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Risk factors for human helminthiases in rural Philippines

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SUMMARY

Background: A cross-sectional survey was performed in 2012 among 18 rural barangays in Northern Samar, the Philippines in order to determine the prevalence of single and multiple species helminth infections and the underlying risk factors of acquiring one or more parasites.

Methods: A total of 6976 participants who completed a medical questionnaire and provided a stool sample for examination were included in the final analysis.

Results: The overall prevalence rates of *Schistosoma japonicum*, *Ascaris lumbricoides*, *Trichuris trichiura*, and hookworm were found to be moderate to high at 28.9%, 36.5%, 61.8%, and 28.4%, respectively. However, the prevalence of harbouring any of the helminths was found to be higher at 75.6%. Significant variation was evident among the predicted barangay-specific random effects for infection with *S. japonicum* (barangay variance of 0.66, 95% confidence interval 0.31–1.40) and for any helminth infection (barangay variance of 0.63, 95% confidence interval 0.30–1.29). The predictive models showed, with greater than 80% sensitivity and specificity, that low socio-economic status, low levels of education, poor sanitation, proximity to water sources, occupation (i.e., farming and fishing), and male sex were all reliable indicators of infection status.

Conclusions: This study will aid in the targeting of limited resources for national treatment and WASH (water, sanitation, and hygiene) efforts in low- and middle-income countries.

1. Introduction

Over one third of the world's human population have disease caused by soil-transmitted helminths (STHs; intestinal parasitic nematode worms), mainly in low- and middle-income countries (LMIC) of Asia, Africa, and Latin America.[1] Collectively, they are the most common of the 13 major neglected tropical diseases (NTDs) and the most widespread of the chronic infections globally.[2] Many individuals harbour more than one STH concurrently, particularly in disadvantaged, rural communities lacking basic hygiene and sanitation.[1,2] *Ascaris lumbricoides* is the most prevalent STH, with an estimated one billion infections; *Trichuris trichiura* and hookworm (*Necator americanus* and *Ancylostoma duodenale*) each infect approximately 600–800 million.[1] Schistosomiasis, caused by blood flukes of the genus *Schistosoma* (phylum Platyhelminthes), afflicts 240 million people globally, with a further 700 million at risk of infection in 78 countries.[2]

STHs are a major public health problem in the Philippines, particularly among school-aged children; these infected children may suffer from profound physical deficits, including anaemia and malnutrition, stunted growth, reduced fitness, and cognitive delays.[2–8] Sixteen out of 17 regions in the Philippines are endemic for STHs with a prevalence of ≥50%.[9] A nationwide survey performed over a period of 10 years found the prevalence in children aged 2–14 years to be 50–90%. Furthermore, up to 30% of the 22 million children in the Philippines were infected with more than one STH species.[10,11]

Schistosomiasis was first reported in 1906 in the Philippines, where approximately 865 000 people are currently infected with *Schistosoma japonicum* and another seven million are at risk of infection.[12] Major endemic foci occur in 28 provinces, 190 municipalities, and 2230 barangays (villages) in the poorest regions of the

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Visayas (Samar and Leyte) and Mindanao.[12] The current schistosome prevalence in endemic foci is estimated to range from 3% to 45%, demonstrating that despite decades of surveillance and treatment with the drug praziquantel, *S. japonicum* is still highly prevalent.[13–19]

The current national control programme for schistosomiasis comprises annual mass drug administration (MDA) with 40 mg/kg of praziquantel in endemic barangays with a human prevalence >10% and annual MDA with 400 mg of albendazole or mebendazole for STHs.[16–18] The purpose of this study was to determine the prevalence of one or more helminthiases (schistosomiasis and STHs) in the rural Philippines, along with their associated risk factors. An improved understanding of the risk factors of multiparasitism could help guide future integrated control strategies leading to the elimination of these NTDs.

2. Methods

2.1. Study design and targeted population

A cross-sectional parasitological survey for intestinal helminths and *S. japonicum* was conducted in 2012 among 18 barangays (villages) in the highly endemic municipalities of Laoang and Palapag, Northern Samar, the Philippines.[12] Villagers there are typically poor rice farmers, with over 50% of the population living below the poverty line. Water, sanitation, and hygiene conditions are most often rudimentary.[12] Most households typically have 6–10 children per family[12] and the prevalence rates of parasitic diseases, acute respiratory infections, diarrhoeal diseases, and other communicable diseases are high.

