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Intervention for the control of Soil -transmitted helminthiasis in the community

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Abstract

The global strategy for the control of soil-transmitted helminthiasis, based on regular anthelminthic treatment, health education, and improved sanitation standards, is reviewed.

The reasons for the development of a control strategy based on population intervention rather than on individual treatment are explained. The evidence and experience from control programmes that created the basis for i) the definition of the intervention package, ii) the identification of the groups at risk, iii) the standardization of the community diagnosis, and iv) the selection of the appropriate intervention for each category in the community are discussed. How to best deliver the appropriate intervention, the impact of the control measures on morbidity and on indicators such as school attendance, cognitive development and productivity are presented. The factors influencing the cost-benefits of helminth control are also considered. The recent progress on the control of soil-transmitted helminth infections is illustrated. Research needs are analysed in relation to the most recent perceptions from private-public partnerships involved in helminth control. The way forward for the control of soil-transmitted helminth infections is described as a multi-disease approach that goes beyond deworming and fosters a pro-poor strategy that supports the aims of the Millennium Development Goals.

1 Population-Based Interventions to Control Soil-Transmitted Helminthiasis

Ascaris lumbricoides, *Ancylostoma duodenale* and *Necator americanus,* and *Trichuris trichiura* constitute the major soil-transmitted helminth (STH) infections. Disease due to these infections is now recognised as a serious public health problem wherever suitable environmental conditions co-exist with inadequate sanitation and poor hygiene. In such

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conditions STH infections are normally highly prevalent with 2 billion people infected worldwide and several million suffering from the chronic debilitating morbidity (Crompton, 1999; Crompton, 2000; de Silva *et al.*, 2003).

The World Health Organization (WHO 2002a) has identified the population-based approach as the main strategy for the control of mortality and morbidity due to STH infections[1], for the following reasons:

- The clinical appearance of STH infection often lacks specific symptoms and may not be recognized by the infected person, even when causing significant health damage. When control measures are limited to curative services, only a small fraction of the infected population receives appropriate treatment.
- Individual diagnosis is relatively expensive requiring the availability of microscopes, laboratory material and trained personnel. The cost of establishing and maintaining an efficient STH diagnosis facility at peripheral level is much more expensive than the cost of treatment, now available for a few US cents per dose (WHO 2002a).
- Identifying risk is usually based on parasitological data that classify communities according to the risk of developing morbidity. To overcome the paucity of epidemiological information, environmental information can be used to predict the large-scale distribution of infection (Brooker *et al.* 2002a). Epidemiological assessments can be undertaken in a limited number of communities, in order to collect reliable data for risk identification and then select the appropriate intervention (Brooker *et al.*, 2002b, Montresor *et al.,* 2002).
- Drugs used in population-based interventions for the control of STH have a secure safety record. The drugs are given orally and because they are usually poorly absorbed they reach and kill the parasites in the digestive tract causing negligible side-effects. Two WHO Informal Consultations have recommended treatment with anthelminthics of pregnant women after the first trimester (WHO, 1996) and of children over 1 year of age (WHO, 2002b) to improve the health and development of these two high-risk groups in endemic countries.
- Delivering population-based interventions for the control of STH requires minimal infrastructure. Due to the safety profile of WHO-recommended anthelminthics, non-medically trained personnel can safely and effectively distribute the drugs after instruction (WHO 2002a, Urbani and Albonico, 2003). Distribution by school-teachers is particularly well accepted by the community (Nwaorgu *et al.*, 1998; Partnership For Child Development, 2001).

[1]WHO promotes the combined control of soil-transmitted helminthiasis and schistosomiasis where both these infections are endemic. Schistosomiasis and soil-transmitted helminthiasis present some similarities in terms of geographical distribution, epidemiology, groups at high risk and control interventions. Although this article focuses on the control of soil-transmitted helminthiasis, it should be noted that where the two infections are often co-endemic, combined control greatly increases impact and cost-effectiveness, and is strongly recommended where appropriate.

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- The morbidity caused by STH is directly related to the number of worms (intensity of infection) and the duration of infection. Infections of moderate to heavy intensity are mainly responsible for the morbidity due to STH. Regular treatment reduces the number of worms in each individual and keeps the worm burden permanently low throughout the year. Regular treatment, despite re-infection, is able to control morbidity in high transmission areas (Savioli *et al.*, 2002) because, even if prevalence of infection remains high, moderate to heavy infections (responsible for morbidity) decline over time (Figure 1).

The use of anthelminthic treatment is no longer limited to the clinical domain; it has become the intervention for large scale prevention and reduction of morbidity in endemic communities.

2 Intervention Package

Three interventions are recommended by WHO to control morbidity due to STH infections: (1) regular drug treatment of high risk groups, aimed at reduction of the worm burden over time; (2) health education to increase population health awareness; (3) sanitation supported by personal hygiene aimed at reducing soil contamination with infected human faeces and the likelihood of re-infection (WHO, 2002a).

An appropriate combination of these three measures should be applied according to different epidemiological situations and to the availability of resources.

2.1 Regular anthelminthic treatment

Regular drug treatment represents the main measure in areas where infections are intensely transmitted, where resources for disease control are limited, and where funding for sanitation is insufficient.

Drug treatment can be administered in the community using different strategies:

- Universal treatment. Treatment is offered to the entire community, irrespective of age, sex, infection status and any other social characteristics.
- Targeted treatment. Treatment is targeted at population groups, which may be defined by age, sex, or other social characteristics, irrespective of the infection status.
- Selective treatment. Individual level application of anthelminthic drug administration, where selection is based on diagnosis to detect the most heavily infected people who will be most at risk of serious morbidity and mortality.

The selection of the distribution strategy and the frequency of treatment is based on analysis of available epidemiological data.

Recommended drugs (WHO, 2004a) for use in public health interventions to control STH infection are:

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- albendazole 400 mg tablets given in single dose, reduced to 200 mg for children between 12 and 24 months
- levamisole 40 mg tablets given in single dose by weight (2.5mg/kg). Levamisole at a dose of 80 mg has been successfully used in primary school-age children (Albonico *et al.*, 2003)
- mebendazole 500 mg tablets given in single dose.
- pyrantel pamoate 250 mg tablets given in single dose by weight (10mg/kg). A combined preparation of pyrantel-oxantel has been proved more effective than pyrantel alone in treating *T. trichiura* infection (Albonico *et al.*, 2002).

These drugs are have undergone extensive safety testing and have been given to millions of individuals with only minimal adverse events (Urbani and Albonico, 2003; Horton, 2000). Anthelminthics can now be safely used in children as young as 12 months (Montresor *et al.*, 2003; WHO, 2002b). Drugs that do not need dosage according to weight, such as albendazole, mebendazole and levamisole (in school-age children) are considered easier to use for population-based interventions (de Silva *et al.*, 1997). All these drugs produce excellent egg reduction rates for *A. lumbricoides* (> 95 percent) and for hookworms (> 80 percent), but are less effective against *T. trichiura* (WHO 1999, Bennet and Guyatt 2000). The efficacy of single-dose anthelminthics is summarised in Table 1.

The patents of the anthelminthic drugs recommended by WHO have expired and therefore the drugs can be produced at very low price by generic manufacturers. The price in the international market for mebendazole 500 mg, produced under Good Manufacturing Practice conditions is approximately 0.02 US $/tablet (Management Science for Health, 2004). The price is further reduced in case of local production, but in this case special attention should be given in assuring the good quality of the product. WHO, with a network of quality control laboratories, may facilitate the quality control exercise (Montresor *et al.* 2002).

2.2 Health education

Health education aims to increase health and hygiene awareness and to change health behaviour in the population. Health awareness is usually increased when communication strategies of proven efficacy are adopted (Kinzie, 2005). Marketing techniques and tools imported from the private sector are increasingly being advocated for their potential value in crafting and disseminating health messages (Bull *et al.*, 2002), but this technology should be appropriately transferred to reconcile differences between commercial marketing and public health (Walsh *et al.*, 1993). Education materials (posters, leaflets, radio and video messages) have been traditionally used to transmit and disseminate health messages. The expansion of commercial advertising in developing countries, however, calls for upgraded skills in designing such tools in order to compete for attention (Bull *et al.*, 2002; Whitelaw *et al.*, 2005).

The adoption of safe behaviour is more difficult to obtain since it is not simply a direct consequence of the health awareness. Especially for diseases related to poverty such STH infection, the suggested solution might not be available or too expensive to adopt. Although

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deprived communities understand the importance of disposing safely faecal matter and of wearing shoes, poverty often hinders the construction of latrines and the purchase of shoes.

For STH infections, the aims are (1) to reduce the faecal contamination of the soil, by recommending the use of latrines, (2) to develop self-protection from re-infection, through personal/family hygiene measures such as washing hands and proper food preparation, and (3) to avoid spraying night soil on vegetables in communities where this habit is common.

Frequently in STH endemic areas, latrines are not available or not in sufficient number for the population needs (Cairncross, 2003), therefore the knowledge and motivation for behavioural change must be sustained with the availability of proper facilities for excreta disposal.

Providing information on the disease and the possible adoption of preventive measures, frequently results in increase of knowledge but not necessarily in behavioural change (O'Cathain *et al.*, 2002). Informed choice in the context of health care, competence (of patients to understand the problem) and the possibility of making a decision (availability of an alternative choice) are also necessary (Reeves, 2002).

Promotion of latrine maintenance and use, washing hands and proper food handling have benefits that go beyond the control of STH infections. From this perspective, it is reasonable to include health education in all STH control programmes when the health education message can be provided in a simple and inexpensive way. Health education messages can be delivered by teachers in schools thereby fostering changes in health behaviour in children which in turn involve their parents and guardians. On the other hand, intensive and sophisticated campaigns can represent the main cost for a STH control programme and impair significantly the cost/effectiveness of the control effort (Mascie-Taylor *et al.*, 1999). The effectiveness of health education campaigns in increasing health awareness and changing defecation habits varies according to different reports (Lansdown *et al.*, 2002; Guanghan *et al.*, 2000).

