A population dynamic approach to evaluating the impact of school attendance on the unit cost and effectiveness of school-based schistosomiasis chemotherapy programmes

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SUMMARY

This paper presents a first attempt at modelling the possible cost and effectiveness of reaching non-enrolled children through school-based programmes using empirical data from Egypt. A sex/school-attendance/age-structured population dynamic model was used to predict trends in infection and early disease. Four treatment delivery strategies were compared: school-based (coverage of 85 %) and school-aged targeted (coverage of 25, 50 and 85 %). The school-aged targeted strategies also included the school-based programme. For each alternative strategy, the maximum unit cost was calculated to obtain a cost-effectiveness ratio equal or smaller to the one obtained with the school-based programme (unit cost of US$ 0·60). The analysis showed that, for *S. mansoni* in Lower Egypt, a programme where only 85 % of children attending school were treated would still prevent 77 % of the early disease cases prevented with a programme where 85 % of all school-age children were treated. However, using the school-aged targeted strategy, from US$ 0·06 to US$ 1·03 extra unit costs could be spent to reach non-enrolled children and still be more cost-effective. Treating non-enrolled children is an important consideration in maximizing the effectiveness of treatment programmes while maintaining a cost-effectiveness comparable to school-based delivery.

Key words: schistosomiasis, population dynamic model, school attendance, school-aged children, chemotherapy, cost-effectiveness analysis.

INTRODUCTION

School-based anthelmintic programmes are becoming increasingly popular as a means of controlling intestinal nematode infections and schistosomiasis (Hall *et al*. 1997; Partnership for Child Development, 1997; Savioli *et al*. 1997). The impetus to this initiative has been the relative ease and cost reductions in using schools to deliver treatment, and the relative effectiveness in targeting the segment of the population most at risk of heavy infection and disease (Anderson & May, 1985), with spin-offs for reducing transmission in the rest of the community (Bundy *et al*. 1990; Butterworth *et al*. 1991; Chan *et al*. 1994, 1995, 1998). One major concern, not just in terms of the effectiveness of these programmes, but also in terms of equity is that such a delivery strategy will not reach the large number of school-aged children who are not enrolled or do not attend school. In Africa in 1996, gross enrolment ratios in primary school males and females were 85·3 % and 71·2 %, respectively (United Nations Education, Scientific and Cultural Organization, 1998). These children not enrolled will be missed by a school-

based initiative though they are equally and may in some instances be at higher risk of disease than those children at school. Indeed, recent studies in Africa showed that school-aged children not enrolled in school had a higher prevalence and intensity of both *Schistosoma mansoni* and *S. haematobium* infection than those children enrolled (Husein *et al*. 1996; Hammad *et al*. 1997; Useh & Ejezie, 1999; Gyorkos, personal communications). Reaching these out-of-school children could be achieved by community based control efforts or by encouraging school-aged children not-enrolled to receive treatment from the school setting, as has already been reported in Egypt (Talaat, Omar & Evans, 1999). Both these control effects would require extra costs, not only in providing additional anthelmintic treatments, but also extra delivery costs in locating these individuals or encouraging them to attend a treatment site.

In the absence of intervention trials to evaluate the relative cost and effectiveness of these alternative control efforts, mathematical modelling can provide useful insights into the predicted patterns. Modelling also lends itself to extensive sensitivity analysis to explore the impact under conditions varying in epidemiology (for instance, infection levels in enrolled and non-enrolled children), coverage, drug efficacy and unit costs for treatment and delivery

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which exist in different localities (Guyatt, 1998; Guyatt & Chan, 1998; Chan *et al.* 1998). Population dynamic models of helminth infection have been used to evaluate the impact of school-based treatment strategies (Guyatt & Chan, 1998; Guyatt, 1999), but these have not considered the potential differences in infection levels of children in and out of school.

In this paper we present a population dynamic model for schistosomiasis which captures these differences by explicitly considering school-aged children in and out of school as discrete segments of the population. Since infection levels can also vary with sex (Gyorkos *et al.* 1995; Hammad *et al.* 1996; Husein *et al.* 1996; Montesor *et al.* 1997; Useh & Ejezie, 1999), these groups are further stratified into boys and girls. Using the published empirical data from studies in Egypt (Husein *et al.* 1996; Talaat *et al.* 1999), we explore the effectiveness of school-based strategies in comparison with school-aged targeted in this setting.

MATERIALS AND METHODS

Empirical data and study population

The data on the prevalence of infection and school enrolment proportions were taken from a large-scale study conducted in Egypt in 1990 as part of Egypt's Schistosomiasis Research Project (Barakat *et al.* 1995; El Khoby, Galal & Fenwick, 1998). This survey was conducted in rural areas of 9 governorates – 4 Lower Egypt governorates, recognized as endemic for *S. mansoni*, and 5 Upper Egypt governorates, recognized as endemic for *S. haematobium* (Husein *et al.* 1996). The primary sampling unit was the village and a representative sample of all gender-age groups was obtained (Barakat *et al.* 1995). All members of selected households were invited to participate in the study by providing stool and urine specimens (Husein *et al.* 1996). The data on age, sex and school attendance for children aged 6–15 years were collected from each individual of the household (or their mothers if children were less than 12 years old). A child was defined as non-enrolled if she/he declared to never have attended school or to have stopped going to school. The presence of infection was measured using the nucleopore filter technique for urine samples and the quick Kato smear for stool samples (Barakat *et al.* 1995).

Table 1 summarizes the school enrolment figures and the prevalences of *S. mansoni* and *S. haematobium* reported by the authors and stratified by sex and school enrolment (Husein *et al.* 1996). These parameters are used in the model to establish the equilibrium condition (i.e. the levels of infection in the different subgroups of the population before treatment).

