A MODEL FOR INTEGRATING PARAGONIMIASIS SURVEILLANCE AND CONTROL WITH TUBERCULOSIS CONTROL PROGRAM

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Abstract. Misdiagnosis of paragonimiasis as pulmonary tuberculosis (TB) due to similar clinical manifestations results in continuing morbidity and loss of productivity. Integration of surveillance and control of paragonimiasis with the TB control program may be important especially in co-endemic areas to prevent misdiagnosis. This study aimed to describe the prevalence of paragonimiasis, TB, and coinfections in six municipalities in Zamboanga Region, Philippines using a model for integrating paragonimiasis surveillance and control with tuberculosis control program, as well as to analyze the cost of implementing the aforementioned model. Active surveillance for TB and paragonimiasis was conducted in nine barangay clusters, while passive surveillance was implemented in two rural health units (RHUs) for at least three months. A simple cost analysis compared the cost of implementing the model with the National Tuberculosis Control Program (NTP). Four hundred patients were included in the active surveillance, seven of whom had paragonimiasis (2%), while three had TB (1%). Out of the 54 patients included in the passive surveillance, one (2%) had paragonimiasis. The marginal cost of implementing the model is lower than the average cost of implementing the NTP indicating that implementing the model may be beneficial in optimizing NTP production outputs. The study showed that the integration of surveillance and control of paragonimiasis with the TB control program is feasible and may contribute in finding and treating misdiagnosed paragonimiasis and TB cases. Optimization of the model and scaling up of its implementation are recommended prior to its proposed integration with NTP.

Keywords: integrated surveillance and control, NaOH concentration technique, National Tuberculosis Control Program, paragonimiasis, TB, Zamboanga Region, Ziehl-Neelsen Technique, Philippines

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INTRODUCTION

Misdiagnosis of paragonimiasis as non-response to pulmonary tuberculosis (TB) treatment or even multi-drug resistant TB is not uncommon, especially in co-endemic areas. Paragonimiasis and TB share similar clinical manifestations including chronic cough, hemoptysis, dyspnea, fever, weight loss, and night sweats (CDC, 2013). In addition, TB and paragonimiasis coinfections may not be uncommon in co-endemic areas (Belizario *et al*, 1997). Acid-fast bacilli (AFB) smear, the laboratory test used in diagnosing TB, destroys *Paragonimus* ova, while chest radiographs prove little or no definitive role in differentiating the two diseases (Singh *et al*, 2005). Misdiagnosis results in inappropriate treatment, continuing morbidity, and loss of productivity. Integrating surveillance and control of TB and paragonimiasis may be important in addressing these diseases in co-endemic areas.

The Philippine Department of Health (DOH) addresses paragonimiasis through the Food and Waterborne Diseases Prevention and Control Program (DOH, 1997), while it tackles TB through the National Tuberculosis Control Program (NTP) (DOH, 2014). The adequacy of these programs, however, comes into question considering that there are no guidelines on integration of surveillance and control strategies in co-endemic areas in the country (Belizario *et al*, 2014). This highlights the need to develop, test, and implement a model for integrating paragonimiasis surveillance and control with the NTP.

In 2012, the University of the Philippines (UP) Manila in collaboration with the Department of Science and Technology-Philippine Council for Health Research and Development (DOST-PCHRD), the DOH, and the local government unit (LGU) of Zamboanga del Norte developed and tested a model for integrating paragonimiasis surveillance and control with the pulmonary tuberculosis (TB) control program (integrated TB-paragonimiasis model) (Belizario *et al*, 2014). Evaluation of the integrated TB-paragonimiasis model is important in determining its utility in enhancing the NTP in areas where paragonimiasis and TB are co-endemic.

This study aimed to describe the prevalence of paragonimiasis, TB, and coinfections in six municipalities in Zamboanga Region, Philippines using the integrated TB-paragonimiasis model, as well as to analyze the cost of implementing the model.

MATERIALS AND METHODS

Study design, sites, and population

The study utilized a cross-sectional design, which involved examination of patients in active and passive surveillance for TB and paragonimiasis using the integrated TB-paragonimiasis model (Belizario *et al*, 2014). Two provinces in Zamboanga Region, namely Zamboanga del Norte and Zamboanga Sibugay, were selected for the implementation and evaluation of the integrated TB-paragonimiasis model (Fig 1).

