Supporting Information

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SI Text

Model Parameterization and Sensitivity to Model Parameters, Calculating Critical Prawn-Density Thresholds Given Variations in Parameter Values. Predation was modeled with a Holling type II saturating functional response parameterized from laboratory data (1), with q being the attack rate and T_h the handling time parameter. The mean prawn density in the intervention site, P, was modeled as a constant parameter that varied from zero to several hundred prawns per site, which considers the predators as a constant managed population controlled by both stocking rates and the survival of prawns after stocking (i.e., P represents the realized, average prawn density at a site). Additional parameter explanations, estimates, and references can be found in Table S1.

We assessed whether the model could qualitatively replicate the observed patterns of reinfection in the human population at the control and experimental sites. To this end, the model assumed that 100 people were treated at each site, out of a total population of *ca.* 2,000 [i.e., 10% mass drug administration (MDA) coverage], which is similar to field conditions. At baseline, the model simulated a double-dose MDA, administered 3 wk apart, as in the field study. In addition, the model simulated prawn stocking in the experimental site by setting prawn density to *ca.* 25 prawns per enclosure, or 0.125 per square meter (which is the estimated average realized prawn density within the experimental enclosure calculated from the starting stocking densities and estimated prawn survival rates based on trapping data).

We used the model to assess uncertainty regarding the prawn densities needed for disease elimination or local snail population extirpation. To this end, we randomly varied each parameter using a normal distribution and a 10% coefficient of variation, with the following exceptions:

i) The attack rate at low density, q, was varied by one order of magnitude below the laboratory-derived value up to the laboratory-derived value (random uniform variation) because we considered the laboratory-derived value as an upper bound, given that factors present in the natural situation were likely to reduce predation efficiency (e.g., habitat complexity, refuges, reduced visibility) compared with predation efficiency measured in laboratory aquaria.

ii) The handling time, T_h, was varied as a random normal variable with mean and SD both estimated by empirical laboratory studies in the study by Sokolow et al. (1).

iii) The dispersion parameter of the negative binomial distribution, k, was varied from empirically derived minimum and maximum values estimated from Senegalese patient field data [collected in this study for *S. hematobium* and in the study by Webster et al. (2), for *S. mansoni*], and k was randomly uniform along that range.

iv) Human life expectancy was left at a constant 60 y and was not varied.

We assembled 100 parameter combinations using the random procedures described above. For each parameter combination, we simulated the system with varying numbers of prawns ranging from 1 to 500 prawns per 200 m^2 (0.005–2.5 prawns per square meter) and estimated the equilibrium number of susceptible, exposed, and infected snails. The minimum prawn density required for quasi-extinction (less than one snail remaining) at equilibrium for infected snails (disease elimination) or all snails (local snail extirpation) was recorded.

The randomly assembled parameter combinations resulted in a range of values of the prawn-free R_0 from 1.7 to 7, which is consistent with the range of published estimates (3, 4). The resultant median and range of prawn densities required for disease elimination or local snail extirpation are shown in Fig. S1. For each individual simulation, we also calculated the ratio of prawn densities required for disease elimination vs. local snail extirpation, and we plotted these ratios in Fig. S2. The results show that as prawn-free R_0 increases, the ratio between the two critical prawn-density thresholds also increases (linearly) approaching 1, meaning that the critical densities for disease elimination approach the critical densities for local snail eradication. On the other hand, as R_0 is reduced, this ratio decreases toward zero, meaning that disease elimination may occur at much lower prawn densities than required for local snail population extirpation. Similarly, as the attack rate of prawns on snails is reduced, the ratio of the two critical densities decreases (Figs. S2 and S3). Thus, for most cases, local snail extirpation is unlikely at the prawn densities required for disease elimination.

Reinfection Rates and Seasonality. Studies from various regions across Africa have suggested seasonality in human schistosome transmission, usually inferred from snail population data, cercarial output measurements, or rodent sentinel studies (5–10). Only a few studies have demonstrated seasonality in transmission and reinfection rates in the natural definitive (human) host. There were three human reinfection periods tracked during this study (Fig. S4).

The first reinfection period occurred over the course of 5 mo after a double-dose praziquantel treatment (40 mg/kg per dose, with two doses 3 wk apart) in February 2012. During this period, which coincided with the dry season, the reinfection rate was very slow at both the treatment and control sites.

