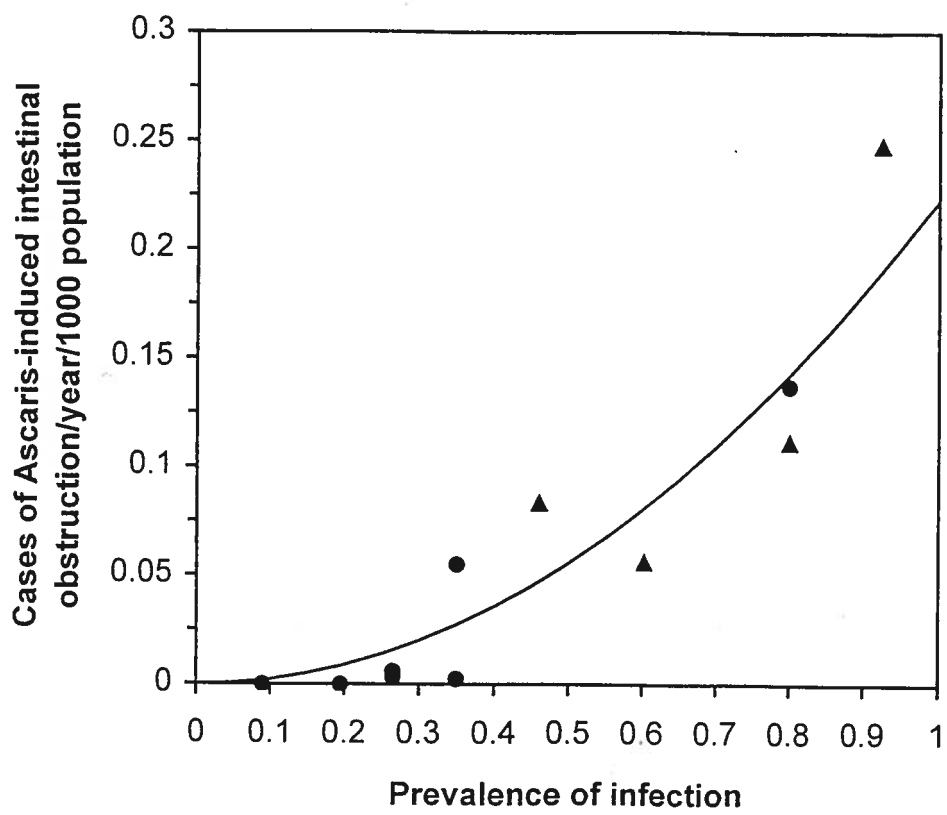Cases of Ascaris-induced intestinal obstruction/year/1000 population vs. Prevalence of infection

● All ages ▲ Children only ── polynomial regression line