2.2. Study procedures

Individuals were asked, over the course of a week, to provide two stool specimens from which six Kato–Katz thick smears were prepared on microscope slides. These slides were examined under a light microscope by experienced laboratory technicians who counted the number of STH and *S. japonicum* eggs per slide. For quality control, 10% of slides were randomly selected and re-examined by a senior microscopist at the Research Institute for Tropical Medicine, Manila. Individual and head of household questionnaires were completed to collect the following information: occupation, level of education, home and land ownership, number of animals owned and raising practices, animal waste disposal practices, pasturing of animals, sanitation, and housing characteristics (roofing, wall, and floor materials). For wealth status, participants were classified as wealthy if their house had a cement floor, a galvanized roof, cement walls, and a tile/marble floor. Participants were classified as poor if they had a house with a nipa (palm) roof, a soil floor, and without cement walls. All other participants were classified as having a moderate wealth status.

2.3. Data management and statistical analysis

Data were double-entered into FoxPro (version 6.0), cross-checked, and subsequently analysed using STATA SE version 13.0 software (StataCorp LP, College Station, TX, USA). All variables including sex, age group, and endemic setting were explored individually by Chi-square statistics. Infection intensity was explored with the Student *t*-test and Kruskal–Wallis test. The standard error (SE) of each estimate was converted to a variance; all variances were summed to provide an overall variance, SE, and 95% confidence interval (CI).

The Chi-square test was used to explore associations of a participant's demographic and socio-economic characteristics and the likelihood of having *S. japonicum*, any STH, and any helminth infection. Significant demographic and socio-economic factors were entered into the mixed-effect logistic regression analyses to obtain the final models for predicting *S. japonicum*, any STH, and any helminth infection separately. Random barangay and household effects were included in the models to account for the correlation among observations within each barangay (village) and household, respectively. Adaptive Gaussian quadrature with 10 points was adopted to approximate the log likelihood for all levels of both random effects in the mixed models. Factors that were not significantly relevant (cut-off for significance = 0.05) were removed in a stepwise backward regression elimination procedure.

To illustrate the predictive power of the diagnostic models, sensitivity and specificity were calculated by randomly dividing the data into half for each type of infection. The observations in one half were used to form a mixed-effect logistic regression model, which in turn was used to make predictions about the other half. A receiver operating characteristic (ROC) curve was generated by plotting the relationship of the true positivity (sensitivity) against the false positivity ($1 - $ specificity) across a series of cut-off points, using the ROCR package.[20] For each ROC curve, the area under the curve (AUC) was calculated; this summarizes the predictive power of the diagnosis model. Moreover, the optimal cut-off point was obtained by maximizing the sum of sensitivity and specificity; this cut-off point optimizes the prediction ability of the model with maximum accuracy rate.

2.4. Study oversight

Ethical consent for the study was obtained from the ethics review boards of the Department of Health in the Philippines (IRB # 2012-13-0) and Griffith University, Australia. Written informed consent was obtained from each individual, or from the parents/legal guardians of those under 15 years of age. All questionnaires were translated into the local dialect and back-translated into English. Individuals found positive for an STH or *S. japonicum* were treated according to the Department of Health clinical guidelines.

3. Results

3.1. Human prevalence and intensity of helminth infections

A total of 6976 participants who completed a medical questionnaire and head of household questionnaire, and who provided a stool sample for examination, were included in the final analysis. The overall prevalence rates of *S. japonicum*, *A. lumbricoides*, *T. trichiura*, and hookworm were found to be moderate to high at 28.9%, 36.5%, 61.8%, and 28.4%, respectively. However, the prevalence of harbouring any of the helminths was found to be higher at 75.6%.

Figure 1 displays the predicted barangay-specific random effects among the 18 endemic barangays surveyed. Significant variation was evident among the predicted barangay-specific random effects for infection with *S. japonicum* (barangay variance of 0.66, 95% CI 0.31–1.40), any STH (barangay variance of 0.69, 95% CI 0.34–1.42), or any helminth infection (barangay variance of 0.63, 95% CI 0.30–1.29). Compared with the other villages, residents from barangay 8 (barangay Nipa) had a significantly higher risk of acquiring a helminth infection, while those resident in barangay 17 (barangay Oleras) had a significantly lower risk of acquiring a parasite. Barangays 1, 5, and 18 (barangays Bangon, Laniwan, and Simora Laoang) also had a relatively lower risk of acquiring an STH infection.