For the active surveillance, nine barangay clusters from six municipalities in the two provinces were selected (Table 1) based on previous reports of paragonimiasis, reports of non-response to TB treatment, as well as other factors including habits of residents of eating freshwater crustaceans, proximity of the area to a body of freshwater, peace and order situation, and willingness of the LGUs to participate. These were selected in consultation with the DOH Regional

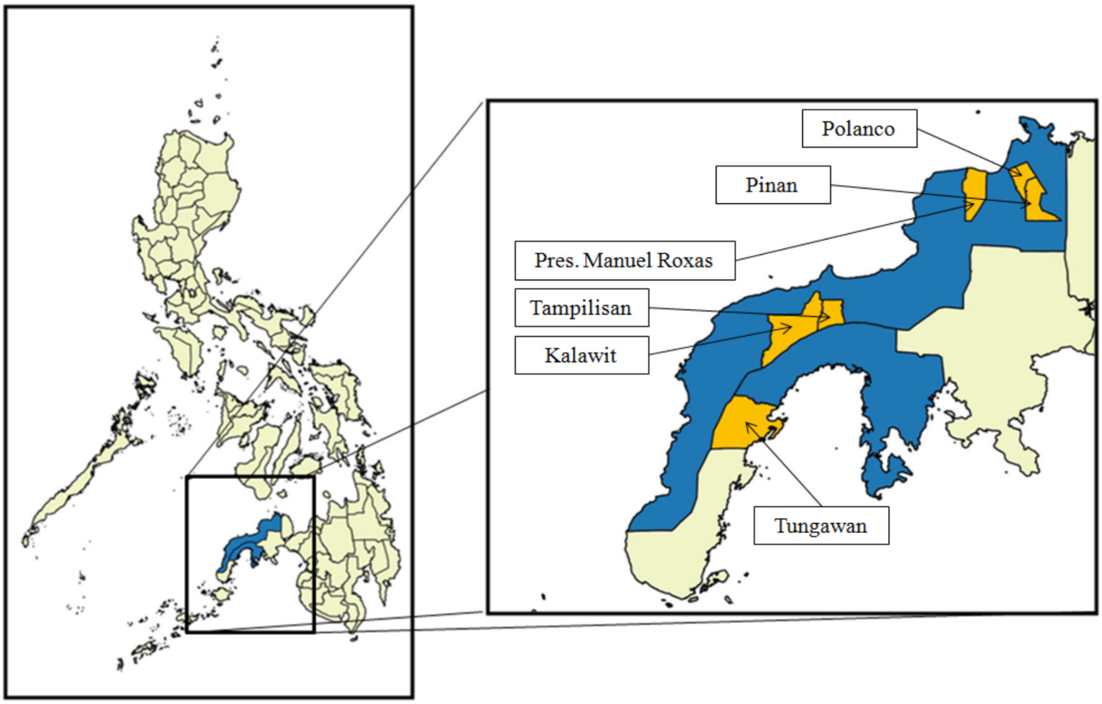


Fig 1–Map of Philippines (left) and the Zamboanga Region (right) showing Zamboanga del Norte, Zamboanga Sibugay (blue) and the municipalities (yellow, bottom to top) of Tungawan, Kalawit, Tampilisan, Pres. Manuel Roxas, Polanco, and Piñan. Map generated using QGIS software.

Office (RO) IX and LGUs. A minimum of 96 patients per selected municipality or a total of 576 patients for the six municipalities were required. The sample size was based on the recommended sample size computation (Lwanga and Lemeshow, 1991).

Patients with a complaint of chronic cough for more than two weeks were included in the active surveillance. Prerequisites for their participation included signed informed consent forms (ICFs) and submission of two sputum samples, an early morning and a spot sputum sample, on the day of the consultation.

Two municipalities in Zamboanga del Norte, namely Pres. Manuel Roxas and Polanco, were selected for the implementation of the passive surveillance based on previous reports of paragonimiasis and willingness of the LGUs to cooperate in the undertaking. Patients consulting the rural health units (RHUs) who satisfied the inclusion criteria were included in the passive surveillance, which was implemented for six months in Pres. Manuel Roxas (March to August 2015) and for three months in Polanco (June to August 2015).