The model

The model is a modification of an age-structured population dynamic model that has been described elsewhere (Chan *et al.* 1995, 1996*a*, *b*). Briefly, this model assessed the instantaneous change in worm burden in different age groups, and included parameters describing the density-dependent mechanism (the establishment rate of new adult worms decreases as the worm burden increases) and the immune response of individuals at each age based on the previous mean worm burden in that group.

In the current model, the transmission dynamics are assumed to differ by sex and school attendance. The population is stratified into 4 groups (g) representing the populations of females in school ($g = 1$), males in school ($g = 2$), females out of school ($g = 3$) and males out of school ($g = 4$). The instantaneous change in the mean worm burden for individuals of age (a) in group (g) is determined by the number of new infections ($\Lambda(g,a,t)$) during a very short period of time (Δt), weighted by immunity response ($e^{-\delta I(g,a,t)}$) minus the sum of the number of deaths of adult worms ($\mu M(g,a,t)$) during that period. The sum of the worm burden over all ages (a) and groups (g) at time (t) is used to evaluate the number of new infections in each group (g) depending on group and age specific contact and contamination rates. In other words, all 4 groups are exposed to a common infection source in the environment, but will acquire the infection and in turn contaminate the environment at different rates. The mixing between groups is considered random. The model is described in detail in Appendix 1. The parameters relating to these biological processes are given in Appendix 2.

It is assumed that there is a total population of 100 000. The proportion of the population in and out of school, by sex, is different in the two regions where *S. haematobium* and *S. mansoni* are endemic. The age distribution was, however, assumed to be the same for males and females, in and out of school, and to be based on a negative exponential distribution and parameter values for the Middle-East, as suggested in the World Bank 'Global Burden of Disease' study (Murray, 1996). For a population with n_g individuals in group (g), the number of individuals of age (a) is

$$n_{a,g} = 0{\cdot}0356 n_g e^{-0{\cdot}33a}.$$

The control programmes and measuring effectiveness

Two main strategies are compared: school-based (where only enrolled children are treated) and school-aged targeted (where non-enrolled children are also treated). The treatment is assumed to immediately reduce the mean worm burden in each group by a percentage defined by the coverage in each group multiplied by the drug efficacy (assumed

Table 1. *The empirical data on study population and prevalence of* Schistosoma mansoni *and* Schistosoma haematobium *in females and males in and out of school in Upper and Lower Egypt*

	Schistosoma mansoni			*Schistosoma haematobium*		
	Study population	Number examined(%)	Prevalence	Study population	Number examined	Prevalence (%)
Females						
Enrolled	5783	5079	1474 (29·0)	2596	4353	581 (5·0)
Not enrolled	2127	1876	722 (38·5)	4156	1750	401 (14·0)
Males						
Enrolled	6887	6001	2538 (42·3)	5265	2118	105 (13·3)
Not enrolled	1316	1130	536 (47·4)	2179	3399	476 (22·9)

Data taken from Husein *et al.* (1996).

to 90 %). Annual treatment is administered over a 5-year programme (a total of 5 treatments).

Effectiveness is assessed as the reduction in the number of infections or in the number of early disease cases (hepatomegaly for *S. mansoni* and upper urinary tract pathology for *S. haematobium*) over 15 years for the 5 years during intervention and for 10 years following) (Chan *et al.* 1996 *a*). The dynamics of the development, resolution and the effect of treatment on early disease have been explained elsewhere (Chan *et al.* 1996 *a*, *b*; Chan & Bundy, 1997). Briefly, the number of new cases of early disease depends on the mean worm burden in group (*g*) of age (*a*) at time (*t*). Fig. 1 illustrates the changes by age groups in the prevalence of *S. mansoni* infection for males in school (B), males out of school (D), females in school (A) and females out of school (C) after a school-based treatment with coverage of 85 %.

The number of cases prevented is measured by the difference between the number of infected (or early disease cases) at equilibrium (before the first round of treatment) and the number of infected (or early disease cases) each year after treatment. To account for the fact that a case prevented today is preferable to a case prevented in the future, a discount rate of 5 % was applied to the number of cases prevented for each of the 15 years after the first round of treatment. The overall effectiveness is measured as the sum of the discounted cases prevented over 15 years. The relative increase in effectiveness was calculated as the ratio between the number of cases prevented with each of the 5 alternative strategies compared with the school-based strategy. The relative number of individuals treated was also calculated.

Simulations

Coverage in school is assumed to be 85 % (Nokes & Bundy, 1993; Hall, personal communication, 1999) and only children aged 6–15 are treated. The coverage in children out of school is varied from zero (school-based programme), to a proportion close to that observed when a programme was implemented

to encourage children out of school to come to school to be treated (85 % – school-aged targeted programme) (Talaat *et al.* 1999). The different control strategies assessed are presented in Table 2.

Cost-effectiveness analysis

Analysis is undertaken to explore the maximum unit cost required for one strategy to be as or more cost-effective than another strategy. Let *x* and *y* be the school-based and school-aged targeted control programmes. Each programme will incur a total cost C_j ($j = x$ or y) (including the delivery costs) and have an effectiveness of E_j (number of discounted early disease or infection cases prevented over 15 years). The aim is to estimate the cost of the alternative strategies compared to the commonly implemented school-based strategy. Programme *y* will be as or more cost-effective as programme *x* if:

$$\frac{C_y}{E_y} \leqslant \frac{C_x}{E_x}.$$

Let N_i represent the number of individuals in each group, V_i the coverage and $i = s$ for children in school and $i = ne$ for school-aged children not in school. Defining U_i as the unit cost of treatment (cost per individual, including delivery), the total costs for programmes *x* and *y* can be calculated as:

$$C_x = U_s N_s V_s$$
$$C_y = U_s N_s V_s + U_{ne} N_{ne} V_{ne}.$$

The threshold unit cost (maximal unit cost) to reach and treat individuals not-enrolled in school while maintaining programme *y* to be as or more cost-effective than programme *x* is given by:

$$U_{ne} \leqslant \left(\frac{E_y}{E_x} - 1\right)\left(\frac{U_s N_s V_s}{N_{ne} V_{ne}}\right).$$