The second reinfection period occurred over 7 mo (July to January) after all patients found to be positive for schistosome infection were treated with a single dose of praziquantel (40 mg/kg) in July. In contrast to the first reinfection period studied, this second reinfection period showed markedly high reinfection rates at both the treatment and control sites. A large portion of this second reinfection period occurred over the rainy season (which lasts from June to October), suggesting that the rainy season and/or the period just before or after the rains may have higher transmission rates than the dry season (which lasts from November to May).

The third reinfection period occurred over 6 mo after positive patients detected at the second follow-up were again treated with a single dose of praziquantel in February (40 mg/kg). The reinfection rate during the third reinfection period was intermediate to the reinfection rate found at the first and second reinfection periods, and, indeed, the third period was of intermediate length (6 mo instead of 5 or 7 mo) and occurred partly in the dry season and partly in the rainy season.

Taken together, these data suggest that reinfection rates are rapid in this region, requiring just a few months to rebound to very high prevalence, and that the rainy season months from June to October may pose a higher human reinfection risk than the dry season months of November to May, similar to results reported by Webster et al. (2), which tracked reinfection in an *S. mansoni* hotspot in a nearby village in northern Senegal.

In Mozambique, *S. hematobium* human reinfection rates after praziquantel treatment were shown to be lower during the cool, dry season, although patients were followed for only 2 mo after

treatment (11). Likewise in South Africa, human reinfection with *S. hematobium* was highest during the warm/wet months and lowest during the cool/dry months (12). In a relatively small study in Nigeria, where warm temperature and rainfall occur in opposite rather than overlapping seasons, the highest transmission rate was seen in the warm/dry season rather than the cool/rainy season (13), suggesting the effects of temperature on transmission may be dominant over the effects of rainfall. Other variables besides snail population growth that might change seasonally to influence reinfection risk include egg survival time outside the host (presumably higher in higher humidity) and the rate of egg passage into the surface freshwaters (presumably higher with more runoff), as well as seasonal differences in human behavior [e.g., the rainy season and the months just before and just after it are the hottest months in the region and may promote more water contact, as has been shown in other areas (14)].

Studies to investigate further the factors involved in the observed, marked differences in transmission of human schistosomiasis across seasons could help to plan the timing of yearly praziquantel administration and/or prawn reintroduction campaigns to maximize their benefits (15).

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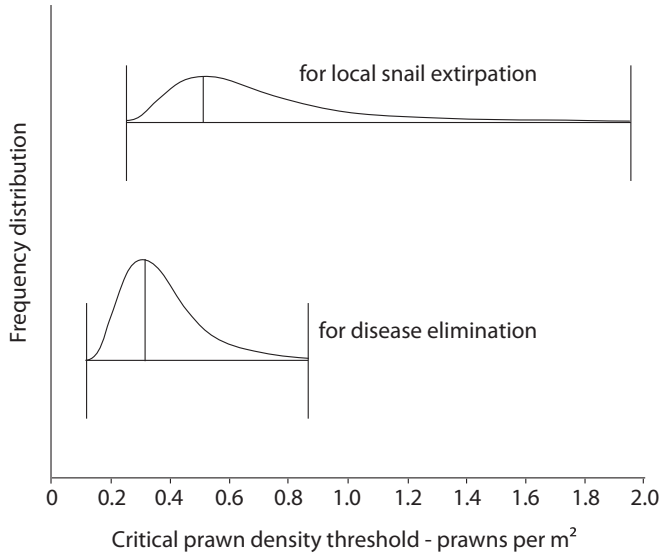

Fig. S1. Frequency distributions for the critical prawn density for snail extirpation (*Top*) and disease elimination (*Bottom*).

