Published in final edited form as:

Trans R Soc Trop Med Hyg. 2009 May ; 103(5): 447–451. doi:10.1016/j.trstmh.2009.01.007.

Cost comparison of rapid questionnaire screening for individuals at risk of clonorchiasis in low- and high-prevalence communities in northern Vietnam

Aya Yajima^{a,*}, Dai Tran Cong^b, Dung Do Trung^c, Thach Dang Thi Cam^c, and Antonio Montresor^b

^aGraduate School of Agricultural and Life Sciences, University of Tokyo, 1-1-1 Yayoi, Bunkyo-ku, Tokyo, Japan ^bWorld Health Organization, Geneva, Switzerland ^cNational Institute of Malaria, Parasitology and Entomology (NIMPE), Tu Liem, Hanoi, Vietnam

Summary

Clonorchiasis is an emerging food-borne trematode infection in Vietnam. Due to the absence of cost-effective preventive measures its control largely relies on morbidity reduction by chemotherapy with praziquantel. We performed a comparative cost estimation of three different diagnostic and intervention approaches in areas of high and low prevalence of clonorchiasis in northern Vietnam in order to select more cost-effective chemotherapy. Our study confirmed that a questionnaire investigating the habit of eating raw, freshwater fish was a rapid, cost-effective and operationally feasible tool for identifying individuals at risk of clonorchiasis in both high-prevalence and low-prevalence areas. The cost of diagnosis and intervention per person and per true positive case was 20-fold higher in low-prevalence areas, regardless of the type of approach. Geographical mapping of high-risk areas prior to screening is, therefore, recommended to maximize the cost-effectiveness of the intervention activities.

1 Introduction

Clonorchiasis and opisthorchiasis are emerging food-borne trematode infections in many tropical countries.^{1,2} Vietnam is one of the most affected countries, with approximately 1 million people estimated to be infected with *Clonorchis sinensis* and *Opisthorchis viverrini*.³ Human infection occurs when a metacercaria of the flukes that parasitize the flesh or skin of a freshwater fish is ingested by a human host. The habit of eating raw freshwater fish is,

*Corresponding author. Tel.: +81 3 5841 5018. yajimaaya@gmail.com (A. Yajima).

Authors' contributions: AY, DTC and AM conceived and designed the study; AY, DDT and TDTC collected the field data; DDT and TDTC administered the questionnaire and conducted the molecular analysis; AY, DTC and AM carried out the statistical analysis, interpreted the data and prepared the manuscript. All authors revised the manuscript and read and approved the final version. AM is guarantor of the paper.

Conflicts of interest: None declared.

Ethical approval: In the first survey the data were collected during the national clonorchiasis control activity conducted by the Ministry of Health, Vietnam in order to improve the performance of the activity; therefore, ethical approval was not required. In the second survey the study protocol was approved by the ethics committee of NIMPE, Ministry of Health, Vietnam, the authority of the Hoa Binh Provincial Department of Health and the Luong Son District Department of Health.

thus, the main cause of clonorchiasis and opisthorchiasis.^{4–7} Disease transmission is influenced by various factors such as the distribution of intermediate host snails, contamination of the aquatic environment by human excreta, methods of culturing freshwater fish, a habit of raw fish consumption and the host-parasite relationship.

Due to the absence of cost-effective preventive measures, clonorchiasis and opisthorchiasis control largely relies on morbidity reduction by chemotherapy with praziquantel.⁸ In this respect, a simple questionnaire to investigate dietary habits has been reported to be a valid tool for screening populations in areas at risk of clonorchiasis and/or opisthorchiasis.⁵ In this study, a comparative cost estimation of three different diagnostic and intervention approaches was performed in areas of high prevalence and low prevalence of clonorchiasis in northern Vietnam, in order to select more suitable and cost-effective chemotherapy.

2 Materials and Methods

2.1 Study area

The data were collected from two surveys conducted separately in northern Vietnam. The first survey was performed in Luong Son district of Hoa Binh province in December 2007, where clonorchiasis/opisthorchiasis had not been reported at the time of the survey. The second survey was carried out in Kim Son district of Ninh Binh province as part of the national clonorchiasis control programme, conducted between 1999 and 2000 by the Ministry of Health, Vietnam to reduce the cost of identifying people infected with *C.sinensis*.