The difference between the maximal unit cost (U_{ne}) and the unit cost for the school-based programme (U_s) indicates the ***maximal extra unit cost*** that could be spent to treat individuals not enrolled and obtain a strategy as cost-effective as the school-based programme.
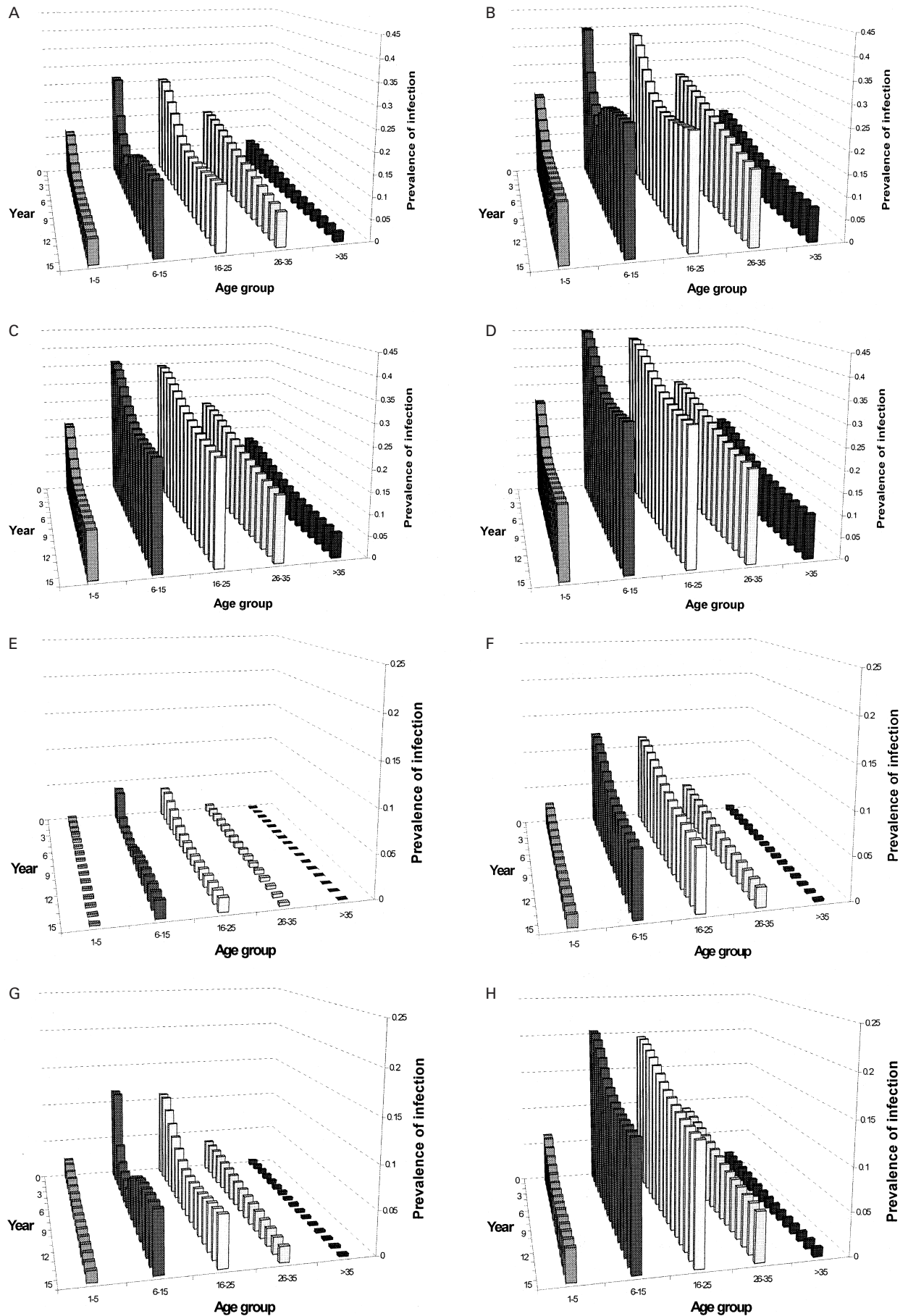
Fig. 1. For legend see opposite.

Table 2. *The proportion of each subgroup treated in the different simulations*

		Population			
		Children in school		Children out-of-school	
Strategy	Target	Coverage (% treated)	Age at treatment (years)	Coverage (% treated)	Age at treatment (years)
1	School	85	6–15	0	6–15
2	School-aged	85	6–15	25	6–15
3		85	6–15	50	6–15
4		85	6–15	85	6–15

A unit cost of US$ 0·60 per child treated is assumed for the school-based programme. This is based on recent data on the cost of school-based drug delivery systems in Tanzania and Ghana (Partnership for Child Development, 1999*a*). Using this unit cost for the school-based strategy, the maximum unit cost for an equivalent effectiveness was assessed for each alternative strategy. The unit cost of the school-based strategy was then varied from US$ 0·2 to US$ 1·00 as a form of sensitivity analysis.

RESULTS

Situation at equilibrium

In the absence of intervention, it can be assumed that there is no change in worm burden through time. This equilibrium situation is used to estimate the transmission parameters, the basic reproductive number in each group (R_{0g}) and acts as the basis for evaluating the number of cases that could be prevented after the implementation of a treatment strategy. Fig. 2 illustrates the equilibrium situation for the prevalence of infection and early disease for *S. mansoni* and *S. haematobium* in females in school (A), males in school (B), females out of school (C) and males out of school (D). This figure clearly shows that the prevalence of infection is highest in school children (aged 6–15 years old), but that the prevalence of early disease tends to be slightly higher in young adults (16 to 25-year-olds). At equilibrium, males out of school have the highest prevalences of infection and early disease for both schistosome species. This reflects the data observed in Egypt.