Data collection

Model for integrated TB-paragonimiasis surveillance and control. The early morning and spot sputum samples collected from each patient in the active and passive surveillance were processed and examined using the integrated TB-paragonimiasis model (Figs 1 and 2). The Ziehl-Neelsen method (DOH, 2014) was

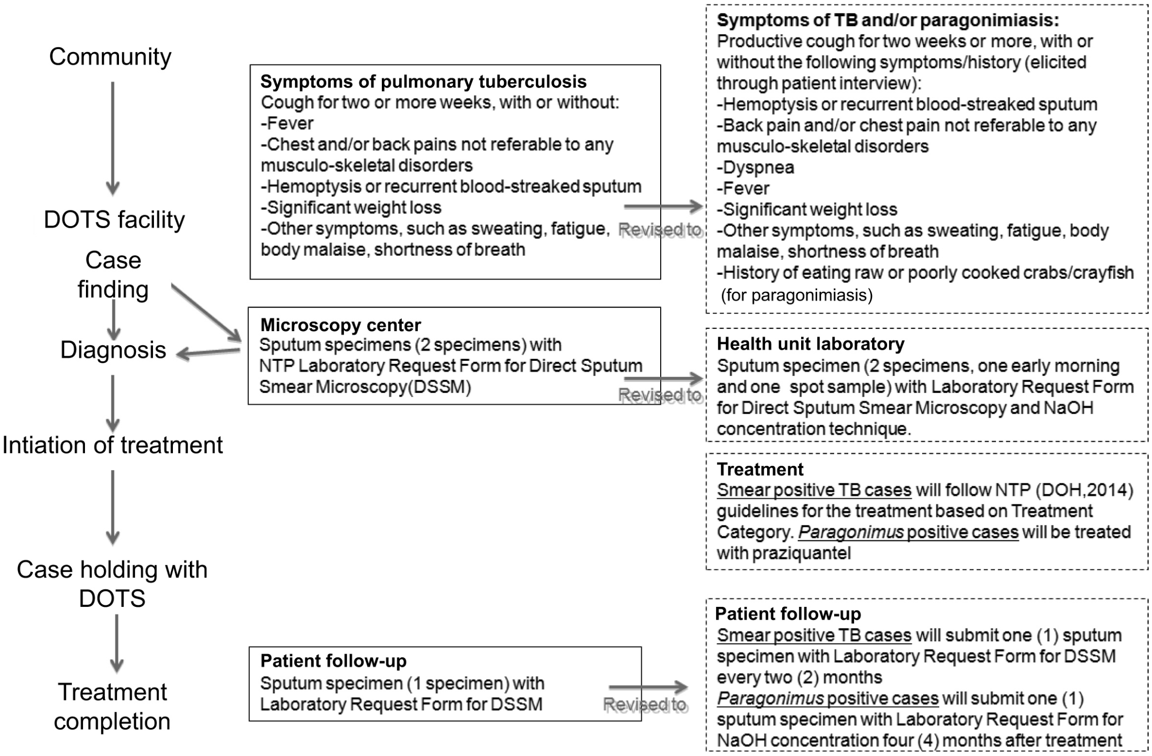


Fig 2–Proposed flow of combined NTP and paragonimiasis control activities (Belizario *at al*, 2012, unpublished report).

used in processing and examining sputum samples for *Mycobacterium tuberculosis*. The remaining sputum specimens from each sample were processed following the NaOH concentration technique (Cheesebrough, 1998) and examined for *Paragonimus* ova.

Quality control of AFB microscopy was performed by the validator in the Provincial Health Office of Zamboanga del Norte. On the other hand, all slides positive for *Paragonimus* ova were cross-checked by a senior microscopist from UP Manila.

