Norhidayu Sahimin <ayusahimin@gmail.com>

Acceptance Letter Manuscript MS : 1498/21
1 message

editor-MSPTM <editor.msptm@gmail.com>  
To: Norhidayu Sahimin <ayusahimin@gmail.com>  
Wed, Jan 15, 2020 at 9:34 AM

Dr. Norhidayu Sahimin  
Tropical Infectious Diseases Research and Education Centre (TIDREC),  
University of Malaya,  
Kuala Lumpur, Malaysia.

Dear Dr,

The Editorial Team of Tropical Biomedicine is pleased to inform you that your manuscript MS 1498/21 “Post-era mass drug administration: an update on intestinal parasitic infections in urban poor communities in Peninsular Malaysia” by Sahimin, N., Abd Khalil, N.S., Lewis, J.W. and Mohd Zain, S.N. has been accepted for the publication. This manuscript will be published in June Issue Volume 37 No 2, 2020. Thank you for submitting your manuscript in Tropical Biomedicine Journal.

If you have any inquiries please contact us at editor.msptm@gmail.com

Yours sincerely,  
Stephen Ambu  
Editor  
Tropical Biomedicine

Important note - new email address for editor

MSPTM have moved to a new website server.

The process of change has terminated the use of our old editor email (editor@msptm.org)

As such our new email address = editor.msptm@gmail.com

Please use the gmail address for all communications and submissions to editor of the Tropical Biomedicine journal

(signature updated on June 2017)
On Mon, Jan 13, 2020 at 10:30 AM Norhidayu Sahimin <ayusahimin@gmail.com> wrote:

Dear Editor,

Thank you for providing us with the comments, suggestions and concerns of the referees. We have now amended our ms taking into consideration all the issues raised by the two reviewers. Thank you.

Regards,

Norhidayu Sahimin, PhD
Post-Doctoral Research Fellow
Tropical Infectious Diseases Research and Education Centre (TIDREC)
University of Malaya, Kuala Lumpur, Malaysia.
Tel: 603 79677027 ext. 2700 / 6012-3639245
Email: ayusahimin@um.edu.my

On Mon, Dec 30, 2019 at 10:29 AM editor-MSPTM <editor.msptm@gmail.com> wrote:

Dear author,

We received two reports for your MS submitted to our journal. Please revise and resubmit to us within 90 days. Please also ensure that your MS will be formatted according to our journal style (i.e., abbreviated author names, references, etc).

Thank you.

Best wishes,
Editor

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(signature updated on June 2017)

On Mon, Nov 11, 2019 at 4:53 PM editor-MSPTM <editor.msptm@gmail.com> wrote:

Dear Dr. Norhidayu Sahimin,

Thank you for submitting your manuscript in Tropical Biomedicine. Your manuscript will be sent for review and we will inform you once we have received a response from reviewer. If you are not a member of MSPTM (Malaysian...
Society of Parasitology & Tropical Medicine) you will be required to pay page charges once your article is accepted.

For future reference regarding your manuscript please quote our reference number MS : 1498/21.

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* The Tropical Biomedicine is a softcopy journal. The paper will not be uploaded unless payment is made.
* USD200 per manuscript for papers accepted for publication starting from January 2016.
* For papers accepted prior to 2016, page charges apply @ USD20 per page.
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Thank you.

Stephen Ambu
Editor

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(signature updated on June 2017)

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On Mon, Nov 11, 2019 at 4:21 PM Norhidayu Sahimin <ayusahimin@gmail.com> wrote:

Dear Editor,

On behalf of corresponding author, Assoc. Prof. Dr. Siti Nursheena Mohd Zain, we are pleased to submit our manuscript entitled "Post-era mass drug administration: an update on intestinal parasitic infections in urban poor communities in Peninsular Malaysia" for consideration as a research article in Tropical Biomedicine. We confirmed that this manuscript has not been previously published and is not under consideration in the same or substantially similar form in any other peer-reviewed media.

Thank you.
Regards,
Dr. Norhidayu Sahimin
012-3639245

Letter Journal Acceptance.pdf
281K
Post-era mass drug administration: an update on intestinal parasitic infections in urban poor communities in Peninsular Malaysia

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Abstract

The health impact of a Malaysian national helminth control program which provided school-based anthelmintic chemotherapy from 1974 to 1983 was assessed after three decades post MDA and also to identify associated risk factors in urban poor communities. Stool samples collected among selected urban poor communities and were screened using the formalin ethyl-acetate concentration technique. Overall, residents were moderately (18.9%; n=39/206) infected with at least one species of helminth and/or protozoan, with a higher infection recorded amongst PPR flat residents (22.5%). Waste disposal was the main risk factor for *Ascaris lumbricoides* infections (n=33; 16.0%), whereas age, education and source of drinking water were significant risk factors for cryptosporidiosis. Infections continue to persist despite the government’s efforts to improve health through the provision of basic amenities to the general public. Higher prevalence values amongst PPR flat dwellers suggests the need to implement targeted preventive and chemotherapeutic measures, in addition to improvements in health awareness and waste management.