Comparison of the effectiveness of alternative control strategies

Effectiveness is assessed as the (discounted) number of infection or early disease cases prevented over a 15 year time-period from the onset of the first cycle of the annual 5-year treatment programme. The effectiveness of the 4 strategies (school-based and variants on school-aged targeted) is summarized in Table 3. Targeting children in school can achieve between 45 and 77 % of the effectiveness of a school-aged targeted approach with 85 % coverage; the relative effectiveness depending on the schisotosome species, the measure of effectiveness and the coverage in those not in school. For instance, the relative effectiveness is greater for *S. mansoni* than *S. haematobium*. The difference between the two schistosome species in the number of infection and early disease cases prevented reflects the variations in baseline prevalences and the proportion of children in each group, and the lower rate of development of early disease for *S. haematobium*.

For the area endemic for *S. haematobium*, the proportion of school-aged children not enrolled in school (45 %) was higher than in Lower Egypt (21 %), where *S. mansoni* is endemic. Reaching these out-of-school children therefore has a greater impact on effectiveness in the case of *S. haematobium*. For instance, if only 25 % of these children could be reached, effectiveness would increase by over 50 % for *S. haematobium* compared to less than 25 % for *S. mansoni*. If as many as 85 % of the school-age children not enrolled could be treated, the relative effectiveness of the school-aged based programme compared to the school-based programme would increase by more than 100 % for *S. haematobium*.

Comparison of the unit costs

Table 4 presents the maximum unit cost for reaching children not in school while achieving the same cost-effectiveness as a school-based strategy at a unit cost of US$ 0·60. The analysis indicates that one could invest more than US$ 0·60 in treating non-enrolled children and still be more or as cost-effective as a school-based approach. The extra cost available per

Fig. 1. Changes in the prevalence of *Schistosoma mansoni* (A–D) and *Schistosoma haematobium* (F–H) infection by age over a period of 15 years as a result of annual school-based treatment (coverage 85 %) for 5 years. (A) Females in school etc. (B) Males in school. (C) Females out-of-school. (D) Males out-of-school. (E) Females in school etc. (F) Males in school. (G) Females out-of-school. (H) Males out-of-school.
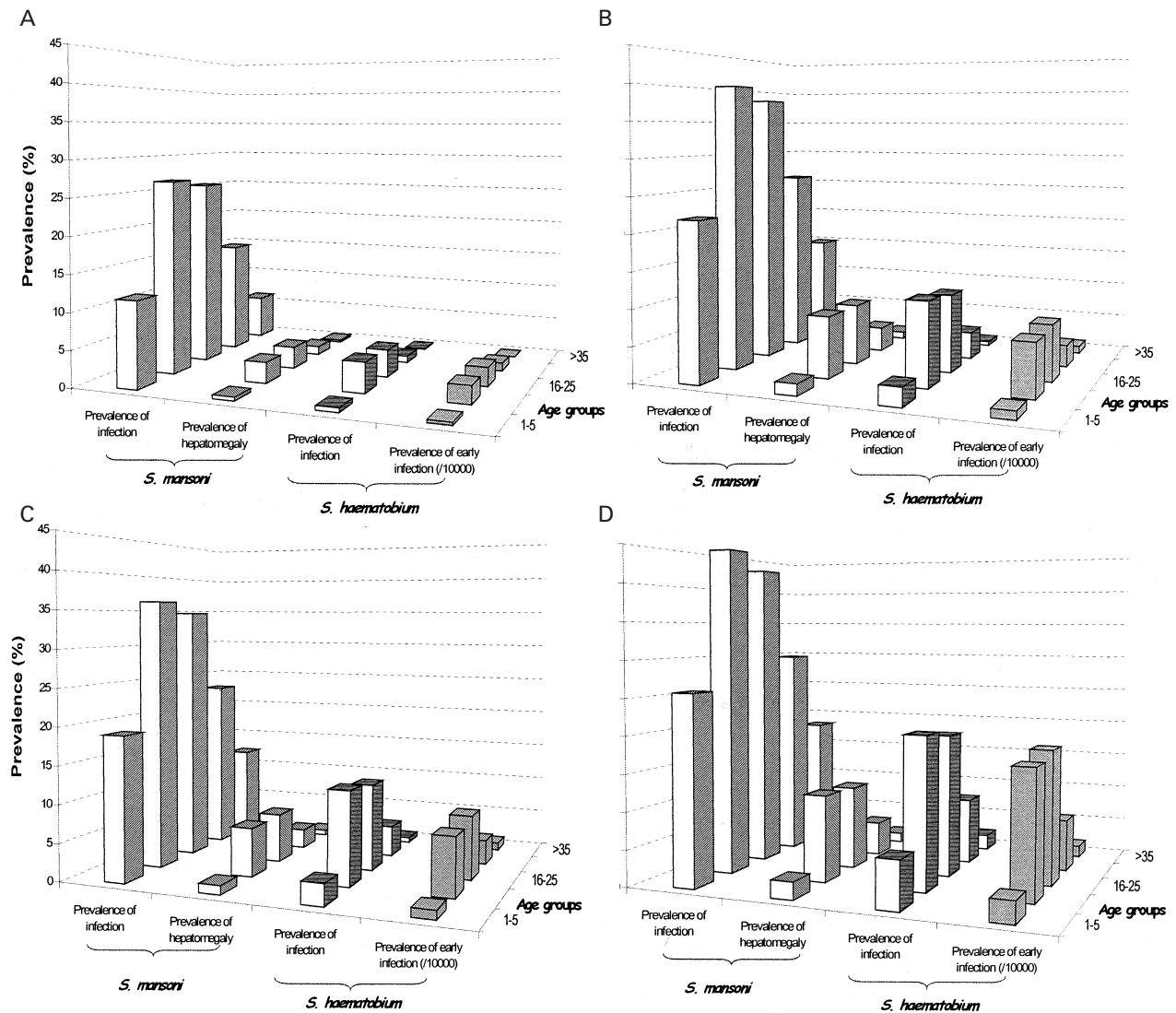
Fig. 2. Equilibrium prevalences for *Schistosoma mansoni* and *Schistosoma haematobium* infection and early disease in (A) females in school, (B) males in school, (C) females out-of-school, (D) males out-of-school.