Active surveillance. The active surveillance was conducted in February 2015 in Pres. Manuel Roxas, Zamboanga del Norte, in May 2015 in Polanco and Piñan, Zamboanga del Norte, and in August 2015 in Kalawit and Tampilisan, Zamboanga del Norte and Tungawan, Zamboanga Sibugay. Barangay health workers (BHWs), who had been oriented on the use of the algorithm, distributed sputum collection kits to patients with complaint of cough for more than two weeks. The patients were instructed to bring early morning sputum samples at the designated area on the scheduled date of the active surveillance. Trained research staff from UP Manila screened the patients for inclusion. The patients were then interviewed for their symptomatology and were examined by physicians from UP Manila, DOH RO IX and the RHUs. Basic information, such as name, birthdate, age and sex of the participants, were recorded

Table 1
List of selected areas for the active surveillance of TB and paragonimiasis (February, May, and August 2015).

Province	Municipalities	Barangay clusters	Barangays
Zamboanga del Norte	Pres. Manuel Roxas	Marupay	Marupay
	Polanco	Macleodes	Macleodes
			Linabo
			La Venta Pera
		Bethlehem	Bethlehem
			New Lebangon
	Piñan	Sta. Fe	Sta. Fe
		Desin	Desin
			Villarico
	Kalawit	Daniel Maing	Daniel Maing
		Botong	Botong
	Tampilisan	Banbanan	Banbanan
			Camul
			Situbo
			Tininggaan
Zamboanga Sibugay	Tungawan	Little Margos	Little Margos

in the Case Record Form (CRF) by the assigned research staff.

Passive surveillance. Trained RHU staff screened the patients for inclusion in the passive surveillance. The patients who presented in the RHUs with complaint of chronic cough for more than two weeks, and thus satisfied the inclusion criteria, were instructed to bring early morning sputum samples. The patients were then interviewed for their symptomatology and examined by the municipal health officer.

Data processing and analysis

Data from CRFs were double encoded using pre-tested Microsoft Excel data forms. Verification of data entries with source documents was done to ensure accuracy. Data was processed using Microsoft Excel 2007. Prevalence rates were computed using the following formulas:

$$\text{Prevalence of TB} = \frac{\text{Number of patients positive for AFB}}{\text{Total number of patients examined}} \times 100$$

$$\text{Prevalence of paragonimiasis} = \frac{\text{Number of patients positive for } \textit{Paragonimus} \text{ ova}}{\text{Total number of patients examinied}} \times 100$$

$$\text{Prevalence of coinfection} = \frac{\text{Number of patients positive for AFB and } \textit{Paragonimus} \text{ ova}}{\text{Total number of patients examined}} \times 100$$