3.2. Risk factors for helminth infection

Table 1 presents the demographic profile of the study participants along with their association with the prevalence of

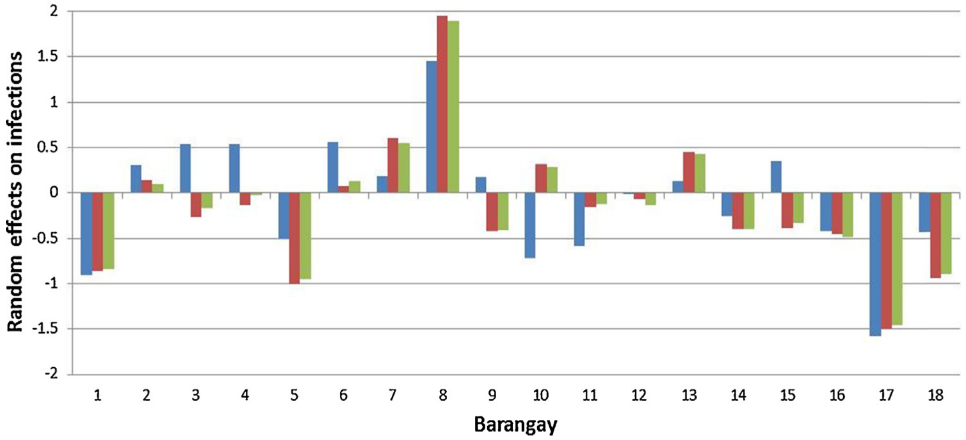

Figure 1. Prediction of barangay-specific random effects for *Schistosoma japonicum* (blue), any STH (red), and any helminth infection (green) among the 18 barangays in Northern Samar, Philippines (STH, soil-transmitted helminth).

Table 1
Demographic profile and the prevalence rates of *Schistosoma japonicum*, any soil-transmitted helminth (STH), and any helminth for the study participants from Northern Samar, Philippines ($N = 6976$)

Demographic variable	Frequency (%)	*S. japonicum* (%)	Any STH (%)	Any helminth (%)
Sex[a]				
Male	3531 (50.6%)	36.9%	79.4%	84.1%
Female	3445 (49.4%)	20.8%	72.2%	76.1%
Age category, years[a]				
< 15	2705 (38.8%)	28.6%	78.2%	82.1%
15–34	1915 (27.5%)	30.9%	74.1%	79.3%
35+	2356 (33.8%)	27.7%	74.5%	78.6%
Education[a]				
None/pre-school	384 (5.5%)	19.3%	71.9%	73.2%
Elementary	4304 (61.7%)	31.9%	79.6%	83.5%
High school/vocational	1829 (26.2%)	27.8%	73.0%	78.8%
College/post-graduate	458 (6.6%)	14.2%	55.2%	59.6%
Occupation[a]				
Student	2826 (40.5%)	30.8%	77.3%	82.1%
Farmer	1122 (16.1%)	41.5%	80.2%	85.7%
Fishing	186 (2.7%)	47.3%	90.9%	92.5%
Professional/worker/other	789 (11.3%)	24.0%	71.2%	74.7%
Unemployed/retired/housewife	2052 (29.4%)	19.8%	71.8%	75.3%
Level of comorbidity (diarrhoea, fever, tiredness, hepatitis, alcohol)[a]				
0				
1	3704 (53.1%)	26.4%	75.2%	79.2%
2	2803 (40.2%)	31.7%	76.8%	81.6%
3+	312 (4.5%)	27.9%	70.2%	74.4%
	153 (2.2%)	41.8%	85.6%	88.2%
Home ownership				
No	692 (9.9%)	28.2%	76.9%	80.9%
Yes	6276 (90.1%)	29.0%	75.7%	80.0%
Land ownership[b]				
No	2832 (40.7%)	30.7%	76.6%	80.8%
Yes	4134 (59.3%)	27.7%	75.3%	79.6%
Farm ownership[c]				
No	4810 (69.1%)	29.0%	77.0%	81.1%
Yes	2150 (30.9%)	28.8%	72.9%	77.7%
Number of animals owned[a]				
0	2555 (36.7%)	30.6%	77.9%	82.0%
1–5	4095 (58.8%)	28.3%	74.9%	79.4%
6+	311 (4.5%)	22.2%	69.5%	74.0%
Go to rivers/lakes in barangay[a]				
No	1710 (24.5%)	19.2%	74.2%	77.7%
Yes	5266 (75.5%)	32.1%	76.4%	80.9%
Type of toilet[a]				
None/open pit	1566 (22.5%)	31.8%	81.4%	84.5%
Antipolo type	251 (3.6%)	37.5%	78.1%	84.1%
Water sealed	5039 (72.4%)	27.9%	74.1%	78.6%
Flush type	107 (1.5%)	14.0%	70.1%	75.7%
Wealth status[a]				
Wealthy	1892 (27.2%)	21.4%	68.9%	73.4%
Medium	4203 (60.4%)	31.8%	76.8%	81.3%
Poor	859 (12.4%)	31.9%	85.9%	88.8%