Table 3. The effectiveness of treatment assessed as the discounted infection and early disease cases prevented over a period of 15 years from the first of the 5 annual treatments

	S. mansoni		*S. haematobium*	
Strategy	Infection	Early disease	Infection	Early disease
1	70 764	17 417	20 279	143
2	86 222	19 966	32 318	223
3	97 353	21 498	39 682	268
4	107 117	22 680	44 889	289

child treated varies with the schistosome species, the measure of effectiveness and the coverage in non-enrolled children.

For *S. mansoni*, if 25 % of non-enrolled children were treated, one could spend, on top of the US$ 0·60 which would cover drug costs and minimum delivery costs, an additional US$ 1·03 per child treated (for infection cases prevented) to reach these

children. This option would still be more cost-effective than a school-based approach. This decreases to US$ 0·49 for early disease cases prevented. As the coverage increases to 50 % and 85 % in this non-enrolled group, the maximal extra unit cost, in the case of early disease cases prevented, decreases to US$ 0·27 and US$ 0·06, respectively. This decrease is a result of a reduction in the

Table 4. *The maximum unit cost (US$) to treat individuals not enrolled in school and achieve the same cost-effectiveness as a school-based strategy (assuming a unit cost of US$ 0·60) and total number of individuals treated for the six strategies*

	S. mansoni			S. haematobium		
Strategy	Number treated	Infection*	Early disease*	Number treated	Infection*	Early disease*
1	84 522	[0·6]	[0·6]	59 513	[0·6]	[0·6]
2	91 273	1·64	1·10	73 618	1·50	1·42
3	98 024	1·41	0·88	87 723	1·21	1·11
4	107 475	1·14	0·67	107 470	1·02	0·92

* Maximum unit cost (US$): this unit cost is the maximum amount one could pay per person in the group of not enrolled individuals (groups 3 and 4) for the strategy to be cost effective as the school-based approach (strategy 1). Effectiveness is measured as infection or early disease case prevented.

difference between the percentage increase in numbers treated and effectiveness of school-aged targeted over school-based approach. This is most pronounced for early disease where the difference is approximately half at 25 % coverage but approaches zero at 85 % (see Fig. 3).

A similar decrease in the extra costs available to reach non-enrolled children as coverage increases is also observed for *S. haematobium*. However, at any given coverage, the maximal unit cost is higher for *S. haematobium* than for *S. mansoni* when effectiveness is assessed in terms of early disease cases prevented. For instance, at a coverage of 50 %, the maximum extra unit cost (for early disease cases prevented) for *S. haematobium* (US$ 0·51) is nearly twice that of the cost for *S. mansoni* (US$ 0·28). This is because reaching out-of-school children in the region endemic for *S. haematobium* has a larger relative impact on cases of early disease prevented than numbers treated (see Fig. 3). Interestingly, the results for infection cases prevented suggest that the maximal unit costs are higher for *S. mansoni*. This observation highlights the importance of the choice of effectiveness measure, particularly for helminths where infection and disease are not linearly related.

The sensitivity analysis showed that with a unit cost as low as US$ 0·20 for the school-based strategy, similar results would have been observed. As the unit cost of the school-based approach increased, the maximal extra unit cost increased for the school-aged targeted approach.

DISCUSSION

Concerns have been raised that a large number of school-aged children are missed by school-based programmes because they are not enrolled in school. Estimates of the proportion of children out-of-school vary by country, locality and sex (United Nations Education, Scientific and Cultural Organization, 1998), but recent studies in Egypt suggest that they can be as high as 45 % (Husein *et al*. 1996).

These studies also showed that the prevalence of infection was higher in those children not in school. Although treating all school-aged children would increase the proportion of infections treated, it is not clear what the relative effectiveness, in terms of both infection and early disease cases prevented over time would be of employing such an approach over a school-based strategy. Furthermore, since reaching these out-of-school children would likely result in additional costs, the relative cost-effectiveness of these approaches also deserves consideration. This paper presents a first attempt at modelling the possible cost and effectiveness of reaching non-enrolled children through school-age targeted programmes using empirical data from Egypt.

As has been shown in other studies (Bundy *et al*. 1990; Butterworth *et al*. 1991; Chan *et al*. 1995, 1998), targeting treatment at children in school will also reduce infection and disease in the rest of the population (including those non-enrolled). The analysis showed that, for *S. mansoni* in Lower Egypt, a programme where only 85 % of children attending school were treated would still prevent 77 % of the early disease cases prevented with a programme where 85 % of all school-age children were treated. The corresponding value for *S. haematobium* was 50 %, given the lower infection levels and the fewer school-aged children enrolled in Upper Egypt. These results support the implementation of school-based approaches, such as those undertaken by the Partnership for Child Development (Partnership for Child Development, 1999*b*).