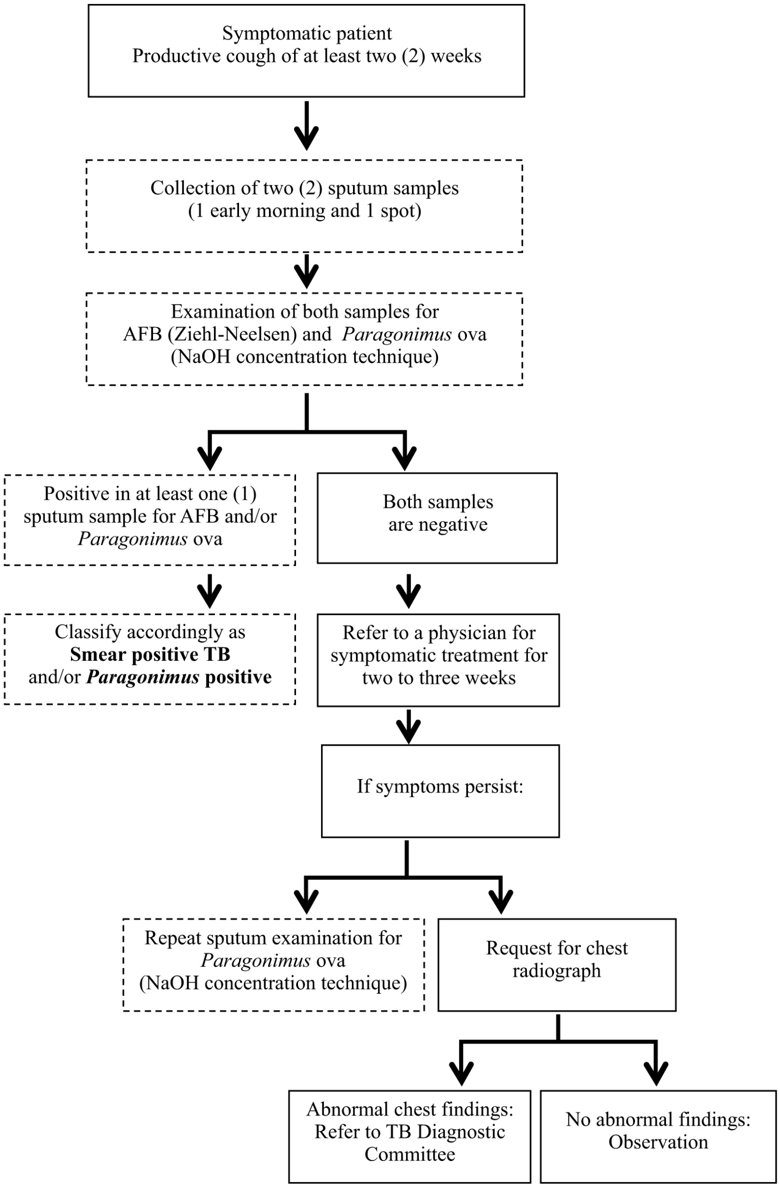
Simple cost analysis

A simple cost analysis was conducted to determine the average monthly cost of implementing the NTP and incremental cost of implementing the integrated TB-paragonimiasis model. Data were collected on the cost items involved in the RHU operation. The cost items for NTD and the integrated TB-paragonimiasis model were identified through consultation with concerned staff of DOH RO IX and RHUs involved. The cost items included person-

Table 2
Number of patients examined and positivity rates for AFB and *Paragonimus* ova according to barangay in selected municipalities in Zamboanga del Norte and Zamboanga Sibugay (February, May, and August 2015).

Province/Municipality/ Barangay	Patients (*n*)	Positive for AFB	Positive for *Paragonimus* spp	AFB and *Paragonimus* coinfection
		n (%)	*n* (%)	*n* (%)
Zamboanga del Norte				
Pres. Manuel Roxas-Marupay	51	0	1 (2.0)	0
Polanco				
Macleodes	49	0	0	0
Bethlehem	67	0	0	0
La Venta Pera	2	0	0	0
Linabo	13	1 (7.0)	0	0
New Lebangon	5	1 (20.0)	0	0
Subtotal (Polanco)	136	2 (1.5)	0	0
Piñan				
Sta. Fe	27	0	0	0
Desin	45	1 (2.0)	0	0
Villarico	31	0	0	0
Subtotal (Piñan)	103	1 (1.0)	0	0
Kalawit				
Botong	10	0	1 (10.0)	0
Daniel Maing	42	0	3 (7.0)	0
Subtotal (Kalawit)	52	0	4 (8.0)	0
Tampilisan				
Banbanan	29	0	0	0
Tininggaan	1	0	0	0
Camul	1	0	0	0
Situbo	1	0	1	0
Subtotal (Tampilisan)	32	0	1 (3.0)	0
Subtotal (Zamboanga del Norte)	374	3 (0.8)	6 (1.6)	0
Zamboanga Sibugay				
Tungawan-Little Margos	26	0	1 (4.0)	0
Overall	400	3 (0.8)	7 (1.8)	0

nel, capacity building, utilities, office supplies, office equipment, laboratory supplies, laboratory equipment, and drugs. Standard ratios of quantity of these cost items with their respective outputs, with respect to quality assurance, were also identified through a review of literature, consultations with DOH RO IX and the concerned RHUs. All costs were collected, either through review of records or key informant interviews. Supporting documents, such as Quarterly Accomplishment Reports of the RHU laboratories were also obtained from the RHUs and other sources. Sunk costs, such as trainings and equipment, were annualized using WHO



Note: Boxes with dashed outline were added to the original NTP flow chart in solid outlines (DOH, 2014)

Fig 3–Proposed algorithm for integrated TB-paragonimiasis surveillance and control.

recommendations (WHO, 2002).

