

Spatial Patterns of Schistosomiasis: A watershed approach to measuring *S. japonicum* environmental risk and human and animal disease outcomes

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ABSTRACT

Schistosomiasis is a water-borne parasitic disease caused by infection with parasitic worms of the genus *Schistosoma*. The disease contributes significantly to the high global burden of helminth disease and affects over 200 million people world wide. The life cycle of *Schistosoma japonicum*, the schistosome species endemic to South East Asia, is dependent on both the presence of an intermediary snail host in the aquatic environment and continued contact with contaminated water by a definitive mammalian host. Ecological and hydrological parameters that shape the suitability of snail habitat are important determinants of the risk of *S. japonicum* transmission to humans and animals. Fecal water contamination and mammalian exposure to infective water are also needed to maintain *S. japonicum* transmission. Because schistosome parasites diffuse through the aquatic environment along aquatic networks, infection risk results from both local and upstream loading of parasites.

The objective of this study is to determine the efficacy of mapping the spatial distribution of population level schistosomiasis in humans and animals using hydrologically defined drainage areas called catchments. A better understanding of how spatial patterns explain the distribution of schistosomiasis at the catchment level may help public health interventions target high transmission areas within the hydrologic network. This thesis explores the potential strengths and weaknesses of defining the catchment as the primary unit of analysis in exploring the spatial relationship between environmental risk of *S. japonicum* and mammalian disease outcomes. Prevalence of infection and an index of potential contamination (IPC) for humans and rats from forty-nine villages in Western Samar Province, the Philippines were mapped, along with the distribution of infected snails, by catchment. Catchment level human, rat, and snail infection was highly variable across the study area. Catchments with high infected snail counts generally had high human IPC. This spatial relationship, however, was not present between snail infection and human prevalence. No clear spatial relationship was present between snail infection and rat infection. These results indicate that a better understanding of how the parasite passes through the aquatic environment and human and animal populations is needed before we can assess the accuracy of using hydrologically define units to capture the spatial relationship between environmental risk and human and animal disease outcomes.

BACKGROUND

Schistosomiasis or Bilhizarias, of the genus *Schistosoma*, is one of the major parasitic worm diseases contributing to the high burden of global helminth infection. An estimated 200 million cases of schistosomiasis occur world wide (WHO, 2002). The five schistosome species producing schistosomiasis in humans include *S. mansoni*, *S. haematobium*, *S. intercalatum*, *S. japonicum*, and *S. mekongi*. These five species are found in endemic regions of Africa, East and South East Asia, the Pacific Islands, Brazil, and the Caribbean Islands. Schistosomiasis is most heavily concentrated in Sub-Saharan Africa where 77% of the total number of disability adjusted life years (DALYs) attributed to schistosomiasis occur (Gryseels, 2006). Though it has a relatively low mortality rate, with estimates between 14,000 (King *et al.*, 2005) and 200,000 annual deaths (WHO, 2002), morbidity from schistosomiasis accounts for the annual loss of an estimated 1.7 to 4.5 million disability adjusted life years, and ranks second to malaria in number of people infected and at risk of disease (WHO, 2002). Based on a meta-analysis by King *et al.* (2005), however, these burden estimates may be seven-fold higher.

Schistosomiasis infection produces a variety of symptoms in humans based on the severity and progression of disease, from cognitive disability in children to nutrient and energy deficiencies and liver fibrosis. The mammalian host experiences a range of disease and functional deficits due to the energetic and immunologic costs of the presence of the worms and the reactions to the eggs produced by adult female worms. The severity of the disease in an individual is related to the immune status of the host, the

duration of disease pathogenesis, intensity of infection (measured in eggs per gram stool (EPG)), and the location of egg deposition in the body. On a population level, researchers generally measure the severity of disease by the prevalence, intensity (mean EPG), and incidence, or the number of new cases in a population per year. These metrics are often correlated and combined to produce better estimates of disease transmission and contamination potential. While prevalence and intensity of infection commonly vary with age, a general pattern of schistosomiasis is an increase in prevalence and intensity of infection with age up to the teenage years and a decline thereafter (Vercruyse, 2001).

Schistosomiasis is both an environmental disease and a disease of poverty. It is environmental because anthropogenic and natural parameters shape the distribution of disease in aquatic systems by defining the ecological niches where the snail intermediate host can survive. Furthermore, schistosomiasis is transmitted from the definitive mammalian host to the aquatic environment through urinary and fecal contamination of waterways. Schistosomiasis is a disease of poverty because its geographic distribution reflects population access to safe water, sanitation infrastructure, socio-economic status, and access to secondary treatment. Praziquantel, the current secondary treatment for schistosomiasis, treats the adult worms once inside the mammalian host. While this drug has proven effective in reducing the burden of disease in many human populations (Jordan and Webbe, 1993) it is not a sustainable treatment because it does not address the persistence of parasitic risk in the environment.

Life Cycle

Schistosome parasites must infect a definitive mammalian host and an intermediate snail host to complete its reproductive life cycle. Schistosome ova pass from the mammalian host to the environment in fecal matter and urine and hatch upon contact with freshwater. Once in water, the ova release free swimming, sexually differentiated miracidia, which search for and penetrate the soft tissue of aquatic and semi-aquatic snails, asexually reproduce, and emerge into the surrounding water as juvenile cercaria. The cercaria infect the mammalian host through skin penetration around hair follicles or wounds, and migrate through the blood stream via the heart to the liver where they develop into mature adults and mate, producing ova that the animal host will repeatedly shed back into the environment, thus completing the schistosome life cycle.

Because schistosomiasis depends on a snail intermediate host to complete its life cycle, it is confined to ecological niches that are suitable for freshwater snail habitat. As a result, environmental and ecological parameters that shape the suitability of snail habitat are important determinants of human and animal risk of contracting schistosomiasis from contact with contaminated water. Both natural parameters (e.g., water temperature and stream ecology) and anthropogenic changes (e.g., dams, agriculture, and reservoirs) shape snail habitat and the distribution of potential snail vectors (Steinmann et al., 2006; Hairston and Santos, 1961).

Although the intermediate snail host inhabits multiple geographic regions, many ecological parameters are known to control its distribution and population size. The intermediate snail host generally inhabits shallow muddy sediments of lentic, still water, and lotic, flowing water, freshwater systems, including streams, rivers, ponds, lakes, irrigation canals, and heavily irrigated agricultural fields. Temperature, sunlight, water flow, presence of macrophytic aquatic plants, and dissolved oxygen are the primary ecological determinants of snail habitat suitability (Thomas and Tait, 1984). High temperatures over long periods of time are known to limit snail fecundity (Appleton, 1976). Direct sunlight may also have lethal effects on snails as experimental evidence shows that snails avoid strong sunlight and prefer shaded areas (Zakaria, 1955).

Human Contamination

While environmental factors may shape the suitability of snail habitat and the resulting distribution of the intermediate snail host, in the end, risk of transmission in humans depends on the frequency and duration of contact with infective water and the level of risk of infection upon contact. Once within the mammalian host, schistosome eggs must pass via the stool or urine to freshwater to complete the parasite's lifecycle. The perpetual contamination of waterways with human waste, and subsequent exposure to contaminated water is essential for the parasite's continued asexual reproduction in the snail host and sexual reproduction within the mammalian host. Thus, in many endemic areas humans contribute heavily to both the parasite's survival and the resulting burden

of disease within the human population through continued fecal and urinary contamination of heavily used water-ways.

Fecal contamination of surface waters with schistosome eggs occurs in rural endemic regions with low sanitation infrastructure. Sanitation levels and fecal contamination patterns in humans and domesticated animals were found to be important contributors to observed levels of local surface water contamination and schistosomiasis prevalence (Li *et al.*, 1998). Contamination events result from overflowing latrines, dumping of treated and untreated sewage into water-ways, and human and animal defecation directly in and around water ways (Jordan and Webbe, 1993). Heavy rains aid contamination by carrying the schistosome eggs to water bodies where they can successfully hatch into viable miracidia. A wet climate is an important contributor to water contamination as seen in the decreased viability of *S. mansoni* ova exposed to the sun within a few days after fecal deposition (Maldonado *et al.*, 1949). The level of contamination is thus dependent on both direct factors such as defecation patterns and indirect factors such as rain events, overflowing latrines, and level of community sanitation.

Animal Contribution

Humans are not the only mammalian hosts contributing to disease transmission. Other animals in a community are also likely to both be exposed to contaminated water and further contaminate waterways with infected feces and urine. *S. japonicum* has the widest variety of mammalian hosts making it even more difficult to quantify the relative

contributions of different mammalian hosts to schistosomiasis transmission. McGarvey *et al.* (2006) found intensity of *S. japonicum* infection in dogs and cats to be strongly associated with that of humans, suggesting that animals may be important reservoirs of infection. More study is needed to understand how related human and animal infection intensities are.

Index of Potential Contamination (IPC)

The index of potential contamination (IPC) reflects a combination of the infection prevalence and the intensity of infection among those infected. The IPC gives an estimate, though limited, of the potential for a community to contaminate surrounding waters with viable *S. japonicum* eggs. Jordan (1963) developed the Index of potential contamination (IPC), previously known as the "infection potential," to quantify the relative contribution by population or age-groups within a population, of schistosome eggs passed in human feces to the infectiveness of locally contaminated surface waters. The crude IPC is calculated by multiplying the prevalence of schistosomiasis in a population by the mean intensity of infection in the population. The resulting value is an estimate of the number of eggs passed per gram of stool in a population.

While the IPC provides a more robust indication of both relative levels of transmission potential in a population and crude estimates of transmission potential between populations than do disease prevalence or intensity alone, more validation of the IPC model is needed to test its accuracy as an estimator of future schistosomiasis

transmission risk (Vercruyssen, 2001). It is highly useful in focusing public health interventions on controlling transmission in those communities with the highest potential for continued transmission by identifying disease and contamination foci within a population. Changes in IPC after public health interventions can also indicate how effective the interventions are in reducing the contamination potential and transmission risk in a community (Vercruyssen, 2001).

The IPC also carries with it high uncertainty as an estimator of the actual contribution to disease transmission of groups in a population. The IPC measures the *potential* for a population to contaminate its surrounding surface waters with schistosome ova and is not a direct measurement of human contribution to contamination. IPC measurements exclude many other significant human contamination variables. The IPC model, for example, does not take into account the hatching rate of eggs, which rises proportionally with infection intensity (Upatham, 1976), or differences in fecal output by age group, or errors in the detection of both presence of eggs and errors in the counting of eggs in fecal specimens (Carabin et al 2005).

Linking environmental risk to human infection

Proximity to contaminated water is a known risk factor for schistosomiasis infection. Huang and Manderson (1999) describe prevalence rates of villagers in one community according to their distance from marshland along the Yangtze River, the snail habitat, and show that prevalence of *S. japonicum* declines with distance of villagers from the marshland. As stated earlier however, proximity to contaminated water alone does

not explain the entire picture. A number of studies have found an association between an individual's occupation and their relative risk of infection (Huang and Manerson, 2005). Yu *et al.* (1992) found fishermen, aquatic workers, and farmers, in that order, to have the highest frequencies of water contact and the highest relative risks of *S. japonicum* infection across three villages in the Dongting Lake region of China. Furthermore, the intensity of agricultural or aquatic production and the percentage of people working in high risk occupations is positively associated with the degree of infection in a community. For example, the total area of rice paddy fields in farming villages of the Hubei Province of China was found to be heavily correlated with *S. japonicum* infection rates, measured over a 9 year period (Zheng *et al.*, 1996). Other researchers have found age-specific patterns to be more significantly associated with schistosomiasis prevalence, showing higher disease rates in school-aged children with greater exposure to infective water through recreational use.