[a] Significant difference between categories for *S. japonicum*, any STH, and any helminth infection.
[b] Significant difference between categories for *S. japonicum* infection only.
[c] Significant difference between categories for any STH and any helminth infection only.

Table 2
Mixed-effect logistic regression analyses of the relationship between *Schistosoma japonicum*, any soil-transmitted helminth (STH), or any helminth infection (*S. japonicum* or STH) with demographic and socio-economic variables

Demographic variable	*S. japonicum*		Any STH		Any helminth	
	aOR (95% CI)	*p*-Value	aOR (95% CI)	*p*-Value	aOR (95% CI)	*p*-Value
Age category, years			NS		NS	
<15	Reference					
15–34	1.66 (1.15–2.39)	0.006				
35+	1.21 (0.81–1.80)	0.361				
Sex						
Male	Reference		Reference		Reference	
Female	0.41 (0.33–0.52)	<0.001	0.59 (0.51–0.69)	<0.001	0.68 (0.57–0.80)	<0.001
Education						
None/pre-school	Reference		Reference		Reference	
Elementary	3.12 (1.98–4.90)	<0.001	1.90 (1.40–2.56)	<0.001	1.90 (1.40–2.56)	<0.001
High-school/vocational	2.23 (1.36–3.67)	0.001	1.55 (1.12–2.13)	0.007	1.62 (1.18–2.22)	0.003
College/post-graduate	0.65 (0.35–1.23)	0.185	0.72 (0.49–1.05)	0.090	0.75 (0.51–1.11)	0.147
Occupation			NS			
Student	2.29 (1.60–3.28)	<0.001			1.33 (1.12–1.59)	0.001
Farmer	1.91 (1.34–2.70)	<0.001			1.47 (1.13–1.91)	0.004
Fishing	3.42 (1.56–7.49)	0.002			1.18 (0.62–2.26)	0.621
Professional/worker/other	1.47 (1.02–2.13)	0.038			1.21 (0.94–1.56)	0.145
Unemployed/retired/housewife	Reference				Reference	
Go to rivers/lakes						
No	Reference		Reference		Reference	
Yes	1.93 (1.47–2.54)	<0.001	1.44 (1.19–1.75)	<0.001	1.42 (1.18–1.72)	<0.001
Wealth status						
Wealthy	0.48 (0.37–0.63)	<0.001	0.67 (0.56–0.82)	<0.001	0.71 (0.59–0.86)	<0.001
Medium	Reference		Reference		Reference	
Poor	1.70 (1.17–2.46)	0.006	1.93 (1.44–2.59)	<0.001	1.85 (1.39–2.46)	<0.001
Number of animals owned	NS		NS			
0					Reference	
1–5					0.84 (0.71–1.00)	0.053
6+					0.66 (0.45–0.97)	0.035
Barangay variance	0.66 (0.31–1.40)		0.69 (0.34–1.42)		0.63 (0.30–1.29)	
Household variance	1.48 (1.04–2.12)		0.98 (0.73–1.31)		0.84 (0.61–1.14)	

aOR, adjusted odds ratio; CI, confidence interval; NS, not significant.