Ethical considerations

The study was granted Ethics Review and Continuing Review approval by the UP Manila Research Ethics Board (UPM-REB 2009-023-01). Following established ethical guidelines, patients were included in the study only after informed consent had been secured. The patients were assured of the confidentiality of their data. All patients diagnosed with TB were treated following NTP guidelines (DOH, 2014). On the other hand, patients diagnosed with paragonimiasis were treated with praziquantel according to national guidelines (DOH, 2010). Drugs were dispensed through the assigned RHU staff.

RESULTS

Prevalence of TB, paragonimiasis, and coinfections in selected sites in the Zamboanga Region

Active surveillance. Four hundred (400) patients were included in the active surveillance, of which 374 and 26 were from Zamboanga del Norte and Zamboanga Sibugay, respectively. Of the 400 patients, seven were positive for paragonimiasis (2%), while three had TB (1%). In Zamboanga del Norte, the municipality of Kalawit had the highest paragonimiasis prevalence at 8%, while no paragonimiasis case was found in the municipalities of Polanco and Piñan. The lone patient from Situbo, Tampilisan was positive for paragonimiasis. On the other hand, Polanco had the highest TB prevalence at 1.5% followed by Piñan at 1%, while no case was found in the municipalities of Pres. Manuel Roxas, Kalawit, and Tampilisan. In Zamboanga Sibugay, a single paragonimiasis case was found (4%), while no TB case was seen. No case of *Mycobacterium tuberculosis* and *Paragonimus* coinfection was seen from either province (Table 2).

Five of the seven patients who were positive for *Paragonimus* ova and two of the three positive for AFB were males. On the other hand, the ages of patients positive for *Paragonimus* ova ranged from 6 to 53 years old, while the ages of the three patients positive for AFB were 39, 53, and 59 years old.

Passive surveillance. None of the 53 patients examined in the passive surveillance in Pres. Manuel Roxas had TB or paragonimiasis. On the other hand, one out of the nine patients included in Polanco had paragonimiasis, while no TB case was found.

Simple cost analysis

The Polanco RHU incurs a monthly cost of PHP 558,465.94 for the implementation of NTP, while the Pres. Manuel Roxas RHU incurs a monthly cost of PHP 718,094.86. In both RHUs of Polanco and Pres. Manuel Roxas, the highest costs incurred in its operation were in personnel, utilities, and laboratory supplies, while the lowest were in office equipment, capacity building and drugs. The average cost per patient for the NTP was PHP 930.78 for Polanco RHU and PHP 1,088.02 for Pres. Manuel Roxas RHU. The incremental cost per patient of the integrated TB-paragonimiasis model was PHP 130.03 for Polanco RHU and PHP 61.75 for Pres. Manuel Roxas RHU. In both cases, the incremental cost of the integrated TB-paragonimiasis model is lower than the average cost of NTP (Table 3).

DISCUSSION

Paragonimiasis was not uncommon in the selected municipalities. Five out of the six selected municipalities had paragonimiasis cases. Cases were also found in barangays where the disease was previously not reported. These may indicate that the true burden of paragonimiasis may be grossly underestimated. Thus, there may be a need to map out endemic areas not only in the region but also in the country. The focal distribution of paragonimiasis observed is consistent with the findings of other studies (Toscano *et al*, 1994; Belizario *et al*, 1997). Identifying focal areas will ensure that resources are maximized. Pediatric paragonimiasis cases found suggest the need for further

Table 3
Monthly cost of production of various cost items, average cost of NTP, and incremental cost of the model for integrated TB-paragonimiasis surveillance and control in the RHUs of Polanco and Pres. Manuel Roxas, Zamboanga del Norte.