A study from the Nile Delta found low numbers (not given) of infected snails and relatively high *S. mansoni* prevalence (10.7% and 30%) in two schistosomiasis endemic villages, Kom el Akhdar and Roda, respectively (Watts, S and Katsha, SE, 1997). The irrigation canals in both villages are part of a greater network of canals and the authors speculate that cercaria and miracidia may originate far from local aquatic sites. The authors attribute the higher prevalence of *S. mansoni* in Roda to a lower frequency of canal drying compared to Kom el Akhdar, resulting in higher probability of cercaria and miracidia survival upon entrance into Roda's canal system. The study, however, only

includes two villages, an insufficient sample size to draw any inference about the relationship between the percentage of infective snails and the prevalence of *S. mansoni* in humans. Furthermore, no data were collected on human fecal or urinary contamination in either village, limiting conclusions about local vs. regional contamination. This study indicates the need for a better understanding of the connection between risk of schistosomiasis at one site and the extent of contamination in the greater hydrological network.

Scale

A major limitation to studies linking behavioral, social, economic and environmental factors to disease transmission in a population is the scale upon which researchers observe and measure these factors. For example, risk of exposure to infective water may be higher for fishermen or agricultural workers within one village, but when assessing exposure of villages on a regional level, environmental variables such as climate, hydrology, and the distribution of water bodies may better predict population disease outcome. Smaller scale studies are able to contextualize nuanced differences in schistosomiasis risk within local economic, social, and behavioral frameworks, an approach that can greatly improve the efficacy of local public health interventions. On the other hand, small scale studies are unable to detect macro-scale determinants of disease outcomes, which effective environmental manipulation may be able to prevent. Furthermore, both macro- and micro-scale environmental and bio-social studies of schistosomiasis have failed to discuss how disease in one village contributes to disease in

another. The IPC model, for example, highlights the importance of understanding how one individual's health influences the environmental risk of disease for an entire community, and should move beyond the individual level to examine this relationship on a village or regional scale.

Research objectives

The primary goal of this thesis is to map infection estimators in snails, rats, and humans by catchment. This thesis explores the potential strengths and weaknesses of defining the catchment as the primary unit of analysis in exploring the spatial relationship between environmental risk of *S. japonicum* and mammalian disease outcomes. A better understanding of how spatial patterns explain the distribution of schistosomiasis at the catchment level may help public health interventions target high transmission areas within the hydrologic network in order to relieve the severity of disease burden already in the population, prevent the emergence of disease in non endemic areas, and reduce the potential for further transmission in highly endemic areas.

Past studies exploring the relationship between snail infection and human disease outcomes have generally used political boundaries or loosely defined ecological regions as units of environmental risk analysis for the waterborne parasitic helminth *Schistosoma japonicum*. Previous studies by McGarvey et al. (2006) and Tarafder et al. (2006) measured *S. japonicum* in the mammalian host population using village boundaries as the geographic unit of analysis. In a study from the Philippines by Pesigan et al. (1958), researchers measured human and animal infection within such political boundaries as barrios (neighborhoods), regions, and provinces. Hairston and Santos (1961) measured

snail infection in different zones defined by surrounding surface waters and the ecology of the immediate area.

Additionally, some researchers have found little correlation between locally infected snail counts and local disease outcomes (Watts and Katsha, 1997). Other field studies have found no definite pattern in the distribution of snails along rivers and streams (Aligui thesis, 1997). Measuring geographic variation in transmission based on disease metrics and environmental variables at the village or household level fails to capture the increased local risk of transmission from allocthonous parasite loading. These studies reveal the limitations of measuring disease and environmental variables with politically defined regions, and highlight the need to develop ecologically and hydrologically sound methods that can more accurately capture the geographic extent of *S. japonicum* transmission.

No studies are currently known that measure infection risk and mammalian host disease outcomes at the catchment level, an area of land topographically defined as draining water to a unique segment of a stream. The failure of previous studies to find a strong correlation between local snail populations and local disease outcomes makes this study an important starting point in developing spatial units of disease analysis that more accurately approximate village level transmission risk. Methods for creating geographic risk boundaries for this study were based on evidence that local risk of transmission results from a combination of both locally produced cercaria and cercaria originating in hydrologically connected areas beyond the village boundary.

METHODS AND MATERIALS

Study area

The island of Samar is located in the Eastern Visayas region of the Philippines and is characterized by a wet climate with rainfall more or less evenly distributed throughout the year. The high annual precipitation supports the ubiquitous and dense year-round distribution of the intermediate snail vector *O. h. quadasi*. Schistosomiasis in Samar occurs in coastal lowlands where the topographic gradient remains constant over wide areas. Schistosomiasis is not present in the mountainous part of central Samar, or in coastal areas where hills of over 200 m hug the shore (Hinz, 1984). According to the National schistosomiasis Control Program *S. japonicum* is estimated to be endemic in 133 villages, known locally as *Barangays*, in 13 municipalities (McGarvey, et al., 2006). Of the 133 endemic villages, 50 villages in Western Samar were selected for the study. Inaccessible villages and villages with less than fifty households were excluded from the selection. All villages chosen had a preponderance of adults working on rice farms. By design one-half of the study villages were selected based on being classified as primarily rain fed rice farms, and the other half were selected due to presence of mostly irrigated rice farms. These two groups of 25 villages each were selected because the original study design was based on detecting a putative effect of rice farming irrigation on schistosomiasis transmission. The rationale, design and village selection is described in more detail elsewhere (McGarvey et al 2006, Tarafder et al 2006).

After village selection and baseline data were collected, a macro-level inspection of the physical geography of the study area led to classification into three regions that were geographically separate from one another (Figure A). The topography, stream

course pattern, and spatial distribution of villages differ across the three regions. Villages in Region A are scattered along narrow river valleys, and are located near streams. Villages in region B are distributed across open foothills along a meandering river network. Villages in region C are concentrated on a flat coastal plain without a major river system. Roads generally follow the stream network in regions A and B and houses within each village are dispersed along roads. The geographic separation of the three regions and their unique topographic and hydrological characteristics allow valuable comparison of *S. japonicum* infection distribution across three distinct environmental settings.

GIS data

Spatial data files representing the physical attributes of fifty villages and surrounding environmental features were imported onto a digital elevation model of Western Samar Province, the Philippines using ArcView version 9.1 (Environmental Systems Research Institute, Redlands, CA, 2006). Vector data include: point files of houses, landmarks, and local water bodies; polyline features of roads and stream networks; polygon features of village and rice field boundaries; and a grid feature of snail survey sites. All raster and vector data were geo-referenced to the Universal Transverse Mercator (UTM) coordinate system Zone 51N with World Geodetic System (WGS) 1984 datum.

Snail sampling

Snail survey data were collected between September 2003 and September 2004. Survey sites for snail counts were selected based on results of preliminary snail surveys of Madsen et al. (2007) and Pesigan et al. (1958), both of which specify the types of

aquatic environments most likely to support *O. quadrasi* snails. Well-shaded areas along streams, creeks, springs, and irrigation and drainage canals were selected as well as swampy areas or grass land and uncultivated rice fields. The margins of streams wider than 1-2 meters were also selected for the snail survey. Streams wider than 1-2 meters with steep banks and rice fields were excluded from site selection as these environments are unlikely habitats for *O. quadrasi*. Sites along all mapped major water bodies falling into the aforementioned habitat criteria were inspected for snail positive sites, and quantitative snail surveys were conducted in these areas.

Thirty 13.5 cm rings were placed at each snail survey site, spaced according to the habitat being surveyed. For streams, creeks, canals, and other surface water features, three ring samples, spaced one meter apart were taken every 10 m along a 100 m transect of the water course. All snails found with each ring were counted and sent to a laboratory for identification and infection analysis. Only quantitative snail counts from each catchment were used in the estimation of catchment level snail infection.

Infection estimators

Human and animal *S. japonicum* infection were estimated on both the village and catchment level using two disease metrics: The index of potential contamination (IPC) and the corrected for error prevalence of infection. The IPC is a metric that combines both infection prevalence and mean infection intensity of those infected. The unit of measurement for the IPC is the mean number of eggs per gram stool (EPG) per 100 individuals. The prevalence of infection, corrected for error in diagnosis, is calculated as the sum of both the prevalence of light infection intensity (1-100 eggs per gram stool) and prevalence of moderate or heavy infection intensity (>100 eggs per gram stool). Rat

infection was measured using the IPC. Snail infection was estimated by summing all infected snails found in each catchment and dividing the total by each catchment's stream link length. The IPC is calculated for each village based on village level prevalence and mean intensity of infection (eggs per gram stool), unadjusted for error in diagnosis. Unadjusted prevalence is estimated by the proportion of egg positive individuals in each village.

Catchment delineation

The ArcHydro9 tool within ArcMap 9.1 was used to delineate the boundaries of watersheds and catchments based on a digital elevation model (DEM) of the Island of Samar. For a full reference to the procedure refer to the web link:

<http://www.crwr.utexas.edu/gis/gishydro05/Introduction/Exercises/Ex3.htm>. ArcHydro9

delineates catchment areas using water accumulation and flow direction models. Each catchment contains within its boundary a unique segment of the stream network. This segment is an un-branching section of a stream network, referred to as a stream link, that begins where two or more streams converge and ends at a drainage point marking the confluence with another stream. Catchments are defined as the total land area draining water to the catchment's unique drainage point. Aggregated upstream catchments comprise a watershed, which is the total land area collecting and draining water to a defined stream network.

Assigning villages to catchments

Disease estimators for humans, animals, and the intermediate snail vector were analyzed at the catchment level. Each village, along with its unique disease metric, was identified by the catchment in which the village was located. If a village or its rice fields

did not geographically fall into a defined catchment, it was left out of the analysis. Two methods were used to designate the catchment in which a village was located. The first method assigned a village to the catchment which contained the geometric center of the houses in a village, referred to as the village centroid. The second method assigned each village to the catchment that contained the village's rice fields. Those villages without identified rice fields, as well as those that did not have a majority of their rice fields falling within one catchment were excluded from the spatial analysis. Only those catchments that completely contained at least one village centroid or group of rice fields were included in the analysis. Of the catchments selected using method one and two, only those catchments that contained at least one quantitative snail survey site were included in the final analysis. Twenty catchments were identified using the village centroid method and thirteen catchments were identified using the village rice field method. I discuss the advantages and limitations of both selection criteria in the discussion section.

Catchment level infection estimators

All selected catchments for final spatial analysis were assigned disease statistics for snail, animal, and human infection. The snail infection statistic for each catchment was estimated as the number of infected snails found within the catchment boundary per kilometer stream link. All snail sites intersecting more than one catchment were excluded from the final calculation of catchment level snail infection to increase the certainty that a catchment's infection risk results from cercaria produced within the catchment's boundary. Village level disease estimators of humans and animals in all villages designated to a particular catchment were averaged to produce a catchment level

human and animal disease estimator. Catchments with only one village were assigned the disease estimator value of the sole village. Catchment level disease estimators for snails, animals, and humans were classified into five categories using natural breaks and mapped using graded colors to visually show the spatial distribution of each disease estimator across catchments.