S. japonicum, any STH, and any helminth infection. Participants were more likely to have *S. japonicum* if male, aged 15–34 years, a farmer or fisherman, with elementary or high school/vocational education, and a high level of comorbidity. Those with *S. japonicum* infection were also more likely to have more water contact in rivers/lakes, have an open pit or antipolo type toilet, be poorer in socio-economist status, not own land, and have few or no animals. The characteristics of participants who were more likely to have any STH infection were similar to those having *S. japonicum*, with the exception being individuals aged less than 15 years, who had a greater risk of STH infection if they lived on a farm. Participant characteristics were the same between any STH and any helminth infection (schistosomiasis or STH).

Table 2 displays the final prediction models for *S. japonicum*, any STH, and any helminth infection. Compared with individuals without any infection, participants with a schistosome infection were more likely to be aged 15–34 years (adjusted odds ratio (aOR) 1.66), with elementary (aOR 3.12) or a high school/vocational school level of education (aOR 2.23). They were more likely to be students (aOR 2.29), farmers (aOR 1.91), fishermen (aOR 3.42), or professional/workers (aOR 1.47), with frequent freshwater contact (aOR 1.93). Females had a lower risk of *S. japonicum* infection (aOR 0.41). Wealthier persons were also less likely to be infected with *S. japonicum* (aOR 0.48), whereas poor persons were more likely to be infected (aOR 1.70).

Compared with uninfected individuals, participants with any STH infection were more likely to have an elementary (aOR 1.90) or high school/vocational school level of education (aOR 1.55), with frequent freshwater contact (aOR 1.44). Females had a lower risk of STH infection (aOR 0.59). Wealthy persons were also less likely to have STH infections (aOR 0.67), but those classified as poor were more likely to be infected (aOR 1.93). Compared to individuals with no infection, participants with any helminth infection were more likely to have an elementary (aOR 1.90) or high school/vocational education (aOR 1.62). They were more likely to be students (aOR 1.33) or farmers (aOR 1.47), with frequent freshwater contact (aOR 1.42). Females had a lower risk of acquiring any helminth infection (aOR 0.68). Wealthy persons were less likely to have any helminth infection (aOR 0.71), with poor individuals again being more likely to be infected (aOR 1.85). Persons who owned more animals had a lower risk of infection with any helminth (e.g., aOR 0.66 for persons with 6+ animals).

3.3. *Receiver operating characteristics (ROC)*

The ROC curves summarizing the operational utility of the predictive models for *S. japonicum*, any STH, and any helminth infection at various cut-off values are displayed in Figure 2. The optimal cut-off level for 'true positives' for *S. japonicum* infection was 87.0%. This corresponded to a sensitivity of 87.0% and a specificity of 81.8% (true negatives). The AUC was 0.921; thus the predictive model was 'excellent' for predicting *S. japonicum*. For any STH infection, the sensitivity and the specificity of the diagnostic model were 80.2% and 80.9%, respectively. The AUC was 0.878; thus the predictive model was 'very good' for predicting any STH infection. For any helminth infection, the sensitivity and specificity were 78.4% and 80.5%, respectively. The AUC was 0.872, and thus again the predictive model was 'very good' for predicting any helminth infection.

4. Discussion

Intestinal helminthiases and schistosomiasis are parasitic diseases of poverty that are ubiquitous in the developing world.