Cost items	Recommended ratio	Cost (Monthly)	
		Polanco	Pres. Manuel Roxas
Personnel			
Physician (MD)	1 MD for 840-1,200 patients	65,000.00	58,000.00
Nurse (RN)	1 RN for 420-600 patients	50,000.00	30,000.00
Medical technologist (MT)	1 MT for 600-2,000 lab tests	25,000.00	23,000.00
Midwife	1 midwife for 2,427-3,747 residents	234,000.00	364,000.00
Barangay health worker (BHW)	1 BHW for 303-312 residents	100,000.00	148,800.00
Barangay nutrition scholar (BNS)	1 BNS for 1,213-1,249 residents	15,000.00	37,200.00
Administrative staff (AS)	1 AS for 840-1,200 patients	12,921.00	4,000.00
Capacity building			
Physicians/Nurses	1 MD/RN per municipality per training	500.00	500.00
Medical technologists	1 MT per municipality per training	500.00	500.00
Utilities			
Rent	N/A	0	0
Electricity	600-660 patients	25,000.00	10,000.00
Water	600-660 patients	4,000.00	4,000.00
Internet	N/A	2,000.00	1,500.00
Office supplies	600-660 patients	6,250.00	6,250.00
Office equipment			
Computer	600-660 patients	163.76	163.76
Printer	600-660 patients	45.49	45.49
Digital camera	600-660 patients	45.49	45.49
IEC materials	1 municipality	2,777.78	2,990.07
T-shirts for activities	200 RHU personnel	0	16,666.67
Lab equipment			
Microscope	2 per RHU (1 for LPO/HPO and 1 for OIO)	5,676.05	1,621.73
Centrifuge	1 centrifuge for 2,000 patients	851.62	851.62
Lab supplies/materials			
Laboratory gown	1 lab gown per personnel	8.01	12.01
Gloves	2 boxes per lab personnel	300.00	300.00
Mask	2 boxes per lab personnel	260.00	260.00
Disinfectant	1 bottle for two weeks	1,200.00	600.00
Sputum collection cup	1 sputum cup per patient	2,175.00	1,450.00
NaOH pellets	1 500 g-bottle per 83 patients	0	2.34
Centrifuge tubes	1 tube per test	0	258.00
Glass slides	1 box per 200 tests	490.00	140.00
Cover slips	1 box per 200 tests	135.00	90.00
Transfer pipettes	1 transfer pipette per test	30.00	177.60
AFB staining set	1 staining set for 100 tests	2,597.00	2,597.00
Applicator stick	1 box for 1,000 tests	200.00	200.00
Drugs			
Praziquantel	1 patient per treatment course	273.09	273.09
TB drugs	1 patient per treatment course	1,066.67	1,600.00
Total cost		558,465.94	718,094.86
Average cost of NTP		930.78	1,088.02
Incremental cost		130.03	61.75

studies on the risk factors and determinants of the disease. The TB prevalence obtained is above the national prevalence estimate in 2014 (WHO, 2015a). This may be related to the active surveillance being conducted in remote areas, which facilitates examination of patients who often do not go to the RHU.

The lower paragonimiasis and TB prevalence obtained compared with a related study conducted in the same region (Belizario *et al*, 2014) may be related with poor compliance with the inclusion criteria and with the sputum collection instructions. Some patients submitted saliva-looking sputum samples. The accuracy of prevalence estimate may have been improved had the study included only those with cough for more than two weeks and had the patients submitted appropriate early morning sputum samples in sufficient amount (Van Rie *et al*, 2008). The proficiency of medical technologists in processing and examining sputum samples is also critical in ensuring accurate diagnosis (Van Rie *et al*, 2008). This highlights the importance of building the capacity of local health unit staff.

The lack of TB-paragonimiasis coinfection case may be due to the low number of patients included and low prevalence of TB and paragonimiasis. A previous study showed that the prevalence of coinfection might be as low as 0.2% in some municipalities in Zamboanga del Norte (Belizario *et al*, 2014). The low turnout of patients was observed in both active and passive surveillance. For the active surveillance, this may be due to challenges in coordination with the community. For the passive surveillance, on the other hand, this may be due to the use of very strict inclusion criteria by the selected RHUs and residents in remote barangays not visiting RHUs. In the latter case, improving the health-seeking behavior through the RHU staff will be very important.

In analyzing program costs, optimal production is achieved whenever incremental cost is equal to average cost. Conversely, there is under-production when incremental cost is less than average cost, and there is over-production (with subsequent cost-inefficiencies) when incremental cost is higher than average cost. In the case of comparing the integrated TB-paragonimiasis model and the NTP, if the computed incremental cost is less than the computed average cost, then the new program can contribute to the NTP in achieving optimal production.