2.3 Sanitation

Sanitation is composed by two elements which are complementary: “hardware” such as toilets, latrines, sewage treatments, and “software” such as personal hygiene and legislation. Sanitation In the context of economic development is the only definitive intervention that eliminates STH infections. STH infections are never a public health problem where hygiene and sanitation standards are appropriate. Improvement of the sanitation standard always has a repercussion on infection and re-infection levels. Studies from West Indies showed that prevalence of STH infections were significantly lower in areas with improved sanitary conditions as was re-infection. Crowding and type of excreta-disposal facility were the only significant predictors of re-infection (Henry, 1988). Similar results were obtained in urban slums of Bangladesh (Henry *et al.*, 1993) and in the plantation sector of Sri Lanka (Sorensen *et al.,* 1994).

Sanitation, however, does not become effective until it covers a high percentage of the population (Esrey *et al.,* 1991). In Zimbabwe, despite the marked increase in the number of

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latrines, no relationship was found between hookworm re-infection intensities and the availability of latrines on individual farms (Bradley *et al.,* 1993). The effect of improved sanitation on helminth transmission is slow to develop and may take decades to achieve a measurable impact. Often, the high costs involved, prevent the provision of sanitation to the communities most in need (Asaolu and Ofoezie, 2003).

A recent experience from STH control in Viet Nam (Montresor, personal communication) based on regular deworming, latrine construction and health education, has shown that the cost /child for each latrine has been estimated at 7.9 US $ (an amount equal to receiving over 200 doses of regular deworming). The building of new latrines was considered important as example for the schoolchildren and a way to providing essential sanitation at least in school. This intervention, however, increased the latrine coverage in each community of less than 1%. To have a significative impact (e.g. 20%) in the latrine coverage, an investment of 50,000 US $ is considered necessary in each community, and a total of over 9 million US $ for one entire province.

In addition, latrine coverage is not a solution, unless the latrine is used and maintained. Studies in Senegal (Sow *et al.*, 2004) demonstrated that, despite high latrine coverage, the majority of the children in a village, interviewed with a questionnaire, claimed to defecate elsewhere. Experience in Mozambique demonstrated that in areas with low latrine coverage, even in houses where a well-maintained latrine existed, the soil in the house-yard was contaminated (Muller *et al.,* 1989).

On the other hand, alternative model which offers a market-based approach that considers the rural poor as customers and not beneficiaries, may accelerate access to sanitation, enhance sustainability, and deliver services more efficiently. An international NGO recently launched a project to stimulate the acquisition and use of sanitation in rural areas of Viet Nam. A range of options that were appealing and affordable to potential customers was developed, the community's willingness to pay was assessed and the perception of benefits of sanitation was promoted through media channels and tailored messages. Within a year coverage of sanitation access has increased by 100% compared with the pre-project access rate. This success indicated that the population's willingness to pay for sanitation is often underestimated, provided that quality product and services are offered with effective information (Mukherjee, 2005).

3 Groups at Risk

3.1 Preschool children

Children between 1 and 5 years of age, are particularly vulnerable to disease caused by STH infections (Carrera *et al.,* 1984; Oberhelman *et al.,* 1998; Crompton and Nesheim, 2002). Though are less likely to harbour heavy infections, such young children, whose worm burdens are housed in smaller bodies, are at higher risk of anaemia and wasting malnutrition (Awashti and Pande, 2001).

The negative effect of STH infection on iron status and nutrition in non-immune children with light infections may be linked to an inflammatory-triggered cytokine response in

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"naive" children, and a consequent suppression of protein metabolism, appetite and erythropoiesis, and not only to iron and micronutrient loss (Stoltzfus *et al.*, 2004).

3.2 School-age children

Children of primary school age (6 - 14 years) should be a major target for regular treatment, because they are the group that usually has the heaviest worm burdens for *A.lumbricoides* and *T. trichiura*, and are steadily acquiring hookworm infections. In addition, they are in a period of intense physical and intellectual growth and benefit most from deworming in terms of growth and school performance (Bundy *et al.* 1992; Crompton and Nesheim, 2002). Schoolchildren are the most accessible group to reach in countries where school enrolment rates are good (Partnership For Child Development , 1999) and even non-enrolled siblings could be effectively outreached by promoting advocacy through the schools (Montresor *et al.*, 2001).

3.3 Women of childbearing age

Women between 15 and 49 years are susceptible to iron deficiency anaemia because of iron loss during menstruation and because of increased nutritional needs during pregnancy (Torlesse and Hodges, 2001; Nurdia *et al.*, 2001). The problem is aggravated if they have diets low in bioavailable iron and if they suffer from hookworm infection. Hookworms feed on blood and iron deficiency is often the consequence of this activity. Hookworm infection invariably reaches peak intensity in this age group (Bundy et al., 1995a). Antenatal anthelminthic treatment in hookworm endemic areas is recommended for the control of maternal anaemia (WHO, 1996). The benefits of deworming after the first trimester far outweigh the health risks and results in improvements in maternal iron status, birth weight and perinatal survival (Christian *et al.*, 2004).

4 Frequency of Treatment

Frequency of regular treatment should vary according to the intensity of transmission and rates of re-infection. These factors must be considered in relation to the resources available and the cost involved in drug purchase and distribution. When there are budgetary constraints it is more efficient to treat a greater proportion of the population less frequently than to treat a smaller proportion of the population more often (Evans and Guyatt, 1995). For *A. lumbricoides* infections, the most cost-effective option is to treat infrequently (every 2 years) when effectiveness is assessed in terms of reduced of mean worm burden and reduction in disease prevalence, both in low and high transmission areas. In contrast, when prevalence reduction is used as the measure of effectiveness (prevalence recovers more rapidly than intensity), the most cost-effective option is to treat every 4 months in high transmission areas and every year in low transmission areas (Guyatt *et al.*, 1993).

- Treatment frequency of twice or three times a year is effective in reducing morbidity in areas of intense transmission (prevalence >70 % and more than 10 % of infections of moderate or heavy intensity) such as in Zanzibar (Albonico *et al.*, 1999a), Nepal (Khanal and Walgate, 2002) and Myanmar (Thein-Hlaing, 1989).

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- In areas with a lower intensity of transmission (prevalence between 40% and 60 % and less than 10 % of infections of moderate and heavy intensity), for example in Oman (Idris *et al.*, 2001), India (Chhotray and Ranjit, 1990) and Brazil (Machado *et al.*, 1996), once-yearly intervention was found to be sufficient to reduce morbidity.

Based on these experiences and on logistic limitations, endemic communities are classified in three categories according the levels of cumulative STH prevalence and intensity estimated in the population (Table 2). An indication of the epidemiological situation of the community can be estimated from the data collected in school-age children (Guyatt *et al.*, 1999) and guidelines on how to conduct school surveys have been proposed by WHO (Montresor *et al.*, 2002).

Each STH infection can be classified as being of light, moderate or heavy intensity according to the thresholds established by a WHO Expert Committee (WHO 2002a) based on the number of STH eggs per gram of faeces (Table 2). Helminths in different areas of the world have different levels of egg output (Hall and Holland, 2000), so the thresholds proposed by WHO are not rigid and should be adjusted for the local situation. The appropriate population-based treatment strategies recommended for each category is illustrated in Table 3 (WHO 2002a).

5 Targets

The World Health Assembly in 2001 endorsed a strategy for the prevention and control of schistosomiasis and soil-transmitted helminthiasis in high transmission areas (WHO, 2001). In the short term morbidity will be reduced by:

- access to drugs (praziquantel and broad-spectrum anthelminthics), and good case management, in all health services;
- regular treatment of at least 75% of school-age children by 2010;
- targeting other high risk groups (young children, women of childbearing age, occupational. groups) through existing public health programmes and channels.

For long-term sustainability, environmental health will be required including:

- improving access to safe water and sanitation;
- improved hygiene behaviour through health education.

Field experience has shown the 75% coverage is an attainable target even in areas where school enrolment rates are low (Montresor *et al.*, 2001) and that a significant reduction in morbidity can be achieved in situations of intense transmission (Albonico *et al.*, 1999b). Cambodia is the first country to have reached this target ahead of schedule and other countries such as Brazil, Equador, Nepal, Tanzania, Uganda, Vietnam are on track to succeed.

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6 Delivering the Intervention

Implementation of any helminth control programme at country level requires strong links with existing interventions that already target women and children. Deworming can readily be added to ongoing public health programmes.

6.1 Helminth control through schools

Helminth control in schools is reckoned to be a most cost-effective public health intervention in low-income countries (World Bank, 1993). Schools represent an ideal setting to reach children. Trained teachers can distribute and administer the drug and give health education messages to the pupils (Montresor *et al.*, 2002). Schools can be used to reach non-enrolled school-age children with a simple child-to-child approach (Montresor *et al.*, 2001). De-worming of school-age children requires minimal financial input (Partnership For Child Development 1999) and gives notable nutritional and cognitive benefits. In addition, enrolment figures and school attendance normally increase after such interventions.

School feeding programmes helps to break the interrelated cycles of hunger, illiteracy, poverty and disease, and serves as a platform for deworming and other interventions (WFP, 2004). Thirty countries worldwide now report active deworming combined with school feeding programmes. Almost 2 million children were reached in 2002, nearly 3 million in 2003, and over 7 million in 2004 (WHO, 2003a). STH control programmes rely strongly on volunteer personnel who are not remunerated but need some basic training for distributing the drug. The safety profile of drugs distributed without the supervision of medical personnel must be explained. In case of any adverse events the child should be referred to the nearest health centre. Close collaboration between the Ministry of Education and Ministry of Health at all levels is mandatory for the success of deworming and other control measures such as health education through the school system.