The relationships between catchment level snail infection and catchment level human and animal disease estimators were analyzed using simple linear regression. The village centroid data set was used to analyze the spatial distribution of rat infection and both the centroid and rice field delineation data sets were used to analyze the spatial distribution of human disease metrics.

Study Area

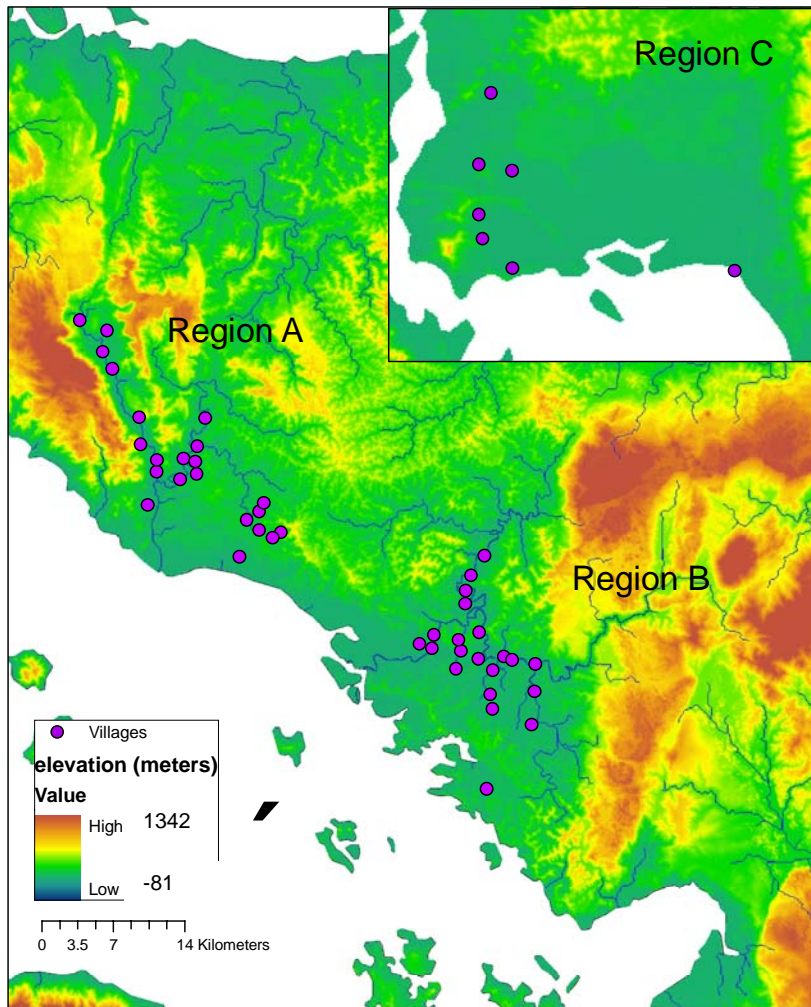


Figure A: Digital elevation map showing distribution of fifty villages across the regions.

RESULTS

Catchment results

Figure B displays the areas of six watersheds, and their catchments, as well as stream links and drainage points within each catchment. Table 1 presents a list of barangays assigned to each catchment, as well as the attributes of each catchment, including catchment area, and stream link length. Based on the Village centroid method of designating catchments to villages, all villages, except one, (N=49) were located within the boundaries of twenty defined catchments. According to rice field designation, twenty-six villages had rice fields within the boundaries of thirteen catchments (Table 2). Rice field polygons were missing from many of the villages, resulting in the exclusion of those villages from the rice field delineated data set. Some villages were found to have their centroids and rice fields located in different catchments, and thus were assigned different catchments according to the two methods of catchment designation. Catchment areas in the study ranged from 114 to 5,848 hectares and catchment stream links ranged from one to fourteen kilometers. Catchment area was generally found to be proportional to the length of the catchment stream links (Figure C).

Regional watersheds, catchments, drainage networks, and drainage points

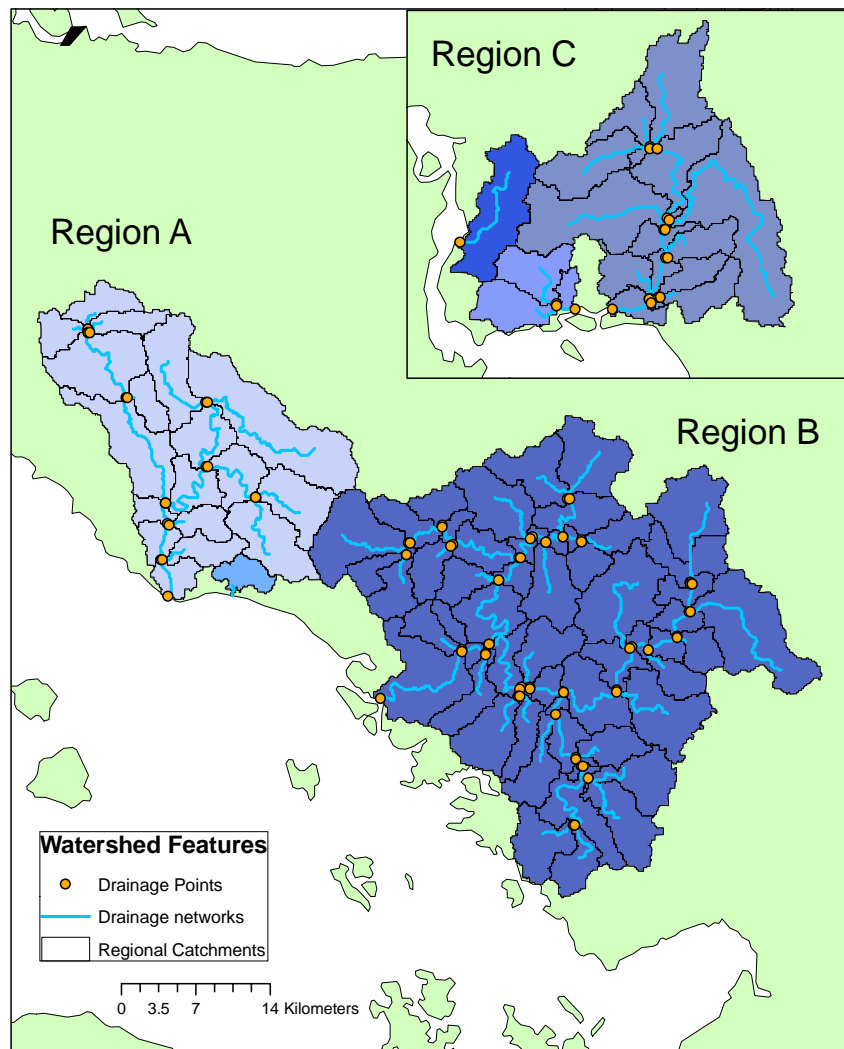


Figure B: Hydrologic map showing boundaries of catchments within watersheds, as well as catchment streams and drainage points

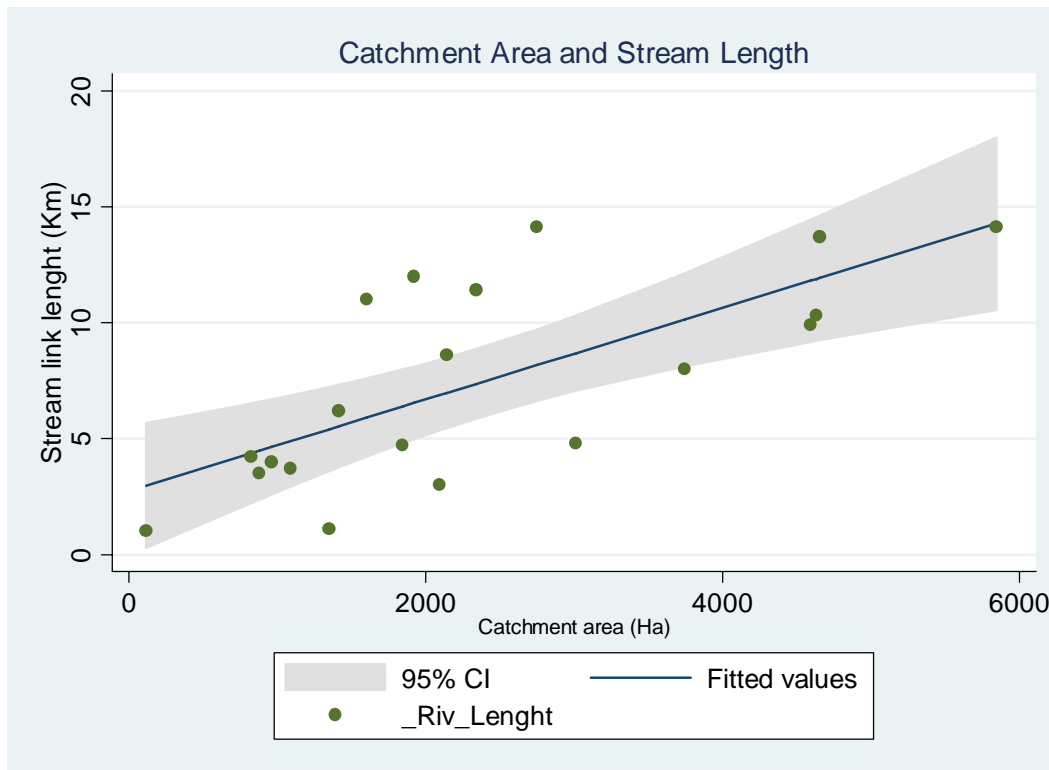


Figure C: Scatterplot with trendline displaying relationship between catchment area and catchment stream link length.

Catchment	Region	BARANGAY (rice field delineated)	BARANGAY (Village centroid delineated)	Catchment Area (Ha)	Catchment Link Length (km)
0000	A	Pilar Bayo Cag-anibong Roxas II	Pilar Bayo Cag-anibong Roxas II	4597	10
1111	A	Cagbilwang	Cabugawan Mawacat Cabatuan Cagbilwang	4656	14
2	A	Cagbayang	Cagbayang	2339	11
3333	A	Nabang Sinidman Oriental Baja	Nabang Sinidman Oriental Baja Mag-ubay	1923	12
4	A		Cabacungan	2142	9
666666	A	Cagboborac Victory Tabawan	Cagboborac Guinbaoyan Norte Guinbaoyan Sur Victory Geragaan Tabawan	3746	8

7	A		Dinagan	1089	4
8	B		Pinaplata	824	4
9 9 9	B	Natimonan Sto. Nino Pizarro/Hiparayan	Natimonan Sto. Nino Pizarro/Hiparayan	2751	14
10	A	Rizal I	Rizal I	1348	1
11 11 11	B	San Pelayo Nacube	Casab-ahan San Pelayo Nacube	5848	14
13 13 13 13	B	San Agustin Hinugacan	San Agustin Diaz Hinugacan	1847	5
14 14 14	B	San Miguel	San Miguel Erenas/San Juan	1605	11
15	B		La Paz	114	1
17 17 17 17	B	Bulao/Guindapunan	Buenavista I & II Bulao/Guindapunan	879	3
19 19 19	B		Mabuhay Rosalim Anquiana/ Sapinit	3013	5
21 21	B		Cantaguic Ranera	1416	6
23 23 23	C		Caticugan Pagsolhugon Dolongan	4633	10
27 27	C	San Fernando	San Fernando	961	4
28 28 28	C	May-it Tingib Can-abay	May-it Tingib Can-abay	2096	3

Table 1: Barangay (village) assignment to catchments by both rice field and village centroid methods, as well as catchment attributes.