The marginal cost of implementing the integrated TB-paragonimiasis model was lower than the average cost of implementing NTP. The low marginal cost may be because the integrated TB-paragonimiasis model uses the NTP as its framework and merely integrates paragonimiasis surveillance and control with the NTP. Implementing the integrated TB-paragonimiasis model will not require additional personnel and equipment. The laboratory supplies and drugs needed are also relatively inexpensive and may be provided by DOH. Thus, implementing the integrated TB-paragonimiasis model will be beneficial and may contribute to NTP in achieving optimal service production.

The marginal cost of implementing the integrated TB-paragonimiasis model in a paragonimiasis-endemic municipality, such as Pres. Manuel Roxas, was lower than that of Polanco where no case was seen in the active surveillance. More people benefit from the additional investments in implementing the integrated TB-paragonimiasis model in an endemic area compared to a seemingly non-endemic area. Thus, while the low marginal costs in both endemic and non-endemic municipalities suggest the economic feasibility of implementing the integrated TB-paragonimiasis model, its implementation may be prioritized in endemic areas where more people will benefit from the program.

Integrating surveillance and control of paragonimiasis with NTP in co-endemic areas, such as Sorsogon and Zamboanga del Norte, may contribute in achieving better health outcomes (Belizario *et al*, 1997, 2014). In particular, this will benefit those who have TB, which reached 410,000 in 2014 (WHO, 2015a), as well as those who live in areas endemic for paragonimiasis, which includes at least 12 provinces (Belizario and Malte, 2004). The integrated TB-paragonimiasis model may also be adopted by other co-endemic countries. This could potentially benefit TB patients worldwide, which reached 9.6 million people in 2014 (WHO, 2015a), as well as the estimated 20 million people in Asia who have paragonimiasis (Strobel *et al*, 2005). The integrated TB and paragonimiasis model may likewise contribute to enhancing the case finding for both TB and paragonimiasis, especially with regards to finding the missed cases. Globally, it is estimated that 3.3 million or a third of those who develop TB cases are missed (WHO, 2014), while there is limited data on paragonimiasis (WHO, 2015b).

The study demonstrated the utility and feasibility of integrating surveillance and control of paragonimiasis with the NTP. The integrated TB-paragonimiasis model may contribute in finding missed TB cases, which may lead to reduced mortality, and in reducing transmission through treatment of patients. Similarly, implementation of the model may lead to diagnosing more paragonimiasis cases, which will reduce morbidity and mortality. Implementation of the model was also shown to have lower marginal cost compared with the average cost of NTP, suggesting that the model is beneficial and may contribute to NTP in achieving optimal service production.

The study recommends optimization of the integrated TB-paragonimiasis model. Selection of study sites may be based on specific criteria, such as reports of paragonimiasis cases, reports of TB cases not responding to treatment, proximity of the area to a body of freshwater, and habit of residents of eating freshwater crabs. The use of questionnaires in identifying transmission foci (Odermatt *et al*, 2009) may also be explored. Indigenous paragonimiasis cases should be confirmed before selecting a site to implement the integrated TB-paragonimiasis model. Capacity building of the local health unit staff, which may include didactics, hands-on trainings, and a means for evaluation of the participants, (Van Rie *et al*, 2008) is also needed. Utilization of the Medical Teleparasitology System, where electronic images of suspected *Paragonimus* ova may be sent for confirmation by diagnostic parasitologists in a reference center, is recommended. Likewise, the possible use of Ziehl-Neelsen method in diagnosing paragonimiasis (Slesak *et al*, 2011) may be explored since AFB smears may be stored for subsequent quality control. The use of triclabendazole (20 mg/kg body weight, two doses, single day), which has simpler regimen compared with praziquantel (25 mg/kg body weight, three doses, three days) in the country for treatment of paragonimiasis may be considered to promote better compliance to treatment. Scaling-up of the implementation of the model to include other co-endemic regions, such as Bicol and Davao Regions, is recommended prior to its incorporation with the NTP. Future surveys on TB and paragonimiasis in barangays that reported cases for the first time, such as Daniel Maing, Botong, and Situbo, may be considered.

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