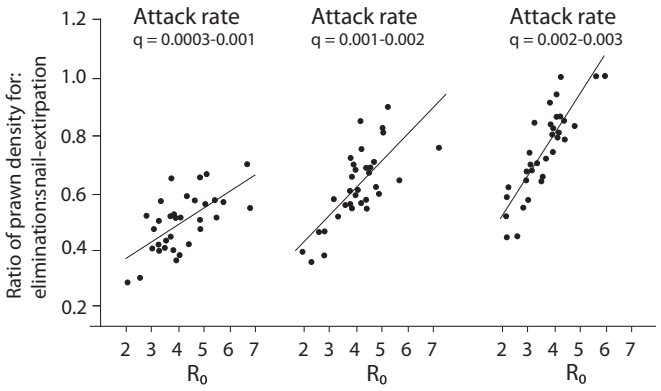

Fig. S2. Relationship between the prawn-free R_0, defined here as the expected number of adult parasites generated per adult parasite, and the ratio of the first and second critical prawn densities (i.e., critical prawn density for disease elimination and snail extirpation, respectively) across varying attack rates (*q*).

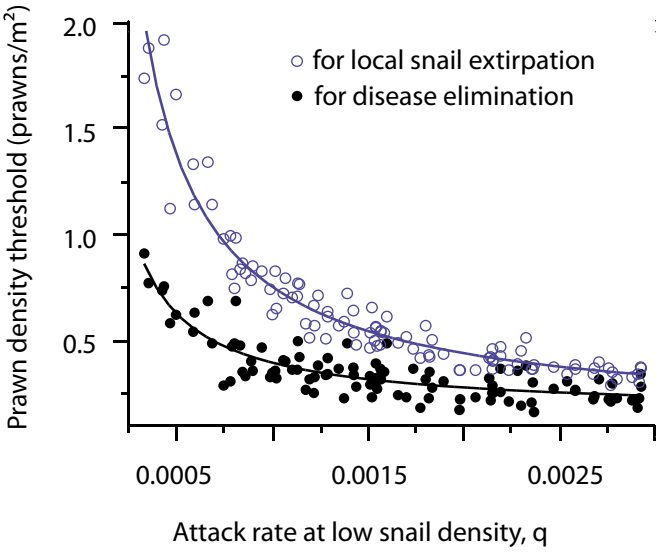

Fig. S3. Relationship between the attack rate (*q*) and the critical prawn densities for disease elimination and snail extirpation.

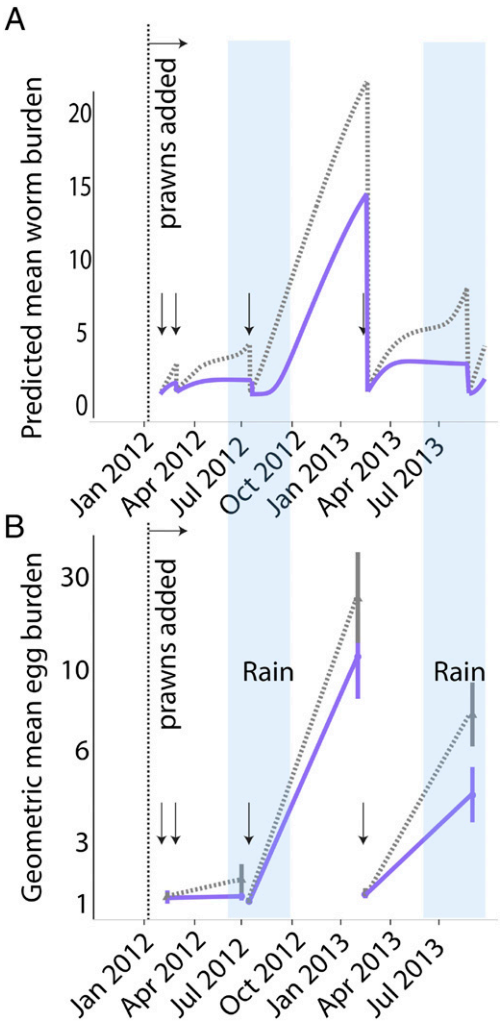

Fig. S4. Seasonal reinfection patterns. (*A*) Reinfection patterns in predicted mean worm burden per capita, based on the schistosome transmission model. (*B*) Actual GM egg burdens at each of three follow-up time periods during the Project Crevette field study (note that GM egg burdens are represented on a log scale). Blue-shaded regions show the timing of the rainy season. Solid lines indicate prawn site, and dashed lines indicate control site. Vertical arrows indicate praziquantel administration to both study populations (intervention and control). The differences between the disease burdens at the prawn vs. control site at each follow-up time point, July 2012 (5 mo), February 2013 (12 mo), and September 2013 (18 mo), are shown in Table S2.