	Catchments	Regions	Area (Ha)	Barangay Count	River Link (km)
Totals (Rice field designated)	13	3	35,687	26	114
Totals (village Centroid designated)	20	3	47,829	49	149

Table 2: Village and catchment Summary

Snail site results

Figure D displays the spatial distribution of catchment level snail infection across the three regions. Table 3 summarizes catchment level snail survey data. A total of 282 snail survey sites were identified within 26 catchments containing at least one snail survey site. Of the 282 sites identified, 254 were located within catchments containing at least one village. Infected snails were found in 22 of the 26 catchments where quantitative snail surveys were conducted. A total of 145 infected snails were found in catchments containing at least one village centroid or one designated rice field across all regions. The total number of infected snails found in each catchment ranged from 0 to 32 snails. The number of infected snails per km stream link in each catchment ranged from 0 to 3.2. The number of snail survey sites conducted was inconsistent across catchments (Figure E): some catchments contained only one survey site while others had over twenty. There is a positive relationship between the number of snail surveys conducted in each catchments and the number of infected snails found (Figure F). No statistically significant difference in average number of infected snail sites was present across the three regions (Table 5).

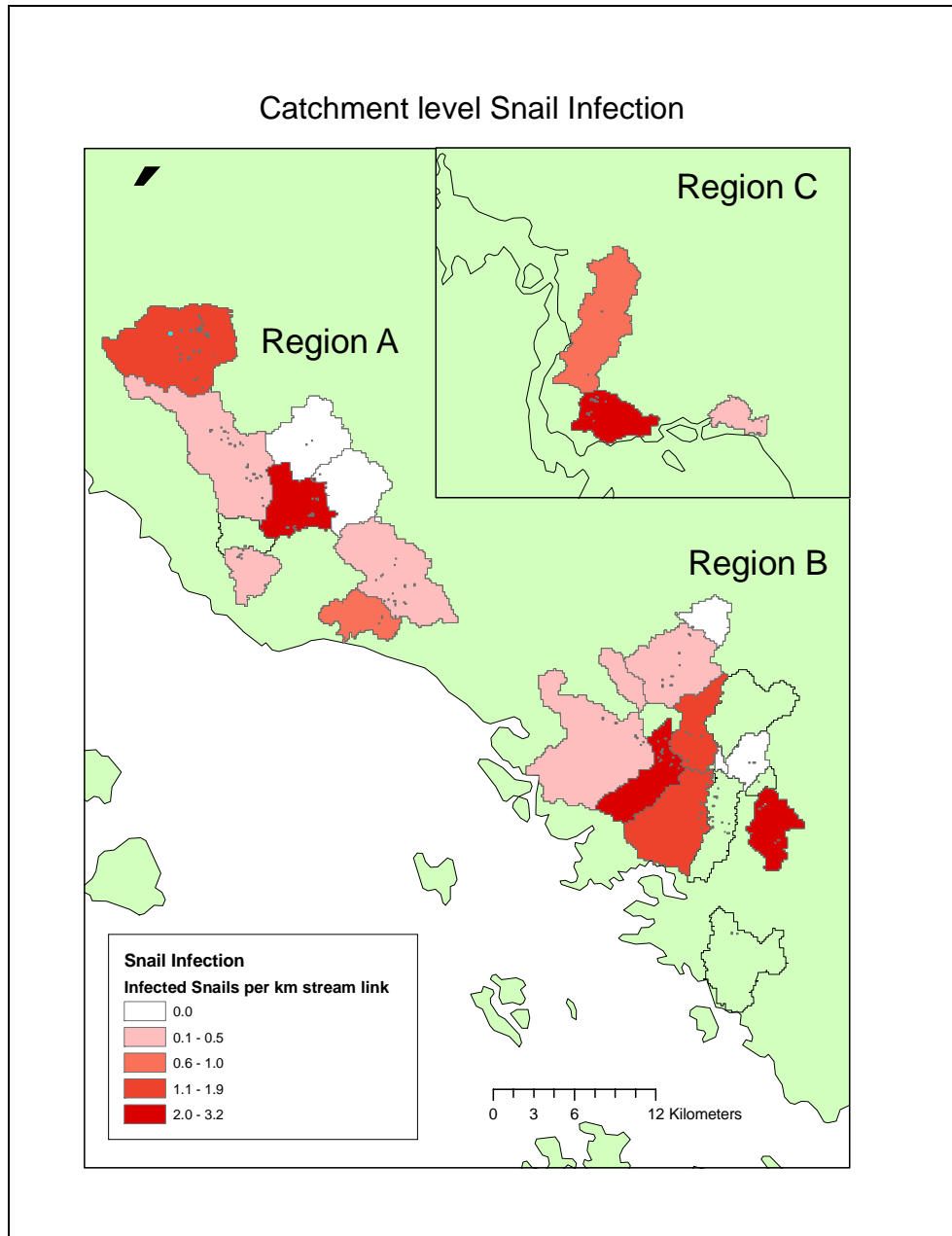
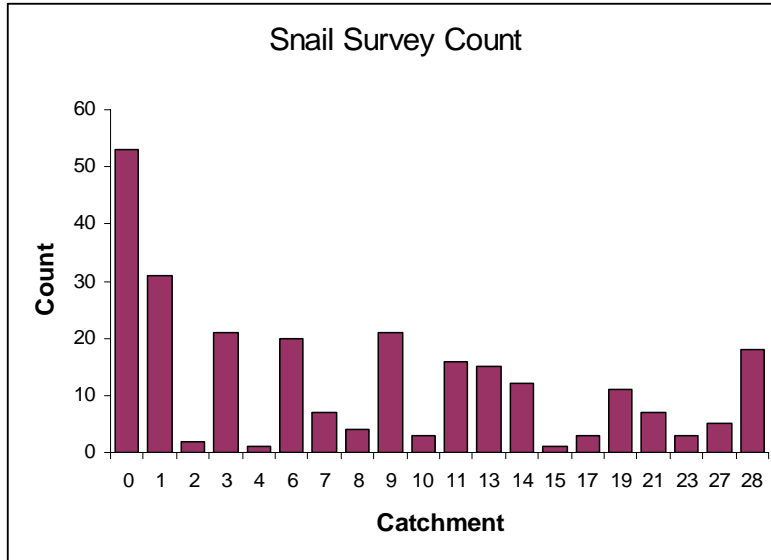


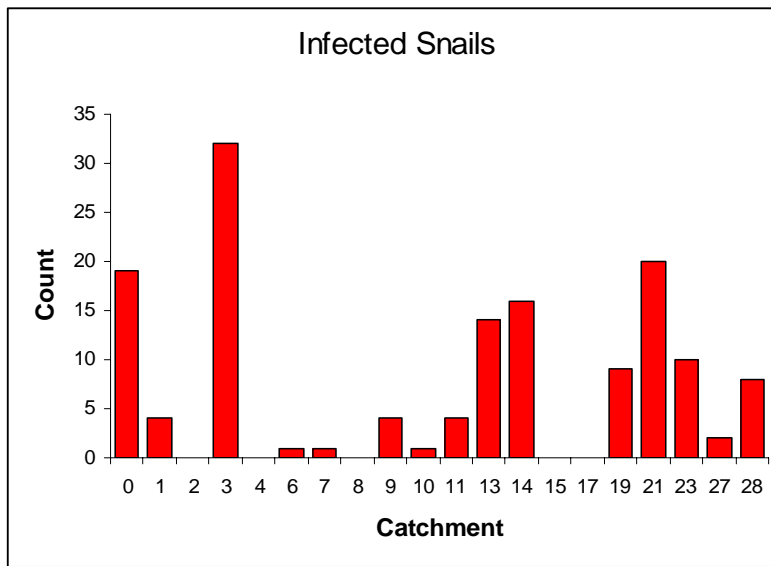
Figure D: Map showing distribution of Snail infection by catchment across three regions with snail survey sites overlaid.

Region	Catchment Number	Snail surveys conducted	O. quadrasi Count	Infected O. quadrasi Count	Infected Snails per Km river	
A	0	53	1361	19	1.9	
	1	31	1206	4	0.3	
	2	2	95	0	0.0	
	3	21	1071	32	2.7	
	4	1	0	0	0.0	
	6	20	666	1	0.1	
	7	7	528	1	0.3	
	10	3	397	1	0.9	
	B	8	4	520	0	0.0
		9	21	2034	4	0.3
11		16	397	4	0.3	
13		15	1354	14	3.0	
14		12	1186	16	1.5	
15		1	718	0	0.0	
17		3	18	0	0.0	
19		11	334	9	1.9	
21		7	1635	20	3.2	
C		23	3	770	10	1.0
	27	5	108	2	0.5	
	28	18	109	8	2.7	
Totals	20	254	14,566	145	20.5	

Table 3: Snail survey attributes by catchment.



(a)



(b)

Figure E: (a) Histogram of snail surveys conducted within each catchment and (b) Histogram of infected snails found at survey sites within each catchment.

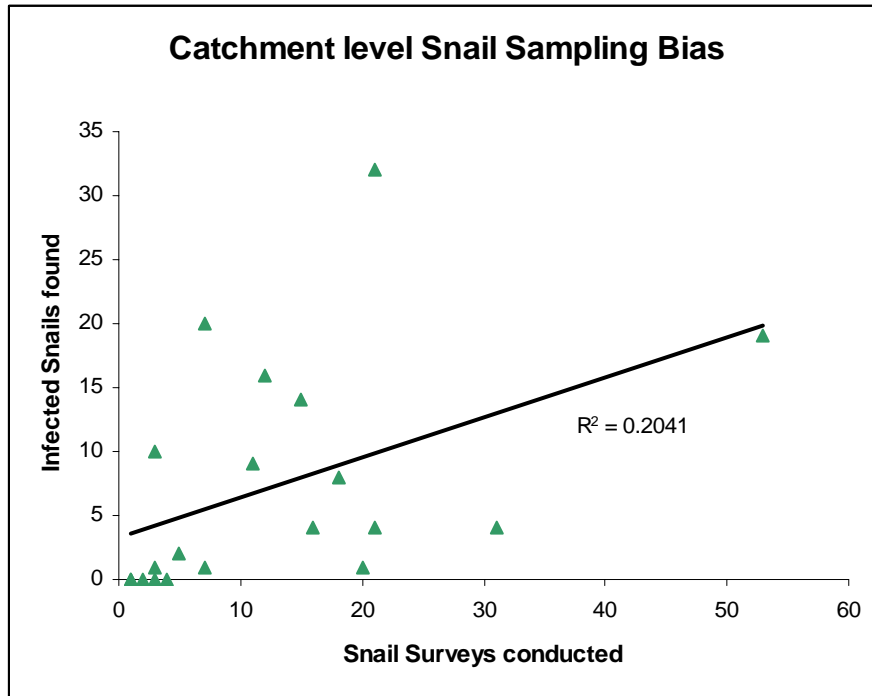


Figure F: Scatterplot with trendline displaying relationship between number of snail surveys conducted and number of infected snails found by catchment.