6.2 Helminth control through community-based intervention

Recent experience demonstrates that many preschool children can be reached by adding de-worming to vitamin A distribution or immunization campaigns. Worms and vitamin A deficiency thrive in impoverished communities where the two problems often co-exist. The advantage to add deworming to vitamin A supplementation is the coverage opportunity: over 167 million children are reached yearly by vitamin A supplementation programmes worldwide and more than 50 countries report more than 70% coverage (UNICEF, 2005). Deworming has been found to increase the vitamin A supplementation coverage and worm-free children have a better vitamin A status than infected children (Curtale *et al.*, 1995). Delivering deworming by using the vitamin A distribution infrastructure reduces costs and takes advantage of the access to remote communities that is already in place.

Nepal is successfully pioneering this approach. Deworming is now offered to children under five by using existing resources and the success of vitamin A distribution campaigns is being reinforced (Khanal and Walgate, 2002). Deworming is also being delivered during the National Child Health Days, a way of reaching children with a package of health measures including immunization and vitamin A supplementation. A similar intervention is proving to

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be successful in Angola, Republic of Korea, Tanzania, Uganda (WHO, 2004b; WHO 2005a). In Cambodia, the Ministry of Health uses monthly outreach services to deliver a minimum package of activities through health centres including immunization, antenatal care, health education, family planning, tuberculosis, leprosy care, vitamin A supplements and deworming (WHO, 2004b; WHO 2005a).

Mother and Child Health (MCH) services offer opportunities to provide regular deworming for childbearing women and children over the age of one year (Savioli *et al.* 2003). The inclusion of routine deworming now reaches 75 percent of pregnant women in Sri Lanka (de Silva, personal communication). STH control measures can also be added to other public health initiatives including Integrated Management of Childhood Illness (IMCI), School Health Programmes, Roll Back Malaria, Micronutrient Initiatives and Reproductive Health – Making Pregnancy Safer.

7 Impact on Morbidity

7.1 Preschool children

Children under five experience the detrimental consequences of acute and chronic STH infections. Recent data from East Africa indicate that hookworms are an important cause of anaemia in preschool children (Brooker *et al.,* 1999) and that regular distribution of anthelminthics has a positive effect on motor and language development in this age group (Stoltzfus *et al.,* 2001). After 12 months of quarterly mebendazole treatment in Zanzibari children, mild wasting malnutrition was reduced by 62% in children < 30 months, moderate anaemia (Hb < 9 g/dl) was reduced by 59% in children < 24 months, and appetite was improved by 48% in all 460 children (Stoltzfus *et al.*, 2004). In India, Awasthi *et al.*, (2000) found that when children aged between 1.5 and 3.5 years received vitamin A and albendazole every six months they gained 3.5 kg in 2 years, compared with 2.5 kg gained by children given vitamin A only. In Nepal twice yearly distribution of vitamin A and albendazole to 2 million children under 5 reduced anaemia by 77% in one year (Mathema *et al.,* 2004).

7.2 School-age children

Deworming school-age children has a considerable benefit on their nutritional status (Stoltzfus *et al.*, 1996, Curtale *et al.,* 1995), physical fitness, appetite, growth (Stephenson *et al.*, 1993) and intellectual development (Partnership For Child Development, 2002). Although re-infection is inevitable where sanitation is lacking (Albonico *et al.,*1995), treatment three times a year with a single dose of 500 mg mebendazole prevented 1260 cases of moderate-severe anaemia and 276 cases of anaemia in the school-children study population (n= 30,000) in Zanzibar (Stoltzfus *et al.,* 1998).

Studies in low-income countries of Africa (Kvalsvig *et al.*, 1991) and The Caribbean (Nokes *et al.*, 1992) have shown that children with intense STH infections perform poorly in learning ability tests, cognitive function and educational achievement. Differences in test performance equivalent to a 6-month delay in development can be attributed to moderate/heavy *T. trichiura* infections (Nokes and Bundy, 1994). Deworming schoolchildren assists

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their ability to learn. Tests have shown that a child's short-term memory, long-term memory, executive function, language, problem solving and attention respond positively to deworming (Watkins and Pollit, 1997). Interestingly, girls display greater improvements than boys. For the most heavily infected children, their educational performance shows an improvement after treatment. For the less heavily infected, deworming may allow them to catch up with uninfected peers over the longer term (Nokes *et al.*, 1992).

Deworming is usually followed by a significant impact on school absenteeism. For example, Jamaican children enduring intense infections with *T. trichiura* miss twice as many school days as their infection free peers (Nokes and Bundy, 1993). A randomized trial in Kenya indicated that school-based targeted treatment with deworming drugs reduced school absenteeism in treatment schools by 25% and that also untreated children in neighbouring schools enjoyed higher school participation and better health (Miguel and Kremer, 2001).

7.3 Pregnant women

Despite understandable concerns about the risk to the unborn child of offering deworming drug to pregnant women, significant benefits follow for mother and infant when hookworm infections are reduced.

A study in Sierra Leone demonstrated that a single dose of albendazole given to pregnant women after the first trimester helped to prevent the decrease in haemoglobin concentrations that continued to occur in the untreated group (Torlesse and Hodges, 2001). An analysis of over 7,000 pregnancies in Sri Lanka reported that mebendazole therapy during pregnancy is associated with a significant improvement in birth weights, fewer stillbirths and perinatal deaths, and that there was no increase of birth-defect rates compared to the untreated women (de Silva *et al.,* 1999).

A controlled study in rural Nepal, where the prevalences of hookworm and *Ascaris* infection were roughly 70% and 50% respectively, demonstrated that deworming greatly improves the health of pregnant women and the birthweight and survival of their infants. After albendazole treatment in the second trimester there was a significant decrease in the prevalence of severe anemia in pregnant women, the birthweight of babies from mothers given two doses of albendazole rose on average by 59g, and the infant mortality rate at 6 months had fallen by 41% (Christian *et al.*, 2004). This work confirms that deworming should be considered as part of routine antenatal care in areas where hookworm infections are endemic. The *Essential Care Practice Guide for Pregnancy and Childbirth* (WHO, 2003b), which provides support to the Integrated Management of Pregnancy and Childbirth (IMPAC), recommends anthelminthic treatment for all pregnant women in the second and third trimester attending clinics if they did not receive such treatment in the last 6 months, and also treatment for all postpartum women.

Women in the first trimester of pregnancy are precautionally excluded from any treatment (including anthelminthic). In developing countries, this principle presents some problem of application because some women in the first trimester of pregnancy may not be aware of their pregnancies. Also the performance of pregnancy test to all women of child-bearing age before administering anthelminthic treatment is not usually affordable. Adolescent girls who

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may be in early pregnancy while still at school and the school is in a deworming scheme are a concern. Results from studies that have evaluated inadvertent deworming during the first trimester, however, have indicated that the risk of extra birth defects is negligible and that benefits in treating hookworm-induced iron deficiency anaemia both for the mother and the newborn far outweight the risk of taking tablets in early pregnancy (de Silva *et al.,* 1999; Torlesse *et al.,* 2001; Diav-Citrin *et al.,* 2003; Christian *et al.,* 2004).

7.4 Adults

Adult populations are also vulnerable to high intensity hookworm infections. Studies conducted in rural China, Brazil, and elsewhere reveal that the elderly often suffer from high intensity of hookworm infection and clinical hookworm disease with impairment of work productivity (Bethony *et al*., 2002; Gandhi *et al.,* 2001). The relationship between STH infections and labour productivity has been studied in various settings, such as tea picking communities in Asia (Gardner *et al*., 1977, Gilgen *et al*., 2001), road workers in Africa (Brooks *et al.,* 1979; Wolgemuth *et al*., 1982) and rural communities in Latin America (Viteri and Torun, 1974). Iron deficiency anaemia, the hallmark of hookworm infection, is the major cause of weakness and fatigue in adults in endemic countries (Crompton and Nesheim, 2002). Not only do the infections significantly reduce the ability to sustain even moderate levels of labour, they also reduce the pace and time spent at work. STH control would increase country productivity and aid economic development (Guyatt, 2000).

8 Cost of the Intervention

The cost-benefits of the control measures for morbidity due to STH infection is influenced by the ecological and environmental situation, by the availability of local anthelminthic drug production, and by the presence of infrastructures and facilities that can be used to reach the high-risk groups.

8.1 Regular chemotherapy

Calculations indicate that a bundle of diseases, including schistosomiasis, soil-transmitted helminthiasis, onchocerciasis, lymphatic filariasis, trachoma and vitamin A deficiency, can be controlled at costs for drug and nutrients ranging from about 1 to 2.50 US $ per patient (Molyneux and Nantulya, 2004). The infrastructure for the delivery of such a package of health care to millions of poor people already exists in many endemic areas through primary health care provision, public and private schools, faith-based organizations and social institutions. In deprived communities, where sanitation is practically non-existent and the prevalence and intensity of infection are high, a suitable infrastructure (such as the school system or a national immunization day) should be used to distribute at least regular treatment to the groups at risk. The cost of adding this intervention is normally marginal.

Over 1,300,000 preschool children were de-wormed during the 2002 vitamin A distribution campaign in Nepal. The yearly cost of the vitamin A intervention is estimated at 1.7 million US $ (Fiedler, 2000). An additional expenditure of 80,000 US $ (about 4 % of the cost of the vitamin A distribution) covered the cost of adding bi-annual deworming to the vitamin A campaign (Mathema *et al.,* 2004).

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Since 1998, the World Food Programme (WFP) has incorporated deworming in the School Feeding Programme (SFP) in Nepal and, in light of the nutritional consequences, decided to include deworming (including schistosomiasis control) in all the countries where SFPs are conducted (Bordignon and Shakya, 2003). Thirty countries now conduct combined deworming and school feeding programmes. The average cost per child per year is 70 US cents: 4 cents for mebendazole, 25 cents for praziquantel, 30 cents for training, monitoring, educational materials, and the remaining 11 cents for delivering both drugs (WHO 2003a).