However, targeting school-aged children increases the effectiveness of the programme. This also requires that more children be treated. The difference between the increased number of children treated and the increased numbers of infection or disease cases prevented is an important consideration, as total cost rises as more children are treated. The analysis suggested that an approach which targeted school-aged children could have a marked effectiveness advantage over school-based treatment,
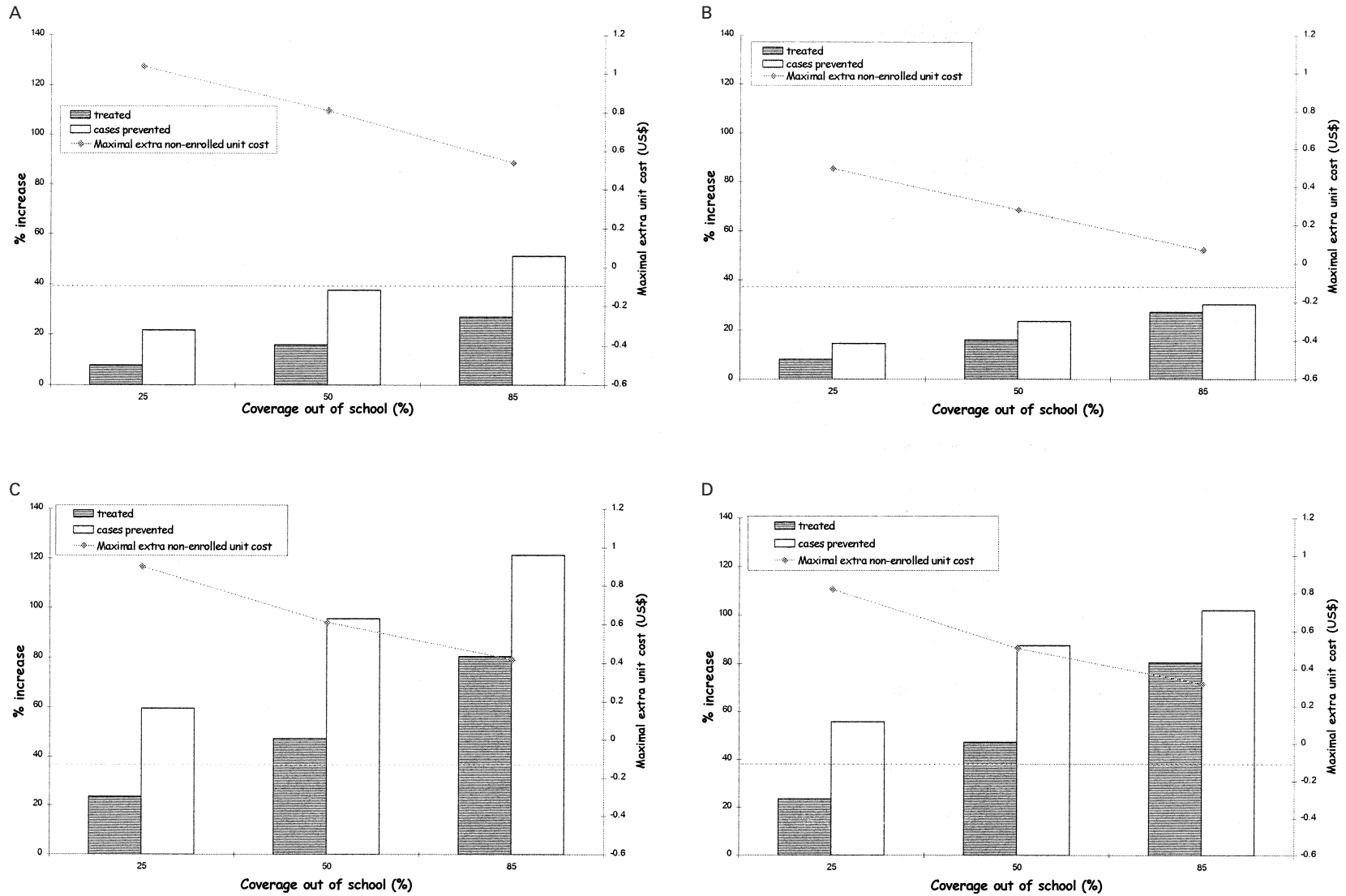
Fig. 3. Relative increase (compared to the school-based strategy) in the number of individuals treated (bar with horizontal lines), discounted cases prevented after 15 years (bar with vertical lines) and maximum extra unit cost in US$ (line) for (A) infection with *Schistosoma mansoni*, (B) early disease with *S. mansoni*, (C) infection with *S. haematobium*, and (D) early disease with *S. haematobium*.

and remain more cost-effective even allowing for additional costs in reaching these children. A recent study conducted in an area endemic for *S. haematobium* in Egypt has shown that using advertisement and recruitment of community leaders, teachers and enrolled children to encourage children out of school to attend the school setting for treatment, more than 85 % of these children could be treated. The additional costs involved in reaching these children are not clear, but the analysis here suggests that if 25 % of out-of-school children are treated, more than US$ 0·80 could be used to get this child to the school setting for treatment in the area endemic for *S. haematobium* as this would be more cost-effective than a school-based approach. Importantly, the maximum unit cost available for reaching these children decreases as the coverage increases. However, even at 85 % coverage, an extra US$ 0·31 per child could be invested and this approach would still minimize the cost per early disease case prevented for *S. haematobium*. Although the same general trends apply to the area endemic for *S. mansoni*, the cost margins are smaller due to the higher school enrolment, and the higher prevalence of infection.

Mathematical models are useful tools for understanding and evaluating the impact of interventions on the disease transmission and dynamics. The population dynamic model used here is based on a set of assumptions regarding transmission rates, immunity, density-dependent effects on worm establishment and the development and resolution of disease. Although the basic model structure and parameter values have been validated with field data (Chan *et al.* 1995, 1996 *a*, *b*), this has not been undertaken for the extended school-attendance/ sex/aged-structured model since empirical data on such interventions are lacking. As a result, the analysis presented in this paper should be seen as a first step in modelling the potential cost-effectiveness of reaching non-enrolled children. There are, for instance, a number of limitations in this model. Firstly, individuals are assumed to stay in the same sex/school enrolment group through time. Secondly, the unit of analysis is the age, sex and enrolment group, not the individual. Therefore, there is no estimate of individual contact or factors that might increase or decrease the risk of contact. Including individual risk factors in a refined model might improve the accuracy of the predictions, though this would have to be considered alongside the availability of data on individual risks. Finally, only prevalence data were available to estimate the equilibrium values in this analysis. The model is set up also to receive intensity data, which would be likely to improve the accuracy of the baseline transmission estimates.