Table S1. Explanation of parameters

Symbol	Explanation	Starting value	Source
P	Prawn density/site (assumed constant, based on periodic stocking)	0–500	Our unpublished data on stocking effort and estimates of prawn mortality
N	(Variable) Total snail population size in ~200 m^2 area encompassing a water access point on a river, pond, or lake	S + E + I	Initially set at prawn-free equilibrium corresponding to absolute densities of ~44 snails/m^2, which is plausible given (1)
h	Initial human population abundance per site	1,000	Our unpublished data on population size at various villages
f	Instantaneous intrinsic fertility rate of snails including survival to detectability (>5.5 mm)	0.16 per day	(1)
φ	Density-dependent parameter for snail population growth (roughly the inverse of carrying capacity per site)	~1/10,000	Equivalent to ~50 snails per square meter on average (1)
β	Per capita snail infection probability	$4 * 10^{-6}$	No data available, calibrated to match expected R_0 of 1–7
η	Fraction of all worms that are breeding females	0.5	Assuming 1:1 sex ratio and M * h >> 1
ω	Miracidial shedding rate per reproductive female divided by miracidia mortality	0.8	Little data available, calibrated to match expected behavior of the system
q	Per capita attack rate of prawns on snails per site at low snail density [scale-dependent, adjusted for size of site (~200 m^2)]	0.003	Laboratory-derived data (2)
T_h	Prawn handling time parameter (*sensu* Holling's disk equation), essentially the inverse of maximum number of snails consumed per prawn per day	0.1	Our laboratory data (2); T_h is the inverse of the sustained daily average consumption of snails by adult prawns: (average, 7.9 ± 1.2; range, 2–20 snails per prawn per day)
z	Fraction of exposed snails that reproduce	0.5	(3)
μ	Natural mortality rate of uninfected (or exposed) snails	1 per 50 d	(4)
σ	Rate of conversion from exposed to shedding	1 per 50 d	Assumed constant here but is really temperature-dependent
α	Additional mortality rate of shedding snails due to infection	1 per 10 d	(3)
λ	Daily infection probability from snail to man, an aggregate parameter that includes cercarial shedding rate divided by cercarial mortality and probability of parasite survival to patency in humans	0.0005	Little data available, calibrated to match expected behavior of the system; compared with estimates (5): ~1 infection per 127–1,176 water contacts per person
k	Dispersion parameter of the negative binomial distribution	0.25	Estimated using data from Yousif et al. (6) and from this project
ν	Adult worm natural mortality	1/3 * 365 d	Estimated life span of 3.3 y (range: 2.7–4.5 y) from Shiff et al. (7)
d	Mortality of adult worms due to rate of human mortality	1/60 * 365 d	Assume an average human life expectancy of 60 y

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Table S2. Observed and predicted (by our model) percentage difference in *S. hematobium* human disease prevalence and egg burden at the experimental site compared with the control site across all follow-up time points

	Observed				Predicted
Parameter	5 mo, %	12 mo, %	18 mo, %	Mean difference ± SE, %	Mean difference, %
Prevalence	−20	−8.2	−25.6	−17.9 ± 5.1	−23.6*
Egg/worm burden	−36.3	−50	−63.5	−49.9 ± 7.9	−56.5†

*Model predicts prevalence of those people with at least two worms (one worm pair), whereas the field data measure the number of people with eggs encountered in 10 mL of urine as a proxy.
†Model predicts actual worm burden, whereas field data measure mean eggs per 10 mL of urine as a proxy.

Table S3. Water contact reporting

Village	Study site % (CI)	Rice fields % (CI)	Garden % (CI)
Lampsar 1 (intervention site), *n* = 152	98% (95–100%)	41% (34–49%)	55% (47–63%)
Lampsar 2 (control site), *n* = 115	100% (97–100%)	52% (43–61%)	64% (55–73%)

Results of an informal query of all enrolled participants during a site visit in 2013 regarding their reported water contact in the study village's designated water access point (study site), individual rice farming allotments when the paddies were flooded (rice fields), or while collecting water to irrigate vegetable garden plots outside the study village (garden). From 40% to 60% of participants at both the intervention and control villages reported having some water contact outside the study site (in or near rice or garden plots). Shown in the table are the percentages of participants who reported having water contact at the three locations (with the CIs). *n*, number of respondents at each site.