Rats

Catchment level rat infection showed very high spatial variability across the three regions in the study area. No infected rats were found in five of the catchments in the study area, while five other catchments contained rats passing thousands of eggs per gram stool (EPG) per 100 rats (Table 4). Infected rats were found in all catchments in region B, whereas no rats were found in three of eight catchments in region A and two of three catchments in region C (Figure G). Village level rat IPC reached over 70,000 EPG per 100 rats in one catchment. High variance of catchment level rat infection was present in all regions and precluded conducting a meaningful comparison of average regional rat IPC. No clear relationship exists between catchment level rat infection and catchment level snail infection (Figure H).

Catchment Number	Village Rat Surveys (Count)	Maximum IPC (EPG per 100 rats)	Average IPC (EPG per 100 rats)
6	5	0	0
7	1	0	0
10	1	0	0
23	3	0	0
27	1	0	0
2	1	2	2
15	1	15	15
11	3	23	8
21	2	69	35
28	3	140	52
4	1	172	172
17	2	405	233
8	1	436	436
1	4	1050	416
14	2	1283	642
13	3	1733	1245
19	3	7222	3863
3	4	14691	3879
0	4	30791	8400
9	3	72617	25621

Table 4: Rat survey and infection estimators by catchment.

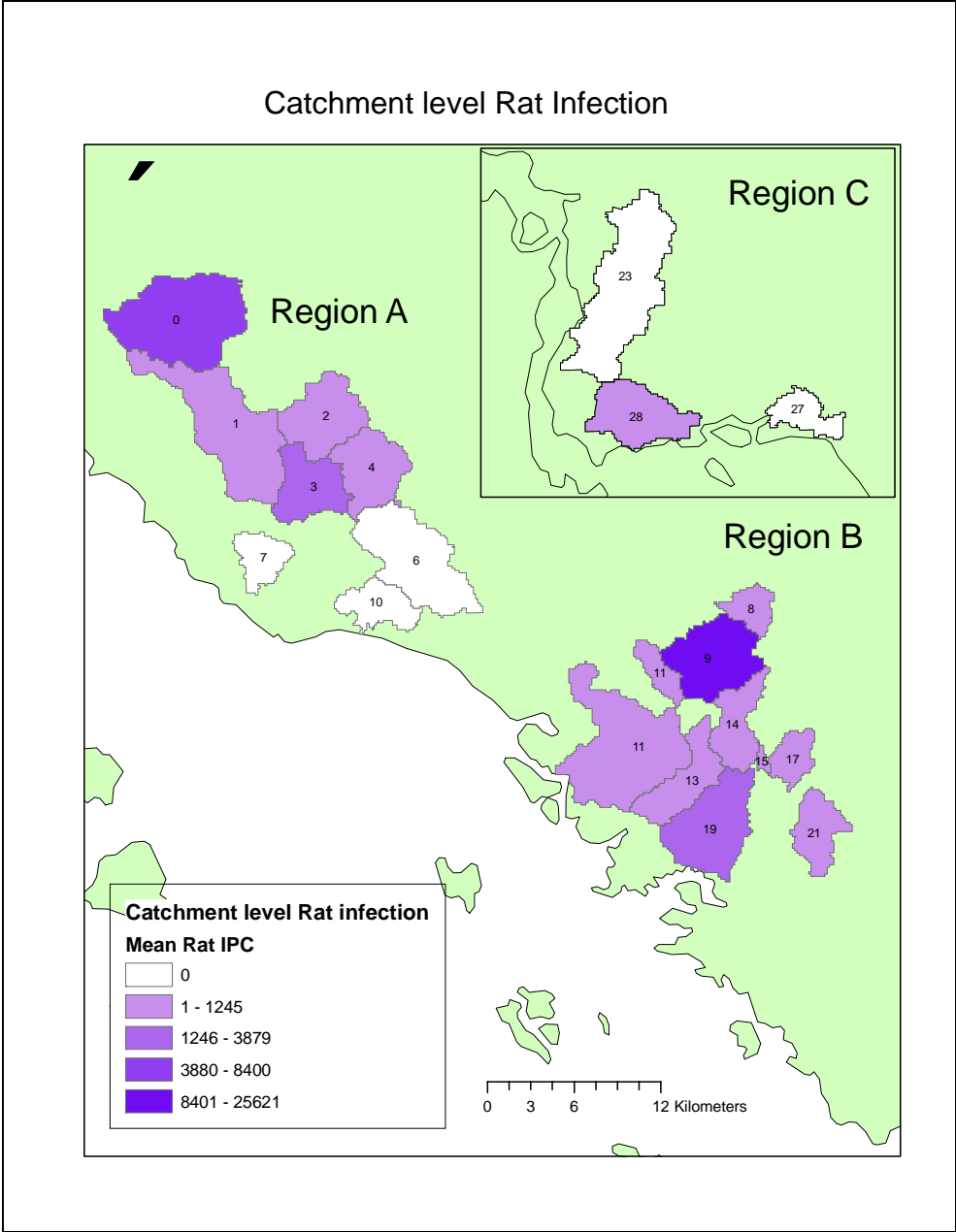


Figure G: Spatial distribution of village centroid delineated catchment level rat IPC across regions A, B, and C.

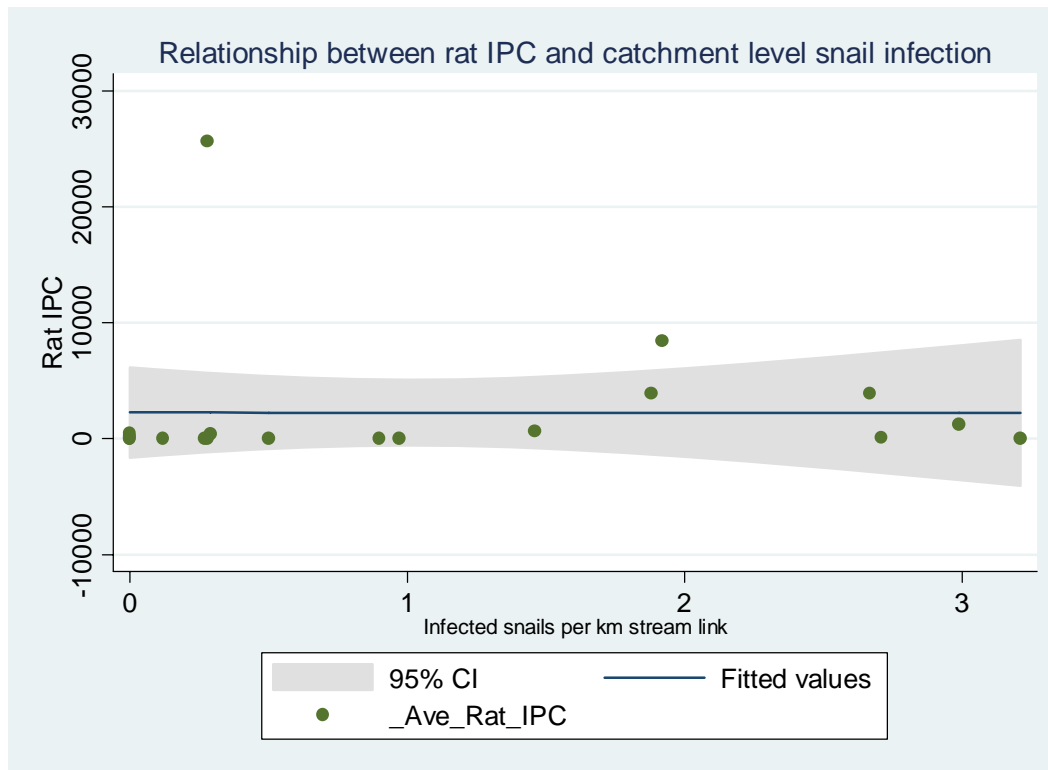


Figure H: Scatterplot with trendline displaying relationship between catchment level snail infection and rat IPC.

Human infection

Figures I, J, K, and L show the high spatial variance in catchment level human disease estimators across the three regions in the study area. The spatial relationship between IPC and corrected prevalence was inconsistent across catchment delineation methods. A positive relationship exists between IPC and corrected prevalence ($R^2 = 0.2499$) using the rice field data set, yet using the village centroid data set, no relationship exists ($R^2 = 0.0090$) (Figure M).

Based on the village centroid delineated catchment dataset, no significant difference in average catchment level infection was present across the three regions in the study area (See summary table 5). The relationship between catchment level snail infection and catchment level human disease outcomes was not consistent across human

disease estimators. This relationship was positive when estimating human disease with IPC (Figure N) and unclear when estimating with corrected prevalence (Figure O).

Relationships between snail infection and human infection were consistent between rice field and village centroid delineated data.

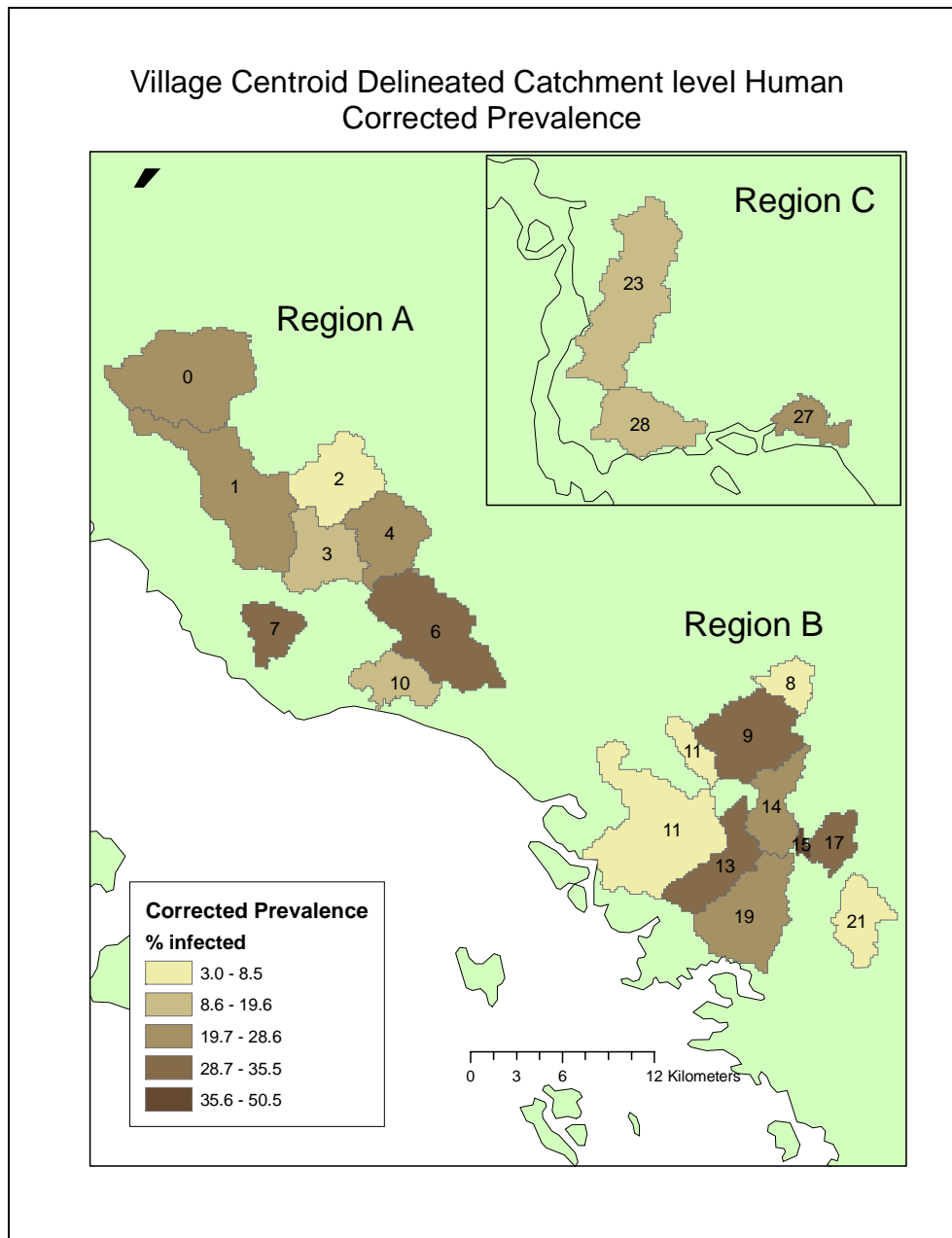


Figure I: Map of spatial distribution of village centroid delineated catchment level human corrected prevalence across three regions.