This study has shown that treatment of non-enrolled children is an important consideration in maximizing the effectiveness of treatment programmes while still maintaining a cost-effectiveness ratio comparable to school-based delivery. As suggested by Jamison & Leslie (1990), children in school could have an important role in encouraging their friends and siblings not enrolled to attend the school setting when treatment is offered. Indeed, this analysis has shown that the benefits for the community as a whole may be large enough to warrant extra money being invested in reaching these non-enrolled children. This is not to mention the ethical issue of improving the access to treatment for children that are the most at risk of being highly infected, of low socio-economical status and from the most unfortunate families.

APPENDIX 1

The Model

The mathematical model used in this paper was developed from an earlier age-structured schistosomiasis model (Chan *et al.* 1995, 1996 *a*, *b*) by the addition of 4 groups (*g*) for children in and out of school and males and females. Structurally, the model now involves 4 sets of differential equations, one each for females in school (*g* = 1), males in school (*g* = 2), females out of school (*g* = 3) and males out of school (*g* = 4). The relative sizes of each group are assumed to be constant with age and individuals are assumed to remain in the same group throughout life (this is a restriction of the modelling method) but the coverage of treatment can be varied within each school-attendance group. The proportion of individuals in each group (*g*) is denoted $\pi(g)$.

The instantaneous change in mean worm burden (*M*) during very short intervals of calendar time and age for individuals of age (*a*) at time (*t*) and in group (*g*) is given by the partial differential equation that follows the conventions of the earlier models:

$$\frac{\delta M(g,a,t)}{\delta a} + \frac{\delta M(g,a,t)}{\delta t} = \Lambda(g,a,t)\,e^{-\delta I(g,a,t)} - \mu M(g,a,t),$$

where $I(g,a,t)$ is the level of immunity (modelled in the same way as the previous model with immunity accumulating with experience of infection in group *g*, age *a*), δ is the strength of immunity and μ is the mortality rate of worms. The immunity factor acts as a modulator for the force of infection (without immunity) represented by $\Lambda(g,a,t)$. The immunity is not lifelong and decays exponentially with age at a

rate of e^{-s} (where $1/s$ is the average duration of immunity). In other words, the larger $I(g,a,t)$, the smaller $e^{-\delta I(g,a,t)}$ which will in turn result in a lower overall acquisition of new infections ($\Lambda(g,a,t)$ $e^{-\delta(g,a,t)}$).

The force of infection at time (t) for individuals for age (a) in group (g) $\Lambda(g,a,t)$ is shown below:

$$\Lambda(g,a,t)$$
$$= \frac{\mu R_{0g}\rho(g,a)f(M(g,a,t))\sum_{g}\int_{a}\pi(g,a)\kappa(g,a)M(g,a,t)da}{\sum_{g}\int_{a}\pi(g,a)\kappa(g,a)\rho(g,a)da}.$$

The functions for age-dependent contamination rate $\kappa_{g,a}$, demography $\pi(g,a)$ and density dependence $f(M(g,a,t))$ are calculated in the same way as in the previous models. Using the equilibrium age distribution of infection intensity $M^*(g,a)$, the group specific R_{0g} can be calculated as follows:

$$R_{0g} = \frac{\alpha_g\sum_{g}\int_{a}\pi(g,a)\kappa(g,a)\rho(g,a)da}{\mu\sum_{g}\int_{a}\pi(g,a)\kappa(g,a)M^*(g,a)da}.$$

Several parameters in the new model are group specific (π_g and α_g in the current study because only the prevalence data were available). Since levels of infection may be different in each of the 4 groups, the parameters for the age-specific contact rate are assumed to depend on the group being considered. This value indicates the contact rate at which each individual is exposed to infection. This gives an age-group specific contact rate (at equilibrium, before treatment) as follows:

$$\rho(g,a) = \alpha_g(a\exp(-(\beta a)^2)+c),$$

where $\rho(g,a)$ corresponds to the contact rate for individuals of age (a) in group (g), α_g is an intermediate scaling factor, β is the contact rate and c is a contact constant. The same numerical value is used for the contamination rate $\kappa(g,a)$, representing the age-group specific rate of contamination of the environment with infectious faeces.

The intermediate scaling factor is determined by the mean worm count at the age of peak intensity of infection (a_p) and the mean worm burden in group (g) as follows:

$$\alpha_g = \frac{\mu m_{p,g}}{a_p e^{-\beta a_p}f(m_{\rho,g})},$$

where a_p is the age of peak intensity, $m_{p,g}$ is the mean egg count at this peak and for group (g), μ is the worm death rate, β is the inverse of the age of peak contact (assumed to equal 0.125) and

$$f(m_{p,g}) = \left(1+\frac{m_{p,g}}{K(m_{p,g})}(1-e^{-\gamma})\right)^{-(K(m_{p,g})+1)}$$

is a density-dependence factor. This factor is modelled here as the reduction in the establishment of new adult worms that depends on the current worm load ($m_{p,g}$) and on a density dependence constant parameter (γ).

The level of infection in each group is input as prevalence of infection from field data. In order to accommodate different distributions of parasite infection in each group, the negative binomial aggregation parameter, k_g, is also allowed to vary between groups. As with the previous model, a linear relationship between the value of k_g and the worm burden is assumed, and both the intercept (k_0) and the slope (k_{lin}) of this function can be group dependent. In the current analysis, the intercept and slope are kept constant because no data on the arithmetic mean of epg were available. Nonetheless, since the mean worm burden depends on group (g) and $k_g = k_0 + k_{lin}*M(g,a)$, k_g will vary according to group (g).

As with the previous studies, the differential equations were solved numerically using a FORTRAN computer program. The simulations are initiated with the endemic equilibrium before treatment. The parameters used were the same as in previous studies (Chan *et al.* 1995, 1996, 1999) unless otherwise stated (see Appendix 2).