2.2 Questionnaire and parasitological investigation

A simple, three-item questionnaire (age, gender and a habit of eating raw fish) was devised. In the first survey 200 residents were randomly selected from a list of the residents of Tien Xuan commune of Luong Son district, Hoa Binh province. In the second survey 300 households were selected randomly from a list of the householders in two communes (Tan Thanh and Yen Loc) in Kim Son district, Ninh Binh province. Informed consent was sought from the staff of a local health centre and each study participant before survey enrolment. It took half a day for five members of staff of the local health centre to interview study participants using the questionnaire in the first survey, and 7 days for the second survey.

The same study participants that took part in the questionnaire survey were subjected to parasitological investigation. Each study participant received a plastic container and was asked to collect a single stool sample of approximately 10 g and return it to the commune health station on the following day. Stool samples were examined by the Kato-Katz thick smear method with a template size of 41.7 mg and multiplication factor of 24.⁹ The number of *C. sinensis*/*O. viverrini* eggs in each sample was counted. As it is known that *C. sinensis* is present exclusively in northern Vietnam, whereas *O. viverrini* is found in both central and northern Vietnam,¹⁰ the eggs identified in the study was assumed to be those of *C. sinensis*. In the first survey the samples were examined at the National Institute of Malaria, Parasitology and Entomology (NIMPE) in Hanoi, Vietnam by four microscopists in 1 day. In the second survey the parasitological investigation was conducted on site in the commune

health station by five microscopists in 12 days. After the stool examination all the participants that were found to be infected with clonorchiasis received treatment with praziquantel (50 mg/kg body weight).

2.3 Cost evaluation and data analysis

Financial expenditure associated with the following three diagnostic and treatment approaches were estimated: (1) stool examination of the whole population in the community, followed by drug treatment for those who were infected; (2) screening using a simple questionnaire to find individuals that had a habit of eating raw fish, followed by drug treatment for those who did eat raw fish; and (3) mass treatment with praziquantel for the whole population, without diagnosis.

Expenditures were estimated in US\$ based on the analysis of direct financial costs (i.e. procurement of drugs and stool examination kits, preparation of the questionnaires and provision of manpower for the survey, stool examination and drug distribution). Costs that were common to all three intervention approaches, such as expenses for committee meetings, transport from Hanoi to each study site, report writing and data analysis were not included in the cost evaluation.

All the data derived from the questionnaires and parasitological examinations were entered and analysed in EpiInfo 3.3.2 (CDC, Atlanta, GA, USA). Univariate analysis of the relationship between the infection prevalence and positive answers to yes/no questions was conducted (gender — ‘Are you male?’; age — ‘Are you over 15 years of age?’; habit of eating raw fish — ‘Do you have a habit of eating raw fish?’). Subsequently, logistic regression analysis was performed in order to confirm that a positive answer to the question on the habit of eating raw fish was a leading factor indicative of clonorchiasis. The diagnostic performance of the questionnaire on the history of raw fish consumption was evaluated by computing the sensitivity, specificity and predictive values.

3 Results

3.1 Prevalence of clonorchiasis

Stool samples and completed questionnaires were obtained from 151 residents in the first survey (Luong Son district, Hoa Binh province) and 1155 residents in the second survey (Kim Son district, Ninh Binh province). The prevalence of infection assessed parasitologically was low in the first survey (1%) and high in the second survey (25%) (Supplementary Table 1). The logistic regression analysis based on the data from Kim Son district showed that a positive answer to the question on the habit of eating raw fish was a leading factor associated with the prevalence of infection, and that this habit was typically observed among adult males (> 16 years of age). Odds ratio analysis was not possible with the data from Luong Son district due to the small number of positive cases. Nonetheless, the two infected individuals found were also adult males with a habit of eating raw fish.

3.2 Diagnostic performance of the questionnaire

The diagnostic performance of the reported habit of eating raw fish to detect the risk of having clonorchiasis in the two surveys is shown in Table 1. Both the surveys reported high negative predictive values of 100 and 99%. The high negative predictive value is of particular importance in diagnostic screening since it allows the safe exclusion of individuals whose risk of being infected is low.^{11,12} Sensitivity was also high (100 and 98%), whereas specificity was moderate (78 and 58%) and positive predictive values were low (6 to 45%).