Rice Field Delineated Catchment level Corrected Prevalence

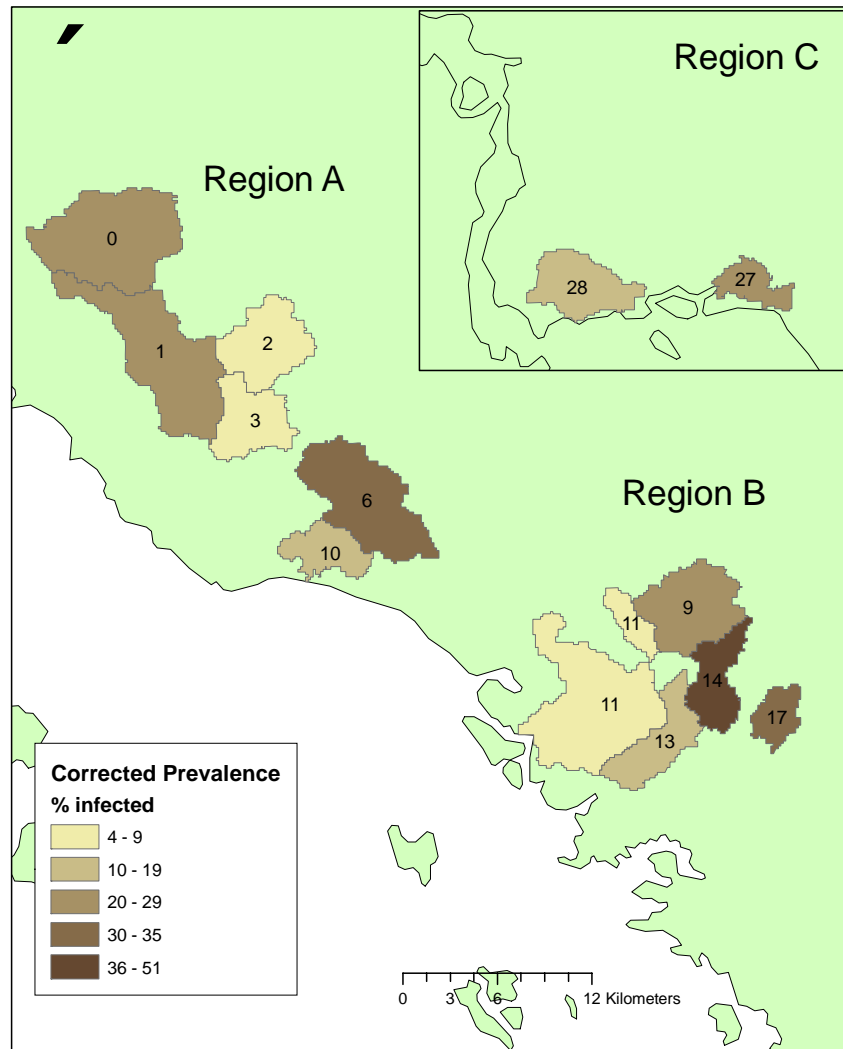


Figure J: Map of spatial distribution of village rice field delineated catchment level human corrected prevalence across three regions.

Village Centroid Delineated Catchment level Human IPC

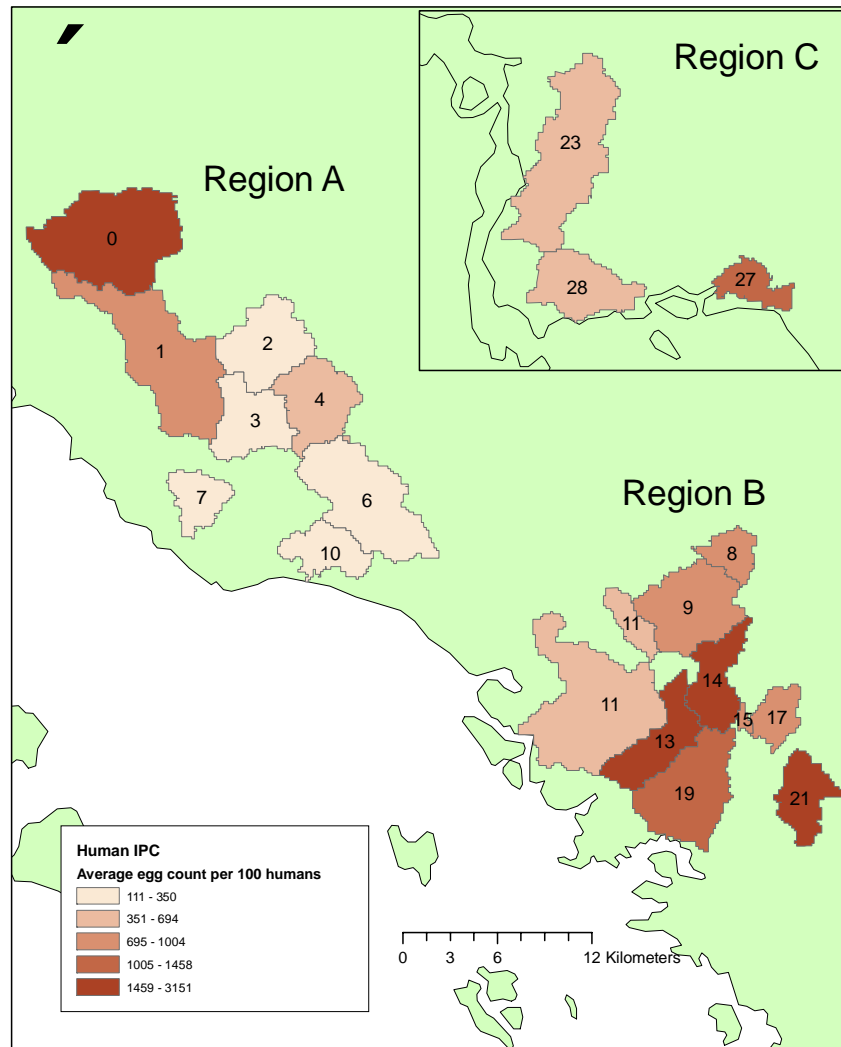


Figure K: Map of village centroid delineated catchment level human IPC across three regions.

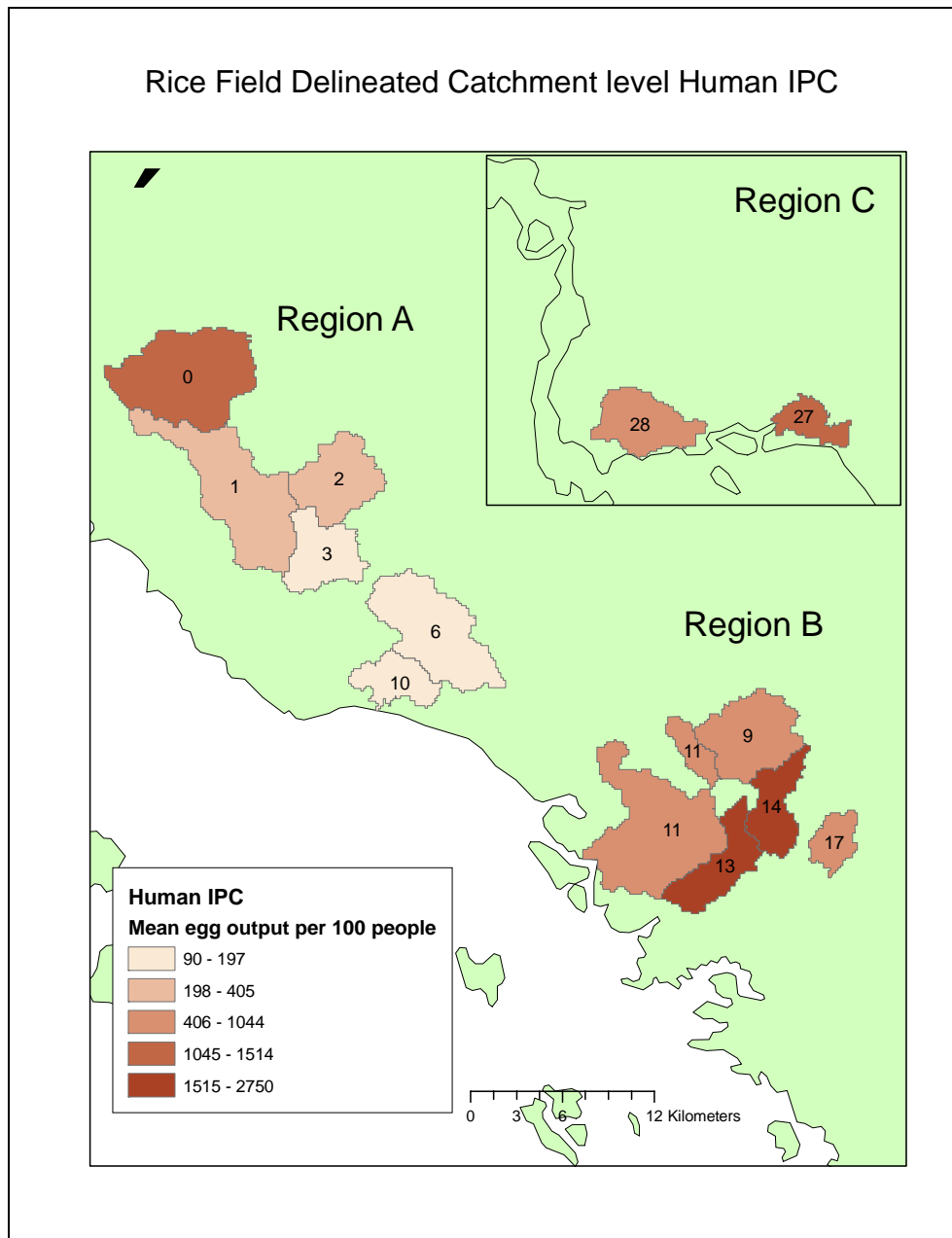
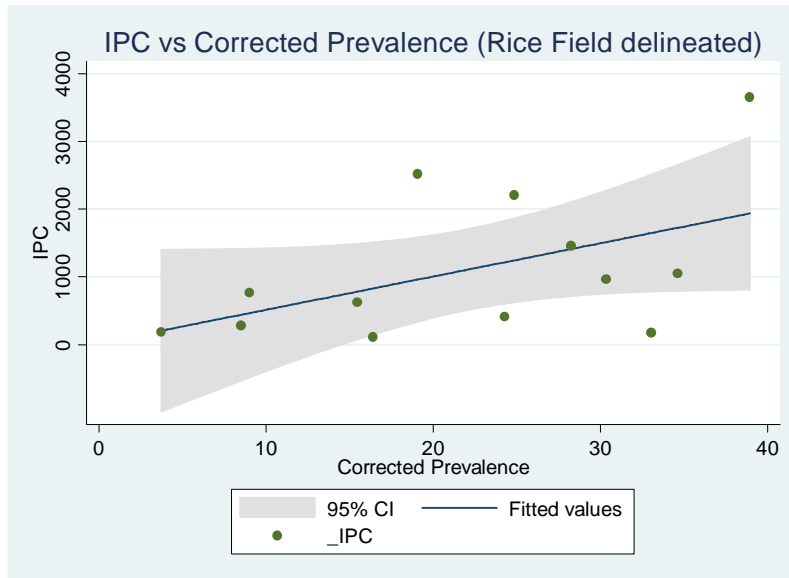