In Ghana with over 80 000 school-age children treated and Tanzania with over 100 000 school-age children treated, the estimated costs for school-based delivery of albendazole was 0.04 and 0.03 US $, respectively (Partnership for Child Development, 1999).

In Cambodian schools, deworming is promoted by means of a school kit which contains deworming tablets, health education posters and pamphlets for teachers, games, and attractive pictures giving simple messages on how to prevent infection. The coverage of primary school-age children was 84% in 2003, and the bi-annual deworming campaign from 2004 onward will cost 0.04 US $ per child treated (Sinoun *et al.,* 2005).

The advantage of regular deworming lies in its simplicity (one tablet/child), cheap delivery (by teachers through schools), and safety record (the benefits of treatment far outweight the risk of minor side effects). Many organizations, including NGOs, could include a STH control package in their routine activities and, even with limited budgets, relieve the burden of STH in the population covered.

8.2 Health education

The contribution of health education towards the control of STH infections and morbidity varies according to different reports. A randomized trial in 25 schools in Viet Nam did not find that intensive health education had any effect on the intensity of re-infection six months after treatment (Partnership For Child Development , unpublished results). Other authors observed increased levels of knowledge and improved health behaviour in the population (Lansdown *et al.*, 2002), and measured a decrease in re-infection rates (Guanghan *et al.*, 2000). Cost analysis of work in Bangladesh indicates that regular mass treatment with albendazole is the most cost-effective control strategy and strategies involving health education were the least cost effective (Mascie-Taylor *et al.*, 1999).

The importance of health education should not be measured merely on cost-effectiveness alone. Health education, in community health, has the same role as the medical information and counselling given by the physician to the patient in clinical medicine. The effects of establishing a good relationship between the health system and the community is not always directly measurable with regard to the success of the control measures. The effect of health education in community health includes improvement in loyalty and trust between the educators and the community. When such a relationship is established, the community is no longer a simple recipient of the medical intervention but becomes one of the partners in the process.

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8.3 Sanitation

The investment needed to provide access to adequate sanitation is beyond the resources of low-income countries. In addition, although improved water and sanitation contribute to reduce incidence of infection (Esrey *et al.,* 1991), morbidity due to infection may persist (Asaolu *et al.*, 2002). The coverage of properly built, used and maintained sanitation has to be higher than 90% to have any effects on worm transmission and critically depends on the general socio-economic status of the community (Asaolu and Ofoezie, 2003). A reliable evaluation of the advantage of investments in sanitation must include the consequences for other health services and for economic development. An efficient sanitation infrastructure removes the underlying cause of most poverty-related communicable diseases and so support the economic development of a country.

The magnitude of the problem of providing sewerage, however, is a big challenge in large metropolis in developing countries. In Lagos, Nigeria, according to population projections, there may be an additional 1240 tons of human stool being deposited daily in the areas where the poor people live. The installation costs of modern sewerage similar to the type found in development countries for the poor population of Lagos could amount to a billion US dollars or more. Progress has been made in developing a variety of latrines for rural communities, but these may not be appropriate for slums and squatter settlements with a shortage of land for dwellings (Crompton and Savioli, 1993). The resources needed to improve hygienic standards can be huge, but the collaboration of different initiatives dealing with hygiene and prevention of diseases related to poor hygiene will help create the synergy needed to reduce both disease and poverty.

9 New Technology for Sustaining Deworming

Regular chemotherapy with single dose anthelminthic drugs will be the mainstay for control of morbidity due to helminths infection in endemic countries for sometime. No new drugs have been recently developed, tested and registered and it is essential to make the best use of existing products. This is particularly important in the light of increasing drug resistance of nematodes of livestock to veterinary versions of anthelminthic products also used in human (Geerts and Gryseels, 2001). Recent evidence suggests reduced efficacy of benzimidazoles against hookworm infections in humans after 15 rounds of treatment (Albonico *et al.*, 2003). Reduced efficacy after drug exposure and treatment failures are signs that drug resistance may emerge. Assessment and monitoring of efficacy of anthelminthic drugs in areas where they are commonly used should be performed in a standard way so to warn of possible treatment failures and stimulate further investigations. In addition to the available measurement of reduction in faecal egg count following treatment, tests such as the Egg Hatch Assay have been developed to monitor benzimidazole efficacy against human hookworms (Albonico *et al.*, 2005). The development of molecular probes with PCR techniques offers a more sensitive technique for drug efficacy monitoring (Roos *et al.*, 1995). Research studies to identify sensitive and resistant genes in worm populations are at an early stage (Albonico *et al.*, 2004).

The creation of a global network for monitoring anthelminthic drug efficacy and resistance, coordinating research efforts, and translating operational research outcome into health policy

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is a much needed response to this emerging threat. Such a network will depend on action by different partners and dedicated funding. A successful example is the concerted action on the use of praziquantel for the treatment of schistosomiasis in Africa , which is funded by the European Union and involves a forum of scientists and public health planners (Hagan *et al.*, 2004).

Combined treatment with two drugs with different modes of action or their alternate use are among strategies to safeguard efficacy and to delay the possible emergence of drug resistance. Combined treatment with mebendazole and levamisole has been proved safe and more effective than either drug alone (Albonico *et al.*, 2003). A pyrantel-oxantel combination is more effective than benzimidazole drugs in curing *T. trichiura* infections (Albonico *et al.*, 2002). Ivermectin and albendazole are effectively and safely given in combination in some countries as mass treatment to eliminate Lymphatic Filariasis and have ancillary benefits in controlling other helminthiasis including strongyloidiasis (Belizario *et al.*, 2003). Co-administration of praziquantel and albendazole is recommended where schistosomiasis and intestinal helminthiasis are endemic (Olds *et al.*, 1999).

In addition to chemotherapy, a new hookworm vaccine against *N. americanus* infection is being developed and tested by the Human Hookworm Vaccine Initiative (Hotez *et al.,* 2003). It is proposed that chemotherapy would be given first to treat existing cases and then a vaccine would be administered to prevent or to delay further re-infection. It is unlikely that a hookworm vaccine will interrupt transmission due to the heterogenicity in hookworm transmission and the need for a vaccine to provide protection for at least two-thirds of an individual's lifetime (Anderson, 1982). The vaccine would decrease the number of L3 larvae invading the gastro-intestinal tract, prevent their development into adult worms (antilarvicidal effect), and it would also reduce the sexual development of female worms (antifecundity effect). The major benefit will be directly reducing individual's worm burden. A first generation product known as *Na*-ASP-2 hookworm vaccine against *N. americanus* has been developed and comprises of a larval hookworm recombinant protein engineered and purified from yeast. Proof-of-concept for the efficacy of the *Na*-ASP-2 vaccine to reduce hookworm burden and intestinal blood loss will be evaluated in a Phase 2b clinical trial in Minas Gerais State, Brazil. An uncertainty is how much such a vaccine will cost to manufacture. Finding an innovative financing mechanism and a cost-efficient delivery represents the major challenges for the successful deployment of hookworm vaccines (Bundy *et al.*, 1995b; Brooker *et al.*, 2005).

10 Scaling up Deworming for School-Age Children

Following the 2001 WHA resolution, WHO was requested to set up a system to monitor each endemic country's progress towards the 2010 target. A global databank has been established at WHO (www.who.int/wormcontrol) to track the number of people who are treated each year for soil-transmitted helminthiasis and schistosomiasis and epidemiological data describing the distribution of infections are regularly collected and displayed using the geographical information system technology. Country profiles, including information on coverage data, plans of action, anthelminthic drugs on the Essential Drug List and their cost, are collected through questionnaires and extensive liaison with other partners, regional

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colleagues, and national programme managers. Global progress in coverage in school-age children from 1999 to 2004 is reported from 73 out of a 104 endemic countries. Although data is awaited from 26 countries in Pan American Health Organization and from India and China, there is a steady increase of coverage over time. Thirty of the 73 countries are known to be expanding control activities (Figure 2) (WHO, 2005b).

The Schistosomiasis Control Initiative (SCI) is assisting Uganda, Burkina Faso, Mali, Niger, Tanzania (including Zanzibar), and Zambia to scale up schistosomiasis and helminthiasis control to National level. SCI has promoted integration of other deworming programmes at the country level , the synergistic deworming in collaboration with the Programme to Eliminate Lymphatic Filariasis (PELF) being an example. SCI, with funds from the Bill and Melinda Gates Foundation, has facilitated registration of drug products in each country, promoted local production by national pharmaceutical companies, and strengthened procurement agencies at country level according to local needs (Fenwick, in press). In addition to these countries, also Cambodia, Nepal, Equador, Brazil, Viet Nam, are examples of good progresses in helminth control.

WHO and other partners are building regional and country capacity to strengthen implementation of control programmes. WHO has provided evidence as to how deworming helps to meet some Millennium Development Goals and progress towards achieving them should be further documented (The Lancet, 2004). In order to meet the target of reaching about 650 million children by 2010, deworming should become part of a multi-disease control approach, by maximising links with chemotherapy-based control of lymphatic filariasis, onchocerciasis, trachoma, and other diseases of poverty, thereby building a pro-poor strategy for sustainable development. (Lancet, 2004; Molyneux & Nantulya, 2004).

11 Questions Needing Answers

Partners for Parasites Control recently gathered to discuss the best way forward in helminth control have perceived the following research needs and priorities (WHO, 2005b).

- Advocacy for sustaining the effort to control helminthiasis requires the latest at best information. The compelling evidence for detrimental effects of helmith infections and the benefits from deworming should be sustained with further knowledge and updated data. The disease burden should be regularly revised and expressed in terms of the most reliable DALYS available.
- There is emerging evidence that concurrent worm infections may have synergistic effects on the severity of malaria, on progression of HIV/AIDS, and on the development and effects of anaemia (Fincham *et al.*, 2003; Spiegel *et al.,* 2003). These interactions and potentially important consequences merit more extensive investigation.
- Impressive benefits of deworming on education, poverty reduction, and contribution towards the Millennium Development Goals have been put forward, though they need further quantification and wider dissemination.