3.3 Cost comparison

Cost estimates for the three diagnostic and intervention approaches for clonorchiasis in the two surveys are shown in Table 2. In both surveys, screening of individuals with a habit of eating raw fish using a simple questionnaire, followed by drug treatment for those eating raw fish resulted in the lowest cost per person (US\$0.18—0.21) and per true positive case (US\$0.83—13.82). The costs of carrying out stool examination of the whole population to identify infected individuals were the highest per person (US\$4.70—4.78) and per true positive case (US\$18.63—354.73). Regardless of the type of approach the estimated cost per true positive was significantly lower in the high-prevalence area (25% infection rate) than in the low-prevalence area (1% infection rate).

In addition, the time necessary to conduct the questionnaire screening (approx. 10 s per person) was much shorter than that necessary to conduct the parasitological investigation (12 min per sample on average).

4 Discussion

The use of a simple questionnaire for a rapid and inexpensive epidemiological assessment to identify the communities and individuals at risk of infection has been discussed and validated for *Schistosoma haematobium* and *S. mansoni* in the past decade.¹³ The present study attempted to validate a simple questionnaire for screening to identify individuals at risk of clonorchiasis in northern Vietnam.

The habit of eating raw freshwater fish, which has been identified as a leading risk factor for clonorchiasis in Vietnam,^{5–7} was used as a key risk indicator in this questionnaire.

The negative predictive values calculated in our first and second surveys (100% and 99%) were higher than those from questionnaires about ‘blood in stool’ and ‘bloody diarrhoea’ for diagnosing *S. mansoni* infection at the community level (32—95%).^{14–19} The diagnostic performance of our questionnaire was equivalent to that of questionnaires regarding ‘blood in urine’ for *S. haematobium* infection (75—100%).^{11,12,20–22} The sensitivity of our questionnaire was also remarkably high (100% and 98%). Our questionnaire was thus proven to be highly effective in excluding from treatment those not at risk of infection. The low positive predictive values we found imply that there are other factors in addition to the habit of eating raw fish that determine infection (e.g. method of cooking freshwater fish and the host-parasite relationship).

In both the first and second surveys the cost of diagnosis and intervention per person and per true positive case was lowest when the questionnaire was used for screening the habit of eating raw fish. This corresponded with the finding of Zhou et al.²³ in China, where infection with *S. japonica* was screened for by a questionnaire on risk factors such as episodes of diarrhoea, frequency of water contact and past history of the infection. Stool examination is not only costly but also time-consuming, as only a limited number of technical staff are capable of conducting stool examination in local settings. While the estimated cost for mass treatment of the whole community without screening was similarly low, screening has the advantage of allowing the allocation of resources for controlling parasites in a more cost-effective way.²⁴ The cost-effectiveness of the screening and intervention approaches seemed to vary with the level of endemicity of the disease in the study community.

Our findings showed that the cost of diagnosis and intervention per person and per true positive case was 20- fold higher in the low-prevalence area, regardless of the approach.

Use of the questionnaire allowed reduction of the number of people necessary to investigate a village. It was estimated that a single person could easily investigate and treat over 700 individuals in a working day, provided that a questionnaire survey was systematically conducted. By contrast, at least 17 microscopists would be necessary to conduct laboratory investigations for 700 people within a day.

Our study confirmed that the questionnaire investigating the habit of eating raw freshwater fish was a rapid, cost-effective and operationally feasible tool for the identification of individuals at risk of clonorchiasis. It can also raise public awareness and promote participation of local residents in clonorchiasis control activities.¹³ The approach would be the most cost-effective when applied in high prevalence areas. Geographical mapping of high-risk areas prior to screening is, therefore, recommended to maximize the cost performance of the intervention activities. Finally, additional validation of the approach is needed before it is widely applied to other local settings. In particular, validation of screening for opisthorchiasis is required, the transmission routes of which are presumably identical to those of clonorchiasis.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

We are indebted to the staff of the National Institute of Malariology, Parasitology and Entomology (Hanoi) for technical assistance. We also thank the active co-operation of the authorities of the Department of Health on a provincial, district and commune level as well as the local health staff and residents of Kim Son district of Ninh Binh province and Luong Son district of Hoa Binh province, Vietnam.