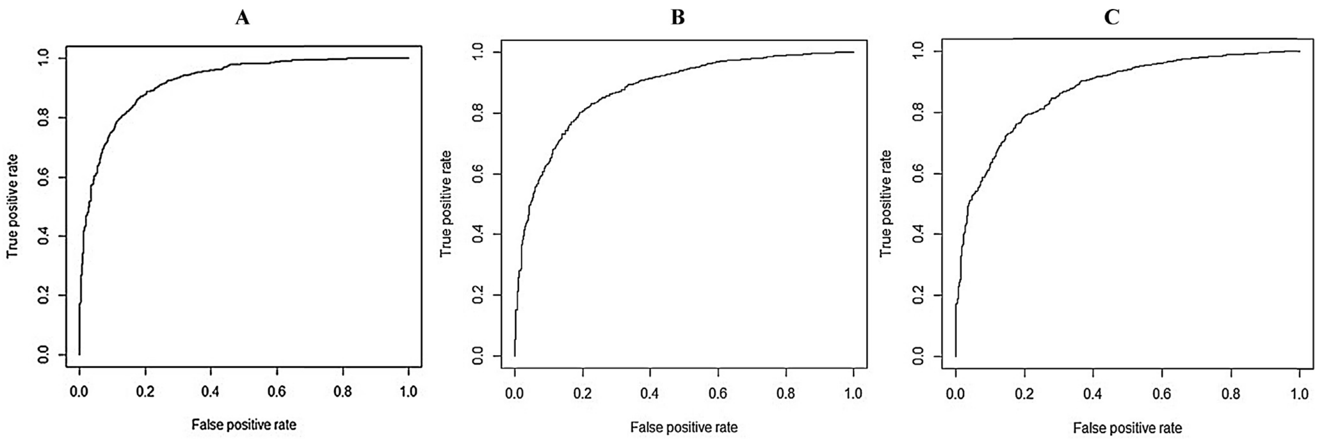

Figure 2. Receiver operating characteristics (ROC) curves of the diagnosis models for (a) *Schistosoma japonicum* infection, (b) any STH infection, and (c) any helminth infection (STH, soil-transmitted helminth).

They have long been neglected by donor agencies as they are perceived to have a very low burden of disease index. However, more than a third of the world's population are currently infected and children suffer from profound physical deficits such as anaemia, malnutrition, stunted growth, and cognitive delays.[2–8] In the Philippines, a nationwide survey found up to 54% of children to be infected.[10] In the present study it was found that 76% of the rural population in the second district of Northern Samar were infected with one or more helminth parasites. This study group has previously found a significant association between co-infection with all four helminthiases and a low intake of energy, thiamine, and riboflavin among children.[15] Thiamine and riboflavin deficiencies are common in Northern Samar, where dairy and meat intake are low and mostly rice-based meals are consumed.[13] Iron deficiency has been associated with impairments in both adaptive and innate immunity and with lowering the body's resistance to infectious diseases.[13] Poor nutrient intake may increase susceptibility to parasitic diseases and together they negatively affect the nutritional status of children and adolescents.[13,15]

These predictive models have shown, with greater than 80% sensitivity and specificity, that low socio-economic status, low levels of education, poor sanitation, proximity to water sources, occupation (i.e., farming and fishing), and male sex are all reliable indirect indicators of infection status. This information was confirmed with the barangay-specific random effects analysis. Residents from barangay 8 (Nipa, Northern Samar) had a significantly higher risk of acquiring a helminth infection. This barangay is known to be one of the poorest in the second district, with most of the men engaged in fishing. It is noteworthy that the wages of fishermen in this locality are far below those of farmers, who are also considered poor. The households of Nipa have high rates of malnutrition, poor sanitation, and little hygiene—the ideal setting for helminth transmission. Thus, the poorest barangays in the rural Philippines should be the focus of future control efforts.

The Philippines Department of Health control programme for intestinal helminths relies largely on chemotherapy with albendazole or mebendazole used for STHs and praziquantel for schistosomiasis. Children aged 1–12 years are targeted for STH treatment, while known schistosomiasis-endemic barangays are targeted through annual MDA with praziquantel. Although this approach provides some short-term benefits, improved access to water, sanitation, and hygiene (WASH) must also be utilized in order to interrupt the lifecycle of these diseases and to achieve sustainable control. This year (2016), the national Department of Health conducted an MDA campaign for STHs in Northern Samar schools using the drug mebendazole. A recent meta-analysis has shown the drug to be largely ineffective.[21,22] Albendazole needs to be combined with WASH, micro-nutrient supplements, and health education[23] for the integrated control of STHs, while bovine treatment, snail control, and irrigation need to be combined with annual MDA of humans for the sustainable control of schistosomiasis. National GIS risk maps must be developed using reliable data generated at the municipal/district level in order to target treatment and integrated control efforts. Unfortunately many LMIC nations (including the Philippines) do not have such data. However, these data could be obtained relatively cheaply, under the coordination of the municipal medical officers (or clinical officers), if local microscopists are properly trained and supervised. These strategies must be deployed if sustainable control is ultimately to be achieved in the Philippines and the developing world.

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