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- Further research on the possible use of “packaging” deworming with other programmes is needed to sustain science –based synergy and integration with Lymphatic Filariasis Elimination Programmes, Vitamin A distribution campaigns, Child Health Days, Malaria, Expanded Programme of Immunization.
- There is inconsistency between WHO recommendation and drug producers’ prescribing information about the use of anthelminthic drugs during pregnancy. The WHO recommendations are based on toxicological evidence presented to experts in two Informal Consultations (WHO 1996, WHO 2002). The full scale toxicological review and the extensive process required by regulation bodies should be undertaken by the pharmaceutical industry. A pressing issue to be addressed is the need to set up a reliable system for pharmacovigilance in community deworming campaigns.
- Sensitive molecular tools to monitor drug efficacy need to be developed. To wait for drug resistance to occur before seeking funds for research on drug efficacy monitoring might be too late an answer if this potential problem emerges.
- The possibility of development of new anthelminthic drugs and the efficacy and safety of available drugs administered in combination should be evaluated.
- Availability of efficient vaccines would make a difference in helminth control. Trials for the development of vaccines against Schistosomiasis and hookworms should be supported and collaboration between research and control should be encouraged.

References

Albonico M, Smith PG, Ercole E, Hall A, Chwaya HM, Alawi KS, Savioli L. Rate of re-infection with intestinal nematodes after treatment of children with mebendazole or albendazole in a highly endemic area. Transactions of the Royal Society of Tropical Medicine and Hygiene. 1995; 89:538–541. [PubMed: 8560535]

Albonico M, Stoltzfus RJ, Savioli L, Chwaya HM, d'Harcourt E, Tielsch JM. A controlled evaluation of two school-based anthelminthic chemotherapy regimens on intensity of intestinal helminth infections. International Journal of Epidemiology. 1999a; 28:591–596. [PubMed: 10405869]

Albonico M, Crompton DWT, Savioli L. Control strategies for human intestinal nematode infections. Advances in Parasitology. 1999b; 42:277–341. [PubMed: 10050275]

Albonico M, Bickle Q, Haji HJ, Ramsan M, Khatib JK, Savioli L, Taylor M. Evaluation of the efficacy of pyrantel-oxantel for the treatment of soil-transmitted nematode infections. Transactions of The Royal Society of Tropical Medicine and Hygiene. 2002; 96:685–690. [PubMed: 12625151]

Albonico M, Bickle Q, Ramsan M, Montresor A, Savioli L, Taylor M. Efficacy of mebendazole and levamisole alone or in combination against intestinal nematode infections after repeated targeted mebendazole treatment in Zanzibar. Bulletin of the World Health Organization. 2003; 81(5):343–352. [PubMed: 12856052]

Albonico M, Wright V, Bickle Q. Molecular analysis of the β-tubulin gene of human hookworms as a basis for possible benzimidazole resistance on Pemba Island. Molecular and Biochemical Parasitology. 2004; 134(2):281–284. [PubMed: 15003848]

Albonico M, Wright V, Ramsan M, Haji HJ, Taylor M, Savioli L, Bickle Q. Development of the Egg Hatch Assay (EHA) for detection of anthelminthic drug resistance by human hookworms. International Journal for Parasitology. (in press).

Europe PMC Funders Author Manuscripts

Europe PMC Funders Author Manuscripts

Anderson, RM. The population dynamics and control of hookworm and roundworm infection. Population Dynamics of Infectious Diseases: Theory and Applications. Anderson, RM., editor. London: Chapman and Hall; 1982. p. 67-109.

Asaolu SO, Ofoezie IE, Odumuyiwa PA, Sowemimo OA, Ogunniyi TA. Effect of water supply and sanitation on the prevalence and intensity of *Ascaris lumbricoides* among pre-school-age children in Ajebandele and Ifewara, Osun State, Nigeria. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2002; 96:600–604. [PubMed: 12625131]

Asaolu SO, Ofoezie IE. The role of health education and sanitation in the control of helminth infections. Acta Tropica. 2003; 86:283–294. [PubMed: 12745145]

Awasthi S, Pande VK, Fletcher RH. Effectiveness and cost-effectiveness of albendazole in improving nutritional status of preschool children in urban slums. Indian Journal of Pediatrics. 2000; 37:19–29.

Awasthi S, Pande VK. Six monthly de-worming in infants to study effects on growth. Indian Journal of Pediatrics. 2001; 68:823–827. [PubMed: 11669028]

Belizario VY, De Leon WU, Amarillo ME, De Los Reyes AE, Bugayong MG, Macatangay BJC. A comparison of the efficacy of single doses of albendazole, ivermectin, and diethylcarbamazine alone or in combinations against *Ascaris* and *Trichuris* spp. Bulletin of the World Health Organization. 2003; 81:35–42. [PubMed: 12640474]

Bennet A, Guyatt H. Reducing intestinal nematodes infection: efficacy of albendazole and mebendazole. Parasitology Today. 2000; 2:71–74.

Bethony J, Chen JZ, Lin SX, Xiao SH, Zhan B, Li SW, Xue HC, Xing FY, Humphries D, Wang Y, Chen G, et al. Emerging patterns of hookworm infection: influence of aging on the intensity of *Necator* infection in Hainan Province, People's Republic of China. Clinical Infectious Diseases. 2002; 35:1336–1344. [PubMed: 12439796]

Bordignon, GP., Shakya, DR. A deworming programme in Nepal supported by the World Food Programme. Controlling Disease due to Helminth Infections. Crompton, DWT.Montresor, A.Nesheim, MC., Savioli, L., editors. Geneva: World Health Organization; 2003. p. 87-92.

Bradley M, Chandiwana SK, Bundy DAP. The epidemiology and control of hookworm infection in the Burma Valley area of Zimbabwe. Transactions of the Royal Society of Tropical Medicine and Hygiene. 1993; 87:145–147. [PubMed: 8337712]

Brooks RM, Latham MC, Crompton DWT. The relationship of nutrition and health to worker productivity in Kenya. East African Medical Journal. 1979; 56:413–421. [PubMed: 520258]

Brooker S, Peshu N, Warn PA, Mosobo M, Guyatt HL, Marsh K, Snow RW. The epidemiology of hookworm infection and its contribution to anaemia among preschool children on the coast of Kenya. Transactions of the Royal Society of Tropical Medicine and Hygiene. 1999; 93:240–246. [PubMed: 10492749]

Brooker S, Hay SI, Tchuem Tchuenté LA, Ratard R. Using NOAA-AVHRR data to model helminth distributions for planning disease control in Cameroon, West Africa. Photogrammetric Engineering and Remote Sensing. 2002a; 68:175–179.

Brooker S, Beasley NMR, Ndinaromtan M, Madjiouroum EM, Baboguel M, Djenguinabe E, Hay SI, Bundy DA. Use of remote sensing and a geographical information system in a national helminth control programme in Chad. Bulletin World Health Organization. 2002b; 80:783–789.

Brooker S, Bethony JM, Rodrigues LC, Alexander N, Geiger S, Hotez P. Epidemiologic, immunologic and practical considerations in developing, and evaluating a human hookworm vaccine. Expert Review Vaccines. 2005; 4(1):1–16.

Bull FC, Holt CL, Kreuter MW, Clark EM, Scharff D. Understanding the effects of printed health education materials: which features lead to which outcomes? Journal of Health Communication. 2001; 6(3):265–79. [PubMed: 11550593]

Bundy, DAP., et al. Chapter 61 in "Disease Control Priorities in Developing Countries". School Health and Nutrition Programs. 2nd Edition. World Bank and Oxford University Press; in press

Bundy DA, Hall A, Medley GF, Savioli L. Evaluating measures to control intestinal parasitic infections. World Health Statistics Quarterly. 1992; 45:168–179.

Bundy DA, Chan MS, Savioli L. Hookworm infection in pregnancy. Transactions of the Royal Society of Tropical Medicine and Hygiene. 1995a; 89:521–522. [PubMed: 8560530]

Europe PMC Funders Author Manuscripts

Europe PMC Funders Author Manuscripts

Bundy DAP, Chan MS, Guyatt HL. The practicality and sustainability of vaccination as an approach to parasite control. Parasitology. 1995b; 110:S51–S58. [PubMed: 7784130]

Cairncross S. Sanitation in the developing world: current status and future solutions. International Journal of Environmental Health Research. 2003; (Suppl 1):S123–S131. [PubMed: 12775388]

Carrera E, Nesheim MC, Crompton DWT. Lactose maldigestion in Ascaris infected preschool children. American Journal of Clinical Nutrition. 1984; 39:255–264. [PubMed: 6695827]

Chhotray GP, Ranjit MR. Effect of drug treatment on the prevalence of intestinal parasites amongst school children in a sub-urban community. Indian Journal of Medical Research. 1990; 91:266–269. [PubMed: 2228055]

Christian P, Kathry KS, West KP Jr. Antenatal anthelminthic treatment, birthweight, and infant survival in rural Nepal. The Lancet. 2004; 364:981–983.

Crompton DWT. How much helminthiasis is there is in the world ? Journal of Parasitology. 1999; 85(3):397–403. [PubMed: 10386428]

Crompton DWT. *Ascaris.* and ascariasis. Advances in Parasitology. 2000; 48:285–375.

Crompton DWT, Nesheim MC. Nutritional impact of intestinal helminthasis during the human life cycle. Annual Review of Nutrition. 2002; 22:35–59.