Funding: None.

References

1. Sayasone S, Odermatt P, Phoumindr N, Vongsaravane X, Sensombath V, Phetsouvanh R, et al. Epidemiology of *Opisthorchis viverrini* in a rural district of southern Lao PDR. *Trans R Soc Trop Med Hyg.* 2007; 101:40–7. [PubMed: 16828134]
2. Keiser J, Utzinger J. Emerging foodborne trematodiasis. *Emerg Infect Dis.* 2005; 11:1507–14. [PubMed: 16318688]
3. WHO. Report of Joint WHO/FAO workshop on foodborne trematode infections in Asia. Manila, Philippines: World Health Organization Regional Office for the Western Pacific; 2004. RS/2002/GE/40 (VTN)
4. Crompton, DWT., Savioli, L. Handbook of helminthiasis for public health. Boca Raton: Taylor & Francis; 2006.
5. Thi Cam TD, Yajima A, Viet KN, Montresor A. Prevalence, intensity and risk factors for clonorchiasis and possible use of questionnaires to detect individuals at risk in northern Vietnam. *Trans R Soc Trop Med Hyg.* 2008; 102:1263–8. [PubMed: 18632126]
6. Kino H, Inaba H, Van De Nguyen, Van Chau Le, Dang Thanh Son, Hoan Thi Hao, et al. Epidemiology of clonorchiasis in Ninh Binh province, Vietnam. *Southeast Asian J Trop Med Public Health.* 1998; 29:250–4. [PubMed: 9886107]
7. Zhang R, Gao S, Geng Y, Huang D, Yu L, Zhang S, et al. Epidemiological study on *Clonorchis sinensis* infection in Shenzhen area of Zhujiang delta in China. *Parasitol Res.* 2007; 101:179–83. [PubMed: 17216484]
8. WHO. The schistosomiasis manual. Geneva: World Health Organization; 1995.
9. Katz N, Chaves A, Pellegrino J. A simple method for quantitative stool thick-smear technique in schistosomiasis mansoni. *Rev Inst Med Trop Sao Paulo.* 1972; 14:397–400. [PubMed: 4675644]
10. De NV, Murrell KD, Cong LD, Cam PD, Chau LV, Toan ND, et al. The foodborne trematode zoonoses of Vietnam. *Southeast Asian J Trop Med Public Health.* 2003; 34(Suppl 1):12–34. [PubMed: 12971505]
11. Mafe MA, von Stamm T, Utzinger J, N'Goran EK. Control of urinary schistosomiasis; an investigation into the effective use of questionnaires to identify high-risk communities and individuals in Niger State, Nigeria. *Trop Med Int Health.* 2000; 5:53–63. [PubMed: 10672206]
12. Lengeler C, Makwala J, Ngimbi D, Utzinger J. Simple school questionnaires can map both *Schistosoma mansoni* and *Schistosoma haematobium* in the Democratic Republic of Congo. *Acta Trop.* 2000; 74:77–87. [PubMed: 10643911]
13. Lengeler C, Utzinger J, Tanner M. Questionnaires for rapid screening of schistosomiasis in sub-Saharan Africa. *Bull World Health Organ.* 2002; 80:235–42. [PubMed: 11984610]
14. Ongom VL, Bradley DJ. The epidemiology and consequences of *Schistosoma mansoni* infection in West Nile, Uganda. I. Field studies of a community at Panyagoro. *Trans R Soc Trop Med Hyg.* 1972; 66:835–51. [PubMed: 4540028]
15. Arap Siongok TK, Mahmoud AA, Ouma JH, Warren KS, Muller AS, Handa AK, et al. Morbidity in schistosomiasis mansoni in relation to intensity of infection: study of a community in Machakos, Kenya. *Am J Trop Med Hyg.* 1976; 25:273–84. [PubMed: 1259088]
16. Hiatt RA, Gebra-Medhin M. Morbidity from *Schistosoma mansoni* infections: an epidemiologic study based on quantitative analysis of egg excretion in two highland Ethiopian villages. *Am J Trop Med Hyg.* 1977; 26:473–81. [PubMed: 869101]
17. Utzinger J, N'Goran EK, Esse Aya CM, Acka Adjoua C, Lohourignon KL, Tanner M, et al. *Schistosoma mansoni*, intestinal parasites and perceived morbidity indicators in schoolchildren in a rural endemic area of western Côte d'Ivoire. *Trop Med Int Health.* 1998; 3:711–20. [PubMed: 9754666]
18. Booth M, Mayombana C, Machibya H, Masanja H, Odermatt P, Utzinger J, et al. The use of morbidity questionnaires to identify communities with high prevalence of schistosome or geohelminth infections in Tanzania. *Trans R Soc Trop Med Hyg.* 1998; 92:484–90. [PubMed: 9861358]
19. Gryseels B. The morbidity of schistosomiasis mansoni in the Rusizi Plain (Burundi). *Trans R Soc Trop Med Hyg.* 1988; 82:582–7. [PubMed: 3151415]