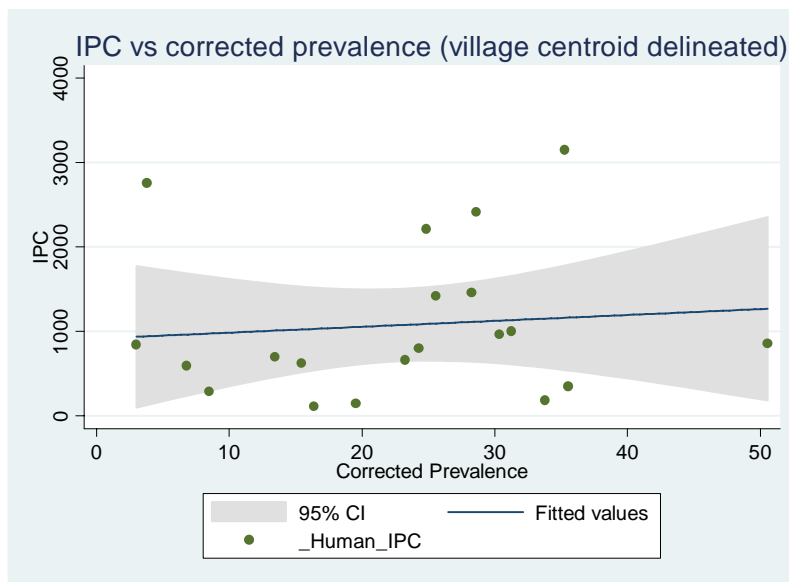
Figure L: Map of village rice field delineated catchment level human IPC across three regions.

Region	Snail Infection	Corrected Human Prevalence
A	0.77 (-0.1 – 1.6)	23.3 (15.9 - 30.6)
B	1.12 (0.12 - 2.1)	23.9 (11.5 - 36.4)
C	1.39 (-1.5 - 4.3)	19.1 (-0.9 - 39.0)

Table 5: Summary of mean catchment level disease estimators by region with 95% CI in bold.

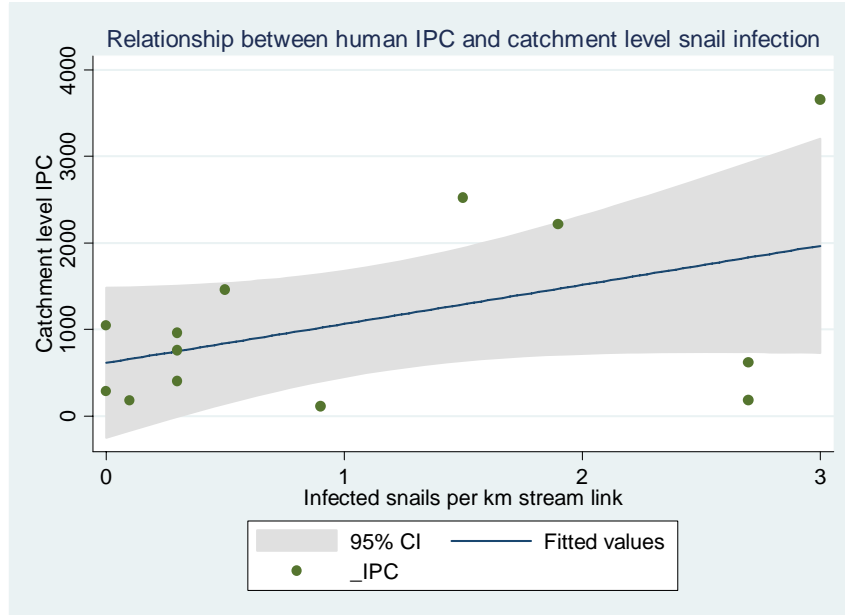


(a)

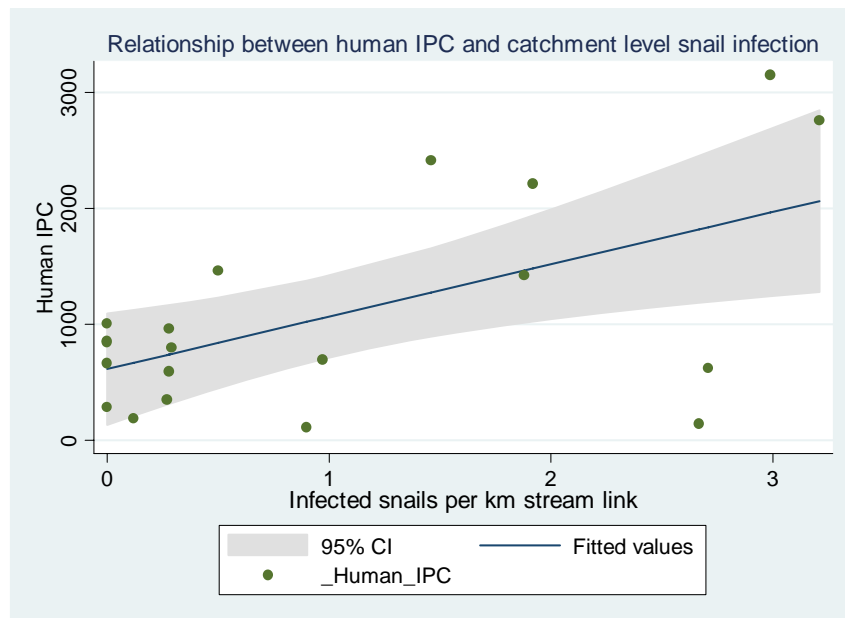


(b)

Figure M: Relationship between catchment level IPC and Corrected Prevalence using (a) rice field data set and (b) village centroid data set

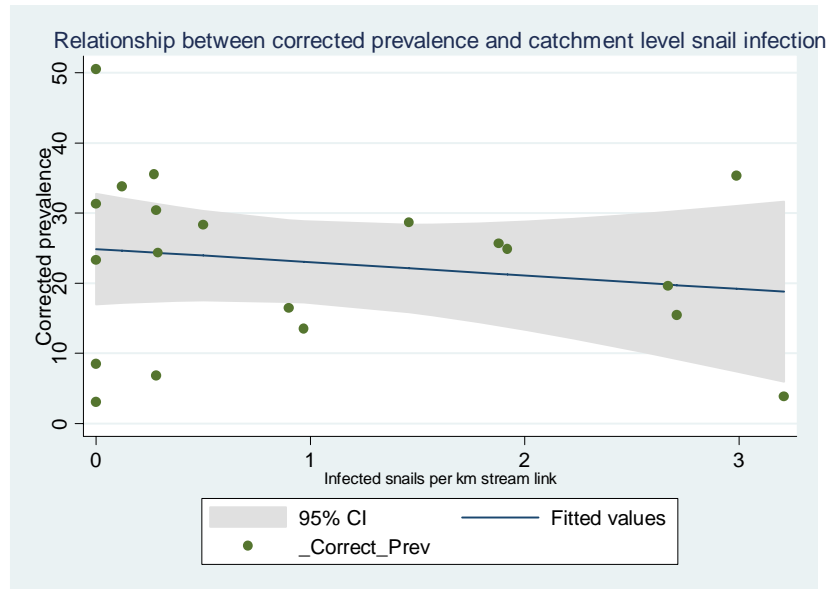


(a)

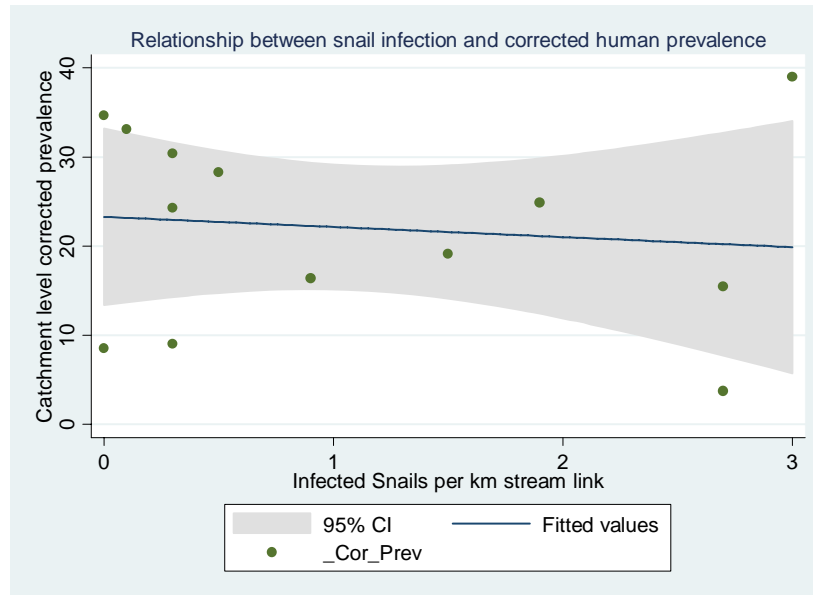


(b)

Figure N: Scatter plots with trend lines displaying relationship between human IPC and snail infection by catchment using both (a) rice field and (b) village centroid data sets



(a)



(b)

Figure O: Scatter plots with trend lines displaying relationship between human corrected for prevalence and snail infection by catchment using both (a) rice field and (b) village centroid data sets.

DISCUSSION

Previous ecological studies from the Philippines have primarily examined relationships between schistosomiasis disease estimators and environmental variables, including the presence of infected snails, at the household and village level. The goal of this study was to capture catchment to catchment variations in *S. japonicum* snail infection and *S. japonicum* human and animal disease across the three regions in the study area in order to understand how human and animal disease indicators vary spatially with snail infection estimates. This study intends to inform ways in which environmental control strategies could most effectively and efficiently reduce transmission of schistosomiasis by identifying high risk areas in the hydrological network where the potential for transmission is high. Spatial analyses of *S. japonicum* infection in snails, rats, and humans were conducted at the catchment level, a geographic unit equal to the total area of land draining water to one point at the confluence of two streams.

A major strength of assessing disease transmission at the catchment level is its ability to capture water contamination and exposure to contaminated water within a hydrologically defined area. Villages in the study area are connected through a vast network of streams and irrigation canals. The perennially wet climate in the study area further justifies defining the transmission area using a hydrological unit of analysis, as heavy year round rains maintain flowing streams, which facilitate the transport of upstream parasites to downstream locations. This study aggregates the total number of infected snails found within the catchment to create one infection estimator as opposed to the more difficult task of capturing small scale heterogeneities in snail distribution through fine local resolution. A major limitation to defining the catchment as the spatial

unit of analysis, however, is that catchments, like villages, are not geographically or hydrologically isolated from one another, and cercaria can potentially travel from one catchment to another via entering streams.