Crompton DWT, Savioli L. Intestinal parasitic infections and urbanization. Bulletin of the World Health Organization. 1993; 71(1):1–7. [PubMed: 8440028]

Curtale F, Pokhrel RP, Tilden RL, Higashi G. Intestinal helminths and xerophthalmia in Nepal. A case-control study. Journal of Tropical Pediatrics. 1995; 41:334–337. [PubMed: 8606439]

de Silva NR, Guyatt H, Bundy DA. Anthelminthics: a comparative review of their clinical pharmacology. Drugs. 1997; 53:769–788. [PubMed: 9129865]

de Silva NR, Sirisena JLGJ, Gunasekera DPS, de Silva HJ. Effect of mebendazole therapy during pregnancy on birth outcome. The Lancet. 1999; 353:1145–1149.

de Silva NR, Brooker S, Hotez PJ, Montresor A, Engels D, Savioli L. Soil-transmitted helminth infections: updating the global picture. Trends in Parasitology. 2003; 19:547–551. [PubMed: 14642761]

Diav-Citrin O, Shechtman S, Arnon J, Lubart I, Ornoy A. Pregnancy outcome after gestational exposure to mebendazole: a prospective controlled cohort study. American Journal of Obstetrics and Gynecology. 2003; 188:282–285. [PubMed: 12548230]

Esrey SA, Potash JB, Roberts L, Shiff C. Effects of improved water supply and sanitation on ascariasis, diarrhoea, dracunculiasis, hookworm infection, schistosomiasis, and trachoma. Bulletin of the World Health Organization. 1991; 69:609–621. [PubMed: 1835675]

Evans DB, Guyatt HL. The cost effectiveness of mass drug therapy for intestinal helminths. Pharmacoeconomics. 1995; 8(1):14–22. [PubMed: 10155598]

Fenwick A. New initiatives against Africa's worms. Transactions of the Royal Society of Tropical Medicine and Hygiene. (in press).

Fiedler JL. The Nepal National Vitamin A Program: prototype to emulate or donor enclave? Health Policy and Planning. 2000; 15:145–156. [PubMed: 10837037]

Fincham JE, Markus MB, Adams VJ. Could control of soil-transmitted helminthic infections influence the HIV/AIDS pandemic. Acta Tropica. 2003; 86:315–333. [PubMed: 12745148]

Gandhi NS, Chen JZ, Khoshnood K, Xing FY, Li SW, Liu YR, Zhan B, Xue HC, Tong CG, Wang Y, Wang WS, et al. Epidemiology of *Necator americanus* hookworm infections in Xiulongkan Village, Hainan Province, China: high prevalence and intensity among middle-aged and elderly residents. Journal of Parasitology. 2001; 87:739–743. [PubMed: 11534635]

Gardner GW, Edgerton VR, Senewiratne B, Barnard RJ, Ohira Y. Physical work capacity and metabolic stress in subjects with iron deficiency anaemia. American Journal of Clinical Nutrition. 1977; 30:910–917. [PubMed: 868783]

Geerts S, Gryseels B. Anthelminthic resistance in human helminths: a review. Tropical Medicine and International Health. 2001; 6(11):915–921. [PubMed: 11703846]

Gilgen D, Mascie-Taylor CGN, Rosetta L. Intestinal helminth infections, anaemia and labour productivity of female tea pluckers in Bangladesh. Tropical Medicine and International Health. 2001; 6:449–457. [PubMed: 11422959]

Europe PMC Funders Author Manuscripts

Europe PMC Funders Author Manuscripts

Guanghan H, Dandan L, Shaoji Z, Xiaojun Z, Zenghua K, Guojun C. The role of health education for schistosomiasis control in heavy endemic area of Poyang Lake region, People's Republic of China. Southeast Asian Journal of Tropical Medicine and Public Health. 2000; 31:467–472. [PubMed: 11289003]

Guyatt HL. Do intestinal nematodes affect productivity in adulthood? Parasitology Today. 2000; 16:153–158. [PubMed: 10725902]

Guyatt HL, Bundy DAP, Evans D. A population dynamic approach to the cost-effectiveness analysis of mass anthelminthic treatment: effects of treatment frequency on *Ascaris*. infection. Transactions of the Royal Society of Tropical Medicine and Hygiene. 1993; 87:570–575. [PubMed: 8266414]

Guyatt H, Brooker S, Donnelly CA. Can prevalence of infection in school-aged children be used as an index for assessing community prevalence. Parasitology. 1999; 118:257–268. [PubMed: 10205801]

Hall A, Holland C. Geographical variation in *Ascaris lumbricoides* fecundity and its implications for helminth control. Parasitology Today. 2000; 16:540–544. [PubMed: 11121853]

Hagan P, Appleton CC, Coles GC, Kusel JR, Tchuem-Tchuentè. Schistosomiasis control: keep taking the tablets. Trends in Parasitology. 2004; 20(2):92–97. [PubMed: 14747023]

Henry FJ. Re-infection with *Ascaris lumbricoides* after chemotherapy: a comparative study in three villages with varying sanitation. Transactions of the Royal Society of Tropical Medicine and Hygiene. 1988; 82:460–464. [PubMed: 3232186]

Henry FJ, Huttly SR, Ahmed MU, Alam A. Effect of chemotherapy in slums and villages in Bangladesh. Southeast Asian Journal of Tropical Medicine and Public health. 1993; 24(2):307–312. [PubMed: 8266234]

Horton J. Albendazole: a review of anthelmintic efficacy and safety in humans. Parasitology. 2000; 121:S113–S132. [PubMed: 11386684]

Hotez PJ, Zhan B, Bethony JM, Loukas A, Williamson A, Goud GN, Hawdon JM, Dobardzic A, Dobardzic R, Ghosh K, Bottazzi ME, et al. Progress in the development of a recombinant vaccine for human hookworm disease: the human hookworm vaccine initiative. International Journal for Parasitology. 2003; 33:1245–1258. [PubMed: 13678639]

Idris MA, Shaban MA, Fatahallah M. Effective control of hookworm infection in school children from Dhofar, Sultanate of Oman: a four-year experience with albendazole mass chemotherapy. Acta Tropica. 2001; 80:139–143. [PubMed: 11600092]

Khanal P, Walgate R. Nepal deworming programme ready to go worldwide. Bulletin of the World Health Organization. 2002; 80:423–424. [PubMed: 12077628]

Kinzie MB. Instructional design strategies for health behaviour change. Patient Education and Counseling. 2005; 56(1):3–15. [PubMed: 15590217]

Kvalsvig JD, Cooppan RM, Connolly KJ. The effects of parasite infections on cognitive processes in children. Annals of Tropical Medicine and Parasitology. 1991; 85:551–568. [PubMed: 1809249]

Lansdown R, Ledward A, Hall A, Issae W, Yona E, Matulu J, Mweta M, Kihamia C, Nyandindi U, Bundy D. Schistosomiasis, helminth infection and health education in Tanzania: achieving behaviour change in primary schools. Health Education Research. 2002; 17:425–433. [PubMed: 12197588]

Machado MT, Machado TM, Yoshikae RM, Schmidt AL, Faria Rde C, Paschoalotti MA, Barata Rde C, Chieffi PP. Ascariasis in the subdistrict of Cavacos, municipality of alterosa (MG), Brazil: effect of mass treatment with albendazole on the intensity of infection. Revista do Instituto de Medicina Tropical de Sao Paulo. 1996; 8:265–271.

Management Science for Health. Electronic resource Center. International Drug Price Indicator. 2004 http://erc.msh.org/dmpguide.

Mascie-Taylor CG, Alam M, Montanari RM, Karim R, Ahmed T, Karim E, Akhtar S. A study of the cost effectiveness of selective health interventions for the control of intestinal parasites in rural Bangladesh. Journal of Parasitology. 1999; 85:6–11. [PubMed: 10207355]

Mathema, P., Pandey, S., Blomquist, PO. Deworming impact evaluation of preschool children deworming programme in Nepal. International Nutritional Anaemia Consultative Group; Lima, Peru: 2004 Nov.

Europe PMC Funders Author Manuscripts

Miguel, E., Kremer, M. Worms: Education and Health Externalities in Kenya Cambridge. MA: National Bureau of Economic Research; 2001. Working Paper No. w8481 (http://www.nber.org/papers/W8481)

Molyneux DH, Nantulya VM. Linking disease control programmes in rural Africa: a pro-poor strategy to reach Abuja targets and millennium development goals. British Medical Journal. 2004; 328:1129–1132. [PubMed: 15130985]

Montresor A, Ramsan M, Chwaya HM, Ameir H, Foum A, Albonico M, Gyorkos TW, Savioli L. Extending anthelminthic coverage to non-enrolled school-age children using a simple and low-cost method. Tropical Medicine and International Health. 2001; 6:535–537. [PubMed: 11469947]

Montresor, A., Crompton, DWT., Gyorkos, TW., Savioli, L. Helminth control in school age children. Geneva: WHO; 2002.