20. Lengeler C, Savigny DD, Mshinda H, Mayonbana C, Tayari S, Hatz C, et al. Community-based questionnaires and health statistics as tools for the cost-efficient identification of communities at risk of urinary schistosomiasis. *Int J Epidemiol.* 1991; 20:796–807. [PubMed: 1955266]
21. Lengeler C, Kilima P, Mshinda H, Morona D, Hatz C, Tanner M. Rapid, low-cost, two-step method to screen for urinary schistosomiasis at the district level: the Kilosa experience. *Bull World Health Organ.* 1991; 69:179–89. [PubMed: 1907220]
22. Guyatt H, Brooker S, Lwambo NJ, Siza JE, Bundy DA. The performance of school-based questionnaires of reported blood in urine in diagnosing *Schistosoma haematobium* infection; patterns by age and sex. *Trop Med Int Health.* 1999; 4:751–7. [PubMed: 10588769]
23. Zhou H, Ross AGP, Hartel GF, Sleight AC, Williams GM, McManus DP, et al. Diagnosis of schistosomiasis japonica in Chinese schoolchildren by administration of a questionnaire. *Trans R Soc Trop Med Hyg.* 1998; 92:245–50. [PubMed: 9861388]
24. Vlassoff C, Tanner M. The relevance of rapid assessment to health research and interventions. *Health Policy Plann.* 1992; 7:1–9.

Table 1

Diagnostic performance of the reported habit of eating raw fish to detect the risk of infection with clonorchiasis in the first survey in Luong Son district, Hoa Binh province in 2007 ($n = 155$) and the second survey in Kim Son district, Ninh Binh province between 1999 and 2000 ($n = 1155$) in northern Vietnam

Study site	Prevalence of infection assessed parasitologically (%)	Prevalence of positive answers to the question (%)	Diagnostic performance (%)			
			Sensitivity	Specificity	PPV	NPV
Luong Son, Hoa Binh	1	23	100	78	6	100
Kim Son, Ninh Binh	25	56	98	58	45	99

PPV: positive predictive value; NPV: negative predictive value.

Table 2

Cost estimates for the three diagnostic and intervention approaches to clonorchiasis in the first survey in Luong Son district, Hoa Binh province in 2007 ($n = 155$) and the second survey in Kim Son district, Ninh Binh province between 1999 and 2000 ($n = 1155$) in northern Vietnam

Diagnostic method by study area	No. targeted	No. (%) positive	No. treated	Total cost (US\$)	Cost per person (US\$)	Cost per true positive case (US\$)
Luong Son, Hoa binh						
Stool examination of the whole population + treatment of those infected	151	2 (1)	2	709.47	4.70	354.73
Screening for a habit of eating raw fish using a questionnaire then drug treatment for those eating raw fish			35	27.63	0.18	13.82
Mass treatment for the whole population			151	45.12	0.30	22.56
Kim Son, Ninh Binh						
Stool examination of the whole population + treatment of those infected	1155	289 (25)	289	5518.06	4.78	19.09
Screening for a habit of eating raw fish using a questionnaire then drug treatment for those eating raw fish			648	244.72	0.21	0.85
Mass treatment of the whole population			1155	327.61	0.28	1.13