APPENDIX 2

Parameter	Symbol (units)	Value	Source
Default parameter set used for simulations of *S. mansoni*			
Concomitant immunity	γ	0·005	Chan *et al.* (1995)
Immunity strength	δ	0·001	Chan *et al.* (1996*b*)
Immunity duration	$1/s$ (years)	10	Chan *et al.* (1996*b*)
Maximum human age	A (years)	80	Estimated
Age at peak contamination	$1/\theta$ (years)	14·29	Present analysis
Age at peak contact	$1/\beta$ (years)	14·29	Present analysis
Contact constant	C	0·35	Present analysis
Timestep	Years	0·05	Present analysis
Maximum worm burden		2000	Cheever (1968)
Demographic constants	be^{-da}	$b = 0\cdot0356$ $d = 0\cdot033$	World Bank data [ ]
Aggregation parameter (intercept)	k_0	0·132	Chan *et al.* (1995)
Aggregation parameter (slope)	k_{lin}	0·002	Chan *et al.* (1995)
Epg per worm	e_I	5·26	Chan *et al.* (1995)
Worm life-span	$1/\mu$ (years)	4	Anderson & May (1991)
Development rate early disease	λ_e	0·0071	Chan *et al.* (1996*a*)
Resolution rate early disease	μ_e	1	Chan *et al.* (1996*a*)
Development rate late disease	λ_l	0·015	Chan *et al.* (1996*a*)
Resolution rate late disease	μ_l	0·0769	Chan *et al.* (1996*a*)
Threshold for heavy infection	(eggs per gram)	200	Present analysis
Group-specific parameters			
Proportion of the population			
Females in school	$\pi(g=1)$	0·3582	Husein *et al.* (1996)
Males in school	$\pi(g=2)$	0·4282	Husein *et al.* (1996)
Females out of school	$\pi(g=3)$	0·1318	Husein *et al.* (1996)
Males out of school	$\pi(g=4)$	0·0818	Husein *et al.* (1996)
Scaling factor*			
Females in school	$\alpha(g=1)$	0·2469	Present analysis
Males in school	$\alpha(g=2)$	0·8253	Present analysis
Females out of school	$\alpha(g=3)$	0·5979	Present analysis
Males out of school	$\alpha(g=4)$	1·2154	Present analysis

*Scaling factor: $\alpha(g) = \dfrac{\mu m_{p,g}}{a_p e^{-\beta a_p} f(m_{p,g})}$

where a_p is the age of peak intensity, $m_{p,g}$ is the mean egg count at this peak and for group (g), μ is the worm death rate, β is the inverse of the age of peak contact (assumed equal to 0·125),

$$f(m_{p,g}) = \left(1 + \frac{m_{p,g}}{K(m_{p,g})}(1-e^{-\gamma})\right)^{-(K(m_{p,g})+1)} \quad \text{and} \quad K(m_{p,g}) = k_0 + k_{lin} * m_{p,g}.$$

APPENDIX 2 (*cont.*)

Parameter	Symbol (units)	Value	Source
Default parameter set used for simulations of *S. haematobium*			
Concomitant immunity	γ	0·001	Chan *et al.* (1995)
Immunity strength	δ	0·001	Chan *et al.* (1996*b*)
Immunity duration	$1/s$ (years)	10	Chan *et al.* (1996*b*)
Maximum human age	A (years)	80	Estimated
Age at peak contamination	$1/\theta$ (years)	14·29	Present analysis
Age at peak contact	$1/\beta$ (years)	14·29	Present analysis
Contact constant	C	0·35	Present analysis
Timestep	Years	0·05	Present analysis
Maximum worm burden			Cheever (1968)
Demographic constants	be^{-da}	$b = 0·0356$	World Bank data [ ]
		$d = 0·033$	
Aggregation parameter (intercept)	k_0	0·184	Chan *et al.* (1996*a*)
Aggregation parameter (slope)	k_{lin}	0·0002	Chan *et al.* (1996*a*)
Eggs per ml per worm	e_I	1	Chan *et al.* (1995)
Worm life-span	$1/\mu$ (years)	4	Anderson & May (1991)
Development rate early disease	λ_e	0·001	Chan *et al.* (1996*a*)
Resolution rate early disease	μ_e	1	Chan *et al.* (1996*a*)
Development rate late disease	λ_l	0·04	Chan *et al.* (1996*a*)
Resolution rate late disease	μ_l	0·1	Chan *et al.* (1996*a*)
Threshold for heavy infection	(eggs per 10 ml)	50	Present analysis
Group-specific parameters			
Proportion of the population			
Females in school	$\pi(g = 1)$	0·1829	Husein *et al.* (1996)
Males in school	$\pi(g = 2)$	0·3709	Husein *et al.* (1996)
Females out of school	$\pi(g = 3)$	0·2928	Husein *et al.* (1996)
Males out of school	$\pi(g = 4)$	0·1535	Husein *et al.* (1996)
Scaling factor*			
Females in school	$\alpha(g = 1)$	0·015	Present analysis
Males in school	$\alpha(g = 2)$	0·0429	Present analysis
Females out of school	$\alpha(g = 3)$	0·0462	Present analysis
Males out of school	$\alpha(g = 4)$	0·1010	Present analysis

*Scaling factor: $\alpha(g) = \dfrac{\mu m_{p,g}}{a_p e^{-\beta a_p} f(m_{p,g})}$

where a_p is the age of peak intensity, $m_{p,g}$ is the mean egg count at this peak and for group (g), μ is the worm death rate, β is the inverse of the age of peak contact (assumed equal to 0·125),

$$f(m_{p,g}) = \left(1 + \frac{m_{p,g}}{K(m_{p,g})}(1 - e^{-\gamma})\right)^{-(K(m_{p,g})+1)} \quad \text{and} \quad K(m_{p,g}) = k_0 + k_{lin} * m_{p,g}.$$

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