Montresor A, Awashti S, Crompton DWT. Use of benzimidazoles in children younger than 24 months for the treatment of soil-transmitted helminthiasis. Acta Tropica. 2003; 86:223–232. [PubMed: 12745139]

Mukherjee, JFN. Harnessing market power for rural sanitation. Water and Sanitation Program; Jakarta, Indonesia: 2005 Feb. WSP Field Notes

Muller M, Sanchez RM, Suswillo RR. Evaluation of a sanitation programme using eggs of *Ascaris lumbricoides* in household yard soils as indicators. Journal of Tropical Medicine and Hygiene. 1989; 92:10–16. [PubMed: 2918573]

Nokes C, Grantham-Mcgregor SM, Sawyer AW, Cooper ES, Robinson BA, Bundy DA. Moderate to heavy infections of *Trichuris trichiura* affect cognitive function in Jamaican schoolchildren. Parasitology. 1992; 104:539–547. [PubMed: 1641252]

Nokes C, Bundy DA. Compliance and absenteeism in school children: implications for helminth control. Transactions of the Royal Society of Tropical Medicine and Hygiene. 1993; 87:148–152. [PubMed: 8337713]

Nokes C, Bundy DA. Does helminth infection affect mental processing and educational achievement? Parasitology Today. 1994; 10:14–18. [PubMed: 15275558]

Nurdia DS, Sumarni S, Suyoko, Hakim M, Winkvist A. Impact of intestinal helminth infection on anemia and iron status during pregnancy: a community based study in Indonesia. Southeast Asian Journal of Tropical Medicine and Public Health. 2001; 32:14–22. [PubMed: 11485075]

Nwaorgu OC, Okeibunor J, Madu E, Amazigo U, Onyegegbu N, Evans D. A school-based schistosomiasis and intestinal helminthiasis control programme in Nigeria: acceptability to community members. Tropical Medicine and International Health. 1998; 3:842–849. [PubMed: 9809919]

O'Cathain A, Walters SJ, Nicholl JP, Thomas KJ, Kirkham M. Use of evidence based leaflets to promote informed choice in maternity care: randomised controlled trial in everyday practice. British Medical Journal. 2002; 324:643. [PubMed: 11895822]

Oberhelman RA, Guerrero ES, Fernandez ML, Silio M, Mercado D, Comiskey N, Ihenacho G, Mera R. Correlations between intestinal parasitosis, physical growth, and psychomotor development among infants and children from rural Nicaragua. American Journal of Tropical Medicine and Hygiene. 1998; 58:470–475. [PubMed: 9574794]

Olds GR, King C, Hewlett J, Olveda R, Wu G, Ouma J, Peters P, McGarvey S, Odhiambo O, Koech D, Liu CY, et al. Double-blind placebo-controlled study of concurrent administration of albendazole and praziquantel in schoolchildren with schistosomiasis and geohelminths. Journal of Infectious Diseases. 1999; 179(4):996–1003. [PubMed: 10068597]

Partnership for Child Development. The cost of large-scale school health programmes which deliver anthelminthics to children in Ghana and Tanzania. Acta Tropica. 1999; 73:183–204. [PubMed: 10465058]

Partnership for Child Development. Community perception of school-based delivery of anthelmintics in Ghana and Tanzania. Tropical Medicine and International Health. 2001; 6:1075–1083. [PubMed: 11737845]

Partnership for Child Development. Heavy schistosomiasis associated with poor short-term memory and slower reaction times in Tanzanian schoolchildren. Tropical Medicine and International Health. 2002; 7:104–117. [PubMed: 11841700]

Europe PMC Funders Author Manuscripts

Reeves D. Provision of information is only one component of informed choice. British Medical Journal. 2002; 325:43.

Roos HM, Kwa MSG, Grant WN. New genetic and practical implications of selection for anthelmintic resistance in parasitic nematodes. Parasitology Today. 1995; 11:148–150.

Savioli L, Stansfield S, Bundy DA, Mitchell A, Bathia R, Engels D, Montresor A, Neira M, Shein AM. Schistosomiasis and soil-transmitted helminth infections: forging control efforts. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2002; 96:577–579. [PubMed: 12625126]

Savioli L, Crompton DWT, Neira M. Use of anthelminthic drugs during pregnancy. American Journal of Obstetrics and Gynecology. 2003; 188:5–6. [PubMed: 12548188]

Sinoun M, Tsuyuoka R, Socheat D, Montresor A, Palmer K. Financial costs of deworming children in all primary schools in Cambodia. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2005; 99:664–668. [PubMed: 15992839]

Sorensen E, Ismail M, Amarasinghe DKC, Hettiarachchi I, Dassenaieke de CTS. The effect of the availability of latrines on soil-transmitted nematode infections in the plantation sector in Sri Lanka. American Journal of Tropical Medicine and Hygiene. 1994; 51:36–39. [PubMed: 8059913]

Sow S, de Vlas SJ, Polman K, Gryseels B. Hygiene practices and contamination risks of surface waters by schistosome eggs: the case of an infested village in Northern Senegal. Bulletin de la Societè de Pathologie Exotique. 2004; 97(1):12–14. [Article in French]. [PubMed: 15104150]

Spiegel A, Tall A, Raphenon G, Trape JF, Druilhe P. Increased frequency of malaria attacks in subjects co-infected by intestinal worms and *Plasmodium falciparum* malaria. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2003; 97:198–199. [PubMed: 14584377]

Stephenson LS, Latham MC, Adams EJ, Kinoti SN, Pertet A. Physical fitness, growth and appetite of Kenyan school boys with hookworm, *Trichuris trichiura* and *Ascaris lumbricoides* infections are improved four months after a single dose of albendazole. Journal of Nutrition. 1993; 123:1036–1046. [PubMed: 8505663]

Stoltzfus RJ, Albonico M, Chwaya HM, Savioli L, Tielsch J, Schulze K, Yip R. Hemoquant determination of hookworm-related blood loss and its role in iron deficiency in African children. American Journal of Tropical Medicine and Hygiene. 1996; 55:399–404. [PubMed: 8916795]

Stoltzfus RJ, Albonico M, Chwaya HM, Tielsch JM, Schulze KJ, Savioli L. Effects of the Zanzibar school-based deworming program on iron status of children. American Journal f Clinical Nutrition. 1998; 68:179–186.

Stoltzfus RJ, Kvalsvig KJ, Chwaya HM, Montresor A, Albonico M, Tielsch JM, Savioli L, Pollitt E. Effects of iron supplementation and anthelminthic treatment on motor and language development of Zanzibari preschool children. British Medical Journal. 2001; 323:1384–1396.

Stoltzfus RJ, Chwaya HM, Montresor A, Tielsch JM, Jape JK, Albonico M, Savioli L. Low dose daily iron supplementation improves iron status and appetite but not anemia, whereas quarterly anthelminthic treatment improves growth, appetite and anemia in Zanzibari preschool children. Journal of Nutrition. 2004; 134:348–356. [PubMed: 14747671]

The Lancet. Thinking beyond deworming. The Lancet. 2004; 364:1993–1994.

Crompton, DWT.Nesheim, MC., Pawlowski, ZS., editors. Thein Hlaing. Ascariasis and its Prevention and Control. Burma. London, New York and Philadelphia: Taylor and Francis; 1989. p. 133-168.

Torlesse H, Hodges M. Albendazole therapy and reduced decline in haemoglobin concentration during pregnancy (Sierra Leone). Transactions of the Royal Society of Tropical Medicine and Hygiene. 2001; 95:195–201. [PubMed: 11355560]

Urbani C, Albonico M. Anthelminthic drug safety and drug administration in the control of soil-transmitted helminthiasis in community campaigns. Acta Tropica. 2003; 86(2–3):215–221. [PubMed: 12745138]

UNICEF. The State of the World's Children 2005. New York: United Nation Children Fund; 2005.

Viteri FE, Torun B. Anaemia and physical work capacity. Clinical Haematology. 1974; 3:609–626.

Walsh DC, Rudd RE, Moeykens BA, Moloney TW. Social marketing for public health. Health Affairs (Bethesda MD). 1993; 12(2):104–119.

Watkins WE, Pollit E. "Stupidity of worms": do intestinal worms impair mental performance ? Psychological Bulletin. 1997; 121:171–191. [PubMed: 9100486]

Europe PMC Funders Author Manuscripts

Whitelaw S, Watson J. Whither health promotion events? A judicial approach to evidence. Health Education Research. 2005; 20(2):214–225. [PubMed: 15367495]

Wolgemuth JC, Latham MC, Hall A, Chesher A, Crompton DWT. Worker productivity and the nutritional status of Kenyan road construction labourers. American Journal of Clinical Nutrition. 1982; 36(1):68–78. [PubMed: 7091036]

World Bank. World Development Report 1993: Investing in Health. London and New York: Oxford University Press; 1993.

World Food Programme. WFP Annual report 2004. Rome: WFP; 2004. p. 36-38.

World Health Organization. Report of the WHO informal consultation on hookworm infection and anaemia in girls and women. Geneva; WHO: 1996. WHO/CTD/SIP/96.1

World Health Organization. Report of the WHO informal consultation on monitoring drug efficacy in the control of schistosomiasis and intestinal nematodes. Geneva: WHO; 1999. WHO/CDS/CPC/SIP 99.1

World Health Organization. Report of the 54th World Health Assembly Control of schistosomiasis and soil-transmitted helminth infections. Resolution N 54.19. Geneva: WHO; 2001.

World Health Organization. Prevention and control of schistosomiasis and soil transmitted helminthiasis Report of a WHO Expert Committee. Geneva: WHO; 2002a. Technical Report Series 912

World Health Organization. Report of the WHO informal consultation on the use of praziquantel during pregnancy and lactation and albendazole/mebendazole in children under 24 months. Geneva: WHO; 2002b. WHO/CPE/PVC 2002.4

World Health Organization. Action against worms. 2003a. Newsletter issue number 2. http://www.who.int/wormcontrol/newsletter/en/

World Health Organization. Integrated Management of Pregnancy and Childbirth. Essential care Practice Guide for Pregnancy and Childbirth. Geneva: WHO; 2003b. Essential Care Series. WHO/RHR/2003

World Health Organization. WHO Model formulary. Based on the 13th Model List of Essential Medicines 2003. Geneva: WHO; 2004a. p. 82-85.