Another limitation to the catchment method is that environmental risk is not homogeneously distributed throughout the catchment's surface waters. Infected snails, and the cercaria they shed, are distributed unevenly along water ways. A disadvantage of scaling beyond the local level is the loss of small scale variations in both disease outcomes and environmental heterogeneities, both of which can inform where to target environmental control at the local level. However, the spatial distribution of village level disease estimators, usually represented geographically by a village's most central point, does not accurately approximate the spatial extent of human and animal exposure to infective water. Most villages in the study are not geographically isolated from one another. Village level environmental features, including rice fields, irrigation canals, and local water bodies, are interspersed among those of other villages. As a result, sites of *S. japonicum* transmission may overlap considerably from one village to another. Until more is known about the spatial and temporal patterns of water contact, we cannot assume that sites of transmission are geographically confined to those surface water features that surround, or pertain to specific villages. Village level water contact patterns in Western Samar Province are currently unknown. Thus, a greater understanding of water contact hotspots needs to be achieved before local environmental control measures can be carried out.

Snails

The distribution of schistosomiasis infection in the aquatic environment is highly focal as a result of its geographic dependence on snail habitats. In this study, the aggregate number of infected snails was used to approximate the relative number of cercaria distributed in the waterways of each catchment, and the resulting transmission risk for mammals exposed to the catchments' waters. An advantage of defining the catchment as the geographic area of transmission is that any cercaria produced within the catchment will be confined to the topographic boundaries of the catchment unless the cercaria reach the most downstream point of the catchment, where they can potentially enter a downstream catchment. A major limitation of using the catchment as the geographic unit of water infection analysis is thus the potential for a cercaria or miracidia produced in one catchment to infect a host in a downstream catchment.

While proximity to infected snails at the time of mammalian water contact increases the probability of cercarial transmission, the absence of infected snails does not preclude transmission. In this study, *S. japonicum* infection in humans was present in all catchments, even those without infected snails. These results support the conclusion that transmission can occur even without the known presence of infected snails. Sampling bias, however, may result in a significant underestimation of catchment level snail infection. The number of snail surveys conducted in each catchment, for example, was not consistent. Many of the catchments lacking infected snails also contained few snail survey sites. Thus, the presence of human and animal infection in catchments lacking infected snails could be also be explained by insufficient snail sampling within the catchment.

Varying spatial distributions of villages within their respective catchments may bias the overall relationship between catchment level snail infection and human disease outcomes. Because catchments are not hydrologically isolated geographic units, cercaria that travel long distances down stream may pose an increased risk to those communities located closer to the drainage point of the upstream catchment. These villages are likely to experience increased risk of cercarial contact from entering waters. Thus, allochthonous cercaria, originating in an upstream catchment and traveling to a downstream catchment, may explain some of the unexplained variance in catchment level disease metrics. Normalizing infected snail counts to the entire length of the stream link may also underestimate the risk of contact with cercaria if snail sites and villages are concentrated near the drainage point of a catchment. Conversely, catchment level snail infection risk will be greatly overestimated if infected snail sites are concentrated down stream from villages and their rice fields. Differences in slope and flow velocities between catchments could also account for high variance in snail counts as those aquatic environments with faster moving water are less likely to provide habitat for snails.

Rats

Infected rats were found in many catchments where no infected snails were found. These results are corroborated by a study by Pesigan et al., 1958, which found infected rats up to 1 km on either side of a river in a municipality without any infected snails. This study highlights rats' ability to forge rivers and travel large distances. Based on the inconclusive relationship observed between catchment level snail infection and rat IPC, and the known ubiquity of rats throughout the aquatic environment, we conclude that rat IPC is not an effective proxy for catchment level environmental risk. While their range

beyond the local level makes rats a desirable catchment level disease indicator, their ability to travel long distances, potentially between catchments, makes them unreliable indicators of catchment level risk.

Humans

Based on comparisons between rice field and village centroid catchment delineations, it is difficult to conclude whether one method more accurately reflects the geographic extent of human transmission. The consistent relationships between snail infection and human disease estimators across both methods suggest that there is no apparent difference in disease outcome between defining rice fields or the immediate vicinity around the village centroid as the primary site of transmission for those participating in the study.

The observed spatial distributions of catchment level disease estimators in the study area reflect the commonly observed spatial heterogeneity of schistosomiasis infection estimators across short geographic distances. As a result of the inconsistent outcomes in the relationships between both disease metrics and snail infection rank, we cannot not make any conclusions about the relationship between catchment level snail infection and human disease. While the observed positive relationship between snail infection and human IPC, on one hand, supports the hypothesis that catchment level snail infection and human disease are tightly coupled, results using corrected prevalence to estimate disease do not corroborate this expected relationship. Results from this study should be interpreted with caution, as the two disease metrics are considerably different from one another based on both the amount of error associated with them and the statistical methods used in their calculations.

Apart from statistical error, the human IPC disease metric has further limitations as a crude estimator of potential contamination of waterways with *S. japonicum* ovum. The mode of causation in the relationship between catchment level snail infection and human infection estimators is not unidirectional. The geographic distribution of infected snails in the aquatic environment is influenced by a number of anthropogenic factors, a major one being fecal contamination. Few data exist on how much contamination is needed, relative to the freshwater snail intermediate host population, to maintain high schistosomiasis transmission rates in a local population (Vercruysse, 2001). Local contamination, however, may not entirely explain the observed levels of local surface water cercarial concentration, as these water bodies may contain snails infected by a combination of both proximal and upstream water contamination (Watts and Katsha, 1997). The human IPC metric alone cannot measure how much local anthropogenic contamination contributes to the observed prevalence of infected snails. A better understanding of parasite diffusion between villages will improve the efficacy of the IPC as a measurement of local contamination. Further study on IPC should examine the spatial relationships between IPCs in hydrologically connected communities. In this respect, spatial proximity to high IPC communities may better explain high prevalence rates in a community with low IPC.

The literature suggests that a combination of environmental and anthropogenic parameters control the distribution of schistosomes within a surface water network (Jordan, 1994). Some studies suggest that the geographic distribution of schistosomes along water ways may have more to do with human behavior and the geographic extent of human travel than on environmental factors alone. Thus, where people live may have

a strong influence on where parasites are located within the surface water network. A study conducted by Raso *et al.*, (2005) in Cote d'Ivoire used demographic and environmental data to produce risk maps weighted by the relative contribution of multiple factors to the geographic distribution of schistosomiasis transmission risk. According to their model, age, sex, and socio-economic status were better predictors of prevalence than ecological and hydrological variables (Fernwick *et al.*, 2006).

Public health interventions

Many public health interventions, especially those before the wide use of effective chemotherapy, have focused on disrupting the environment suitable for the intermediate snail host's survival as a means of breaking disease transmission. Some snail control studies have found mollusciciding to be a highly effective disease control measure (Yi *et al.*, 2005; Wang, 1999). In order to permanently reduce the risk of schistosomiasis transmission, snail control must occur from the upper to the lower reaches of an endemic watershed (Yi *et al.*, 2005) because local snail control alone cannot prevent free swimming miracidia located in upstream parts of the watershed from infecting snails in a down stream location. Mollusciciding, however, is expensive and ecologically unsustainable because of the high risk of environmental externalities from chemical contamination (Thomas and Tait, 1984).

Other snail population control regimes have physically manipulated aquatic environments to reduce their suitability for snail habitat. An early study on the ecological control of the snail host of *S. japonicum* in a small village in Leyte Province, the Philippines, found that eradication of the snail population is possible where complete control and manipulation of aquatic environments can be achieved through activities such

as draining or filling snail habitats (Pesigan, 1958). Snail habitat reduction, however, has certain limitations as a disease control measure. Eradicating the entire population of snails would require highly disruptive environmental change on a large scale to be sustainable. Certain environmental engineering is also very expensive for resource poor areas where schistosomiasis is heavily endemic.

In order to reduce morbidity and mortality associated with schistosomiasis and reduce the risk of further transmission, public health interventions must first treat already infected individuals with chemotherapy to lessen the severity and duration of disease in the population and reduce the potential for further contamination. Secondly, primary interventions must identify geographic sites of high transmission as well as human and animal groups in a community that contribute the most to local contamination. To accomplish this, more sophisticated risk prediction models should incorporate local behavioral, occupational, and economic contexts that drive human exposure and continued water contamination. Finally, further research should focus not only on the cycle of disease transmission within one single community, but also on how that cycle contributes to the risk of transmission in another. In this way, public health interventions can identify and target autochthonous foci of disease that contribute to greater contamination to ensure that schistosomiasis does not continue to emerge in new geographic locations or intensify in already endemic ones.

Recommendations and further study

Can the catchment, as a geographic unit, accurately define the boundaries of *S. japonicum* environmental risk and the resulting human and animal infection?

Catchments are defined based on the location of predetermined drainage points, which,

for this study, were selected as the point where two unique streams converge or the point where a unique stream segment diverges. Other methods of selecting drainage points should also be considered when defining hydrologic regions of disease analysis. Further study could define catchments or drainage areas by the area of land draining to a location where humans and animals are exposed to potentially infective water, such as the area surrounding a village. In this way, the environmental risk posed to individuals at a particular point, like a population in a village, would be captured in the upstream region draining water to that defined point. This method would allow the comparison of environmental and hydrological features within upstream areas of different sites of exposure to assess how these features might contribute to the loading of parasites to a specific point.

Additionally, the catchment units used in this analysis may not be representative of the proper scale to capture environmental risk. Smaller catchments along waterways where snails are more likely to inhabit may capture more focal risk as opposed to large catchments with vast areas without any human, animal, snail, or parasite foci. For example, catchment 0 in the study area extends West to East, but the distribution of villages, rice fields, and snail sites fall along the Pilar river, which flows from North to South. The boundaries of this catchment thus extend beyond the probable sites of human and animal transmission and may misrepresent the actual environmental risk to humans that tend to be more focal in nature.

High uncertainty in the sampling methods and limitations to the disease estimators, especially IPC, prevent concluding whether the catchment more or less accurately captures the spatial distribution of environmental risk and human disease than

other methods of disease mapping. Inconsistent results from this study, however, do not suggest that the catchment method is an ineffective or inaccurate unit of disease analysis. What these results do suggest is that more consistent snail and cercarial sampling methods should be conducted, including water sampling, in order to better quantify smaller scale environmental risk within the catchment. Methods of measuring the relative infectiousness of water for *S. japonicum* have already been developed (Pesigan et al. 1958). Future studies should conduct cercaria sampling at different points along water courses within the catchment, as well as measure the transfer of cercaria from one catchment to another at the drainage points of each catchment.

Once catchment level environmental risk estimation is improved, research on the village level can more accurately describe how local environmental, behavioral, and economic forces help mediate or reduce transmission of *S. japonicum* to humans and animals. Until better methods are developed to explore the spatial relationship between *S. japonicum* distribution in the environment and human and animal disease outcomes, the catchment method should continue to be explored as a geographic boundary of environmental and population disease estimation. Further research on the spatial distribution of *S. japonicum* in the environmental and within the mammalian host should avoid assigning politically isolated boundaries or ecologically defined geographic areas as independent units of disease analysis. Given the complexity of the life cycle of schistosomiasis, the many possible definitive hosts, and the multiple forces shaping disease in human populations, public health interventions need to take an integrated approach to address the most important proximal pathways of exposure within hydrologically defined units.

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