World Health Organization. How to add deworming to vitamin A distribution. Geneva: WHO; 2004b. WHO/CDS/CPE/PVC/2004.1

World Health Organization. Action against worms. 2005a. Newsletter issue number 6. http://www.who.int/wormcontrol/newsletter/en (in press)

World Health Organization. Deworming for health and development. Report of the third global meeting of the partners for parasites control. Geneva: WHO; 2005b. WHO/CDS/CPE/PVC/2005.14

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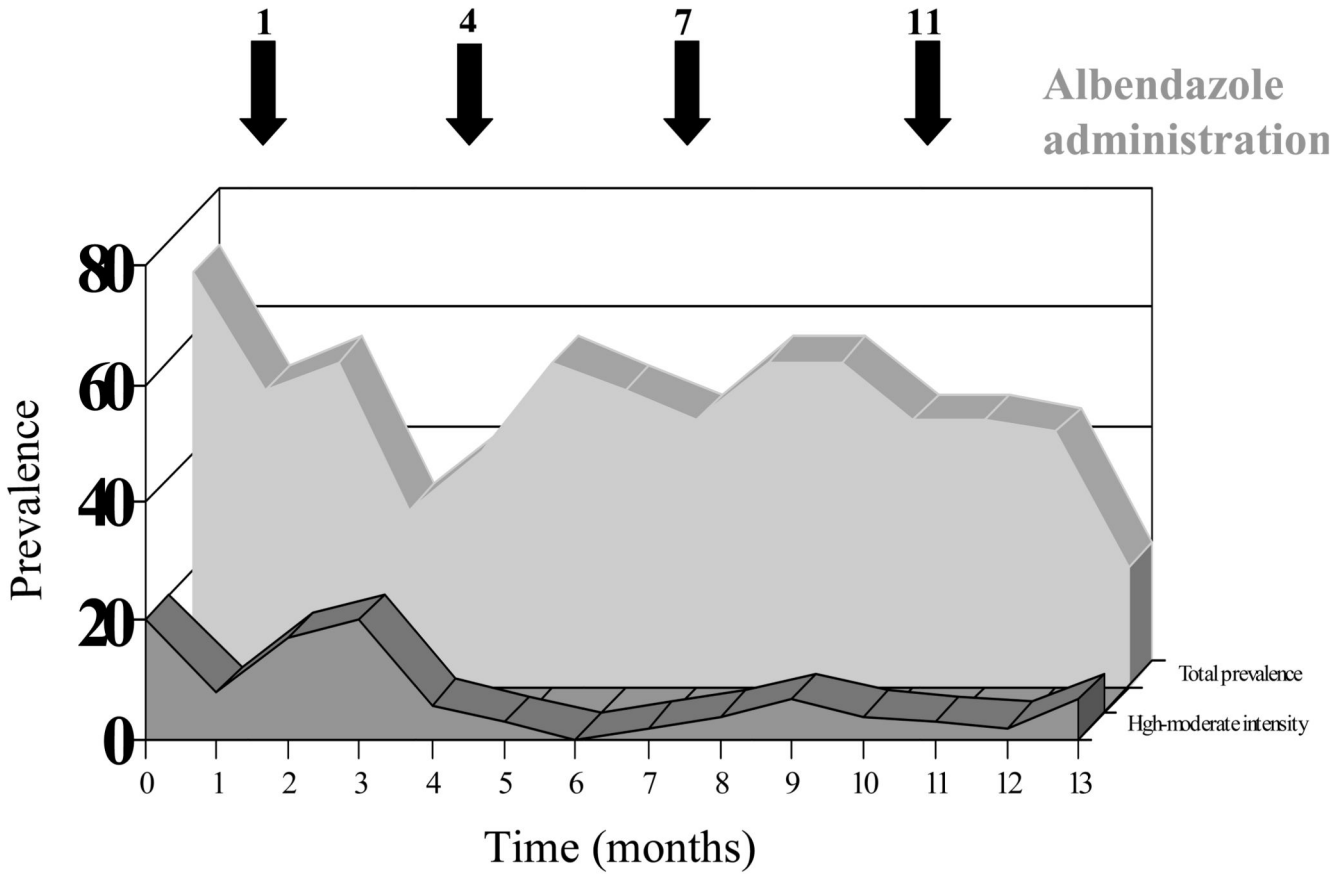

Figure 1.

Effects of periodical treatment with mebendazole on total prevalence and prevalence of moderate-heavy *T. trichiura* infections (Montresor et al., unpublished data from the control programme in Zanzibar, United Republic of Tanzania).

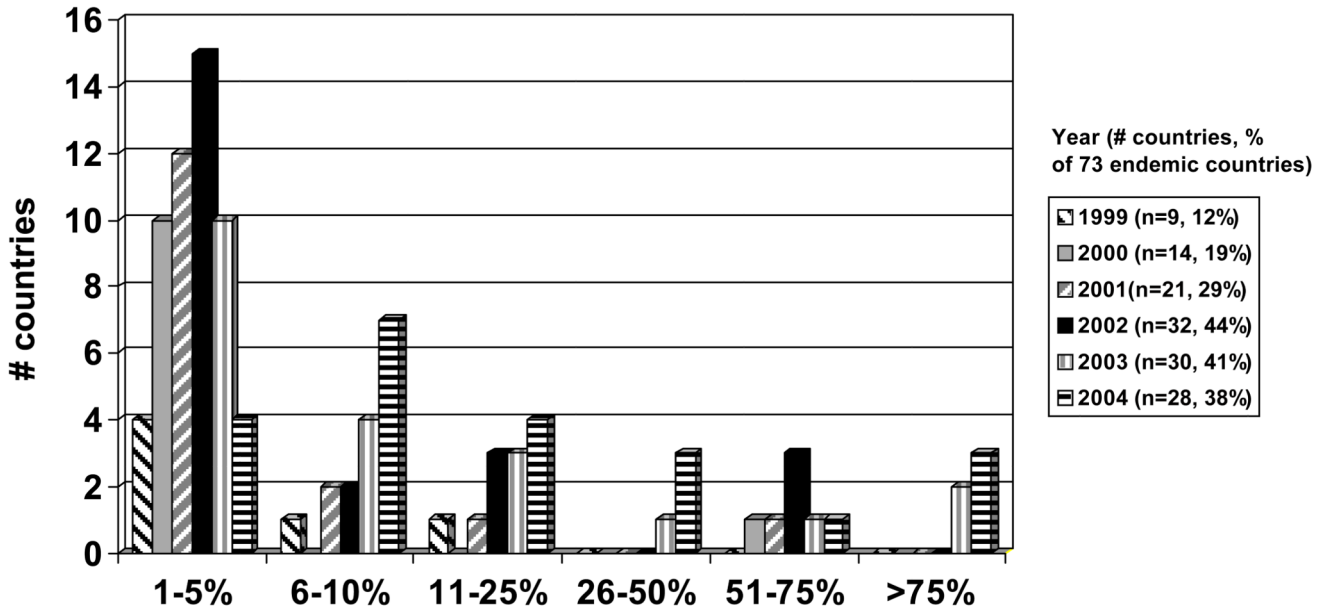

Figure 2.
Global coverage of deworming school-age children 1999-2004. Data from 73 endemic countries. (WHO, 2005).

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Table 1

Recommended drugs for the treatment of soil-transmitted nematode infections in public health.

Substance	Therapeutic activity		Dosage	Use in pregnancy and in children
Albendazole (tablet 200 and 400 mg, suspension 100 mg/ 5ml)	*A. lumbricoides*	+++	400 mg single dose	Not recommended in the first trimester of pregnancy. In children between 12 and 24 months use 200 mg
	T. trichiura	++	400 mg single dose	
	Hookworm infections	+++	400 mg single dose	
Ivermectin (tablet 6 mg)	*A. lumbricoides*	+++	200 μg/kg single dose	Not recommended in the first trimester of pregnancy and in children less than 5 years
	T. trichiura	+	200 μg/kg single dose	
	Hookworms	-	200 μg/kg single dose	
Levamisole (tablet 40 mg, syrup 40 mg/5 ml)	*A. lumbricoides*	+++	2.5 mg/kg single dose (80 mg single dose in school age children)	No evidence of teratogenicity
	T. trichiura	+		
	Hookworms	++	2.5 mg/kg single dose (80 mg single dose in school age children)	
			2.5 mg/kg single dose (80 mg single dose in school age children) For heavy Necatoriasis repeat after 7 days	
Mebendazole (tablet 100 and 500 mg, suspension 100 mg/ 5ml)	*A. lumbricoides*	+++	500 mg single dose	Not recommended in the first trimester of pregnancy and in children under 1 year
	T. trichiura	++	500 mg single dose	
	Hookworms	+++	500 mg single dose	
Pyrantel (tablet 250 mg, suspension 50 mg/ml)	*A. lumbricoides*	+++	10 mg/kg single dose	Not recommended in the first trimester of pregnancy
	T. trichiura	-	10 mg/kg single dose	
	Hookworms	++	10 mg/kg single dose. For heavy Necatoriasis repeat for 3 days	

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Table 2

Community classification for soil-transmitted helminth infections (WHO 2002a)

Each community can be classified according to prevalence and (if available) intensity of infection.

Intensity of infections are classified as below:

Ascaris lumbricoides: Light 1-4,999 epg; Moderate 5,000-49,999 epg; Heavy > 50,000 epg

Trichuris trichiura: Light 1-999 epg; Moderate 1,000-9,999 epg; Heavy > 10,000 epg

Hookworms: Light 1-1,999 epg; Moderate 2,000-3,999 epg; Heavy > 4,000 epg

	Results of school survey	
Community category	prevalence of any soil-transmitted helminthiasis	percent of moderate-to-heavy infections
I high prevalence or high intensity	≥ 70 percent	≥ 10 percent
II moderate prevalence and low intensity	≥ 50 percent < 70 percent	< 10 percent
III low prevalence and low intensity	< 50 percent	< 10 percent

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Table 3

Recommended treatment strategies for soil-transmitted helminth infections (WHO 2002a). These treatment strategies always need to be accompanied by efforts to improve water supply, Sanitation, and information, education and communication.

Soil-transmitted helminth infections		
Community category	Intervention in schools (enrolled and non-enrolled children)	Community-based intervention
I	Targeted treatment of school-age children, 2-3 times / year	Systematic treatment of preschool children and women of childbearing age in mother and child health programmes
II	Targeted treatment of school-age children, once per year	Systematic treatment of preschool Children and women of childbearing age in mother and child health programmes
III	Selective treatment	Selective treatment