Keywords: Anthelmintic drugs, Malaysia, Parasitic infection, Urbanization
Introduction

Malaysia has undergone a cumulative growth in urbanization from 43.2% (1989) to 76% (2018) resulting in an urban population boom from 27% (1970) to 71% (2010) (Siwar et al., 2016) and a downward trend in the incidence of urban poverty over the past three decades from 16.5% in 1970 to 1.0% in 2012 (Sherina et al., 2011; CIA, 2019). However, the number of urban poor residents in cities is still considerably large (Zainal et al., 2012), with pockets of urban poverty remaining in different states of the country due to the migration of low-income groups from rural to urban areas. This has also been accompanied by the inflow of foreign workers and a rise in the cost of living. The population boom over such a short time scale has exerted pressure on local governments especially in fulfilling provision for services and infrastructures, creating job opportunities and providing houses for urban dwellers (Elhadary & Samat, 2012). Inadequate amenities and a housing shortage have led to the deterioration of living standards and an increase in urban environmental deterioration, pollution, congestion, diseases, squatters, improper dumping of garbage and a mismanagement of sanitation services (Elhadary & Samat, 2012). The more recent deterioration of living standards among the urban population was highlighted by UNICEF (2018) in that 99.7% of children occupying low cost flats in Kuala Lumpur live in poverty and 7% in absolute poverty.

Southeast Asia (SEA) has the highest reported prevalence of soil-transmitted helminths (STHs) worldwide with infections occurring in 11 SEA countries (Jex et al., 2018). STHs have not only been recognized as a major public health problem since the 1970s in Malaysia (Bisseru & Ahmad, 1970), but also continue to be a concern especially among the poverty-stricken
communities (Sinniah et al., 2014). Studies on different population groups and demographic profiles have provided evidence of variable prevalence of gastrointestinal helminths and protozoans especially among groups such as the Orang Asli (44.33-99.2%) (Al-Mekhlafi et al., 2008; Nas et al., 2013) plantation and rural communities (32.3-70.0%) (Chia et al., 1978; Al-Mekhlafi et al., 2008; Sinniah et al., 2014) urban dwellers (20.6-90.9%) (Chia et al., 1978; Sinniah et al., 2014), fishing communities (54.2-98.0%) (Anuar et al., 1987; Sinniah et al., 1988), flat dwellers (5.1-57.0%) (Kan, 1987; Sinniah et al., 2002; Sinniah et al., 2014) and migrant workers in Malaysia (13.1%-62.9%) (Sahimin et al., 2016; Sahimin et al., 2018).

A national helminth control program was undertaken by the Ministry of Health Malaysia from 1974 to 1983 to improve the standards of education, sanitation and anthelminthic treatment exclusively for school children. Several studies have shown a dramatic decline in infections among urban dwellers (90.9% in 1978 to 20.6% in 2014) (Chia et al., 1978, Sinniah et al., 2014), flat dwellers (57% in 1983 to 5.5% in 2014) (Kan, 1983; Sinniah et al., 2014) and rural communities (90.0% in 1970 to 32.3% in 2014) (Bisseru & Ahmad, 1970; Sinniah et al., 2014) reflecting an improvement in their living conditions. However, a rapid increase in the urban population over a relatively short period of time exerts pressure on city living that may impact on the quality of life especially as the population becomes more vulnerable to a range of communicable and non-communicable disease. Poverty can also restrict accessibility to quality healthcare and education, whilst a poor educational background perpetuates health problems through little or lack of awareness of good health practices. Therefore, the present study was undertaken to assess the prevalence of STHs and protozoan infections following the lapse of
MDA more than 3 decades and also to identify associated risk factors in urban poor communities.

**Materials and Methods**

**Recruitment of volunteers, questionnaire and ethical clearance**

The present investigation was carried out through a social well-being community program in the states of Wilayah Persekutuan Kuala Lumpur, Selangor and Malacca. The study cohort comprised residents from Program Perumahan Rakyat (PPR) flat developments and other urban poor settlements, which consisted of communities from villages within the urban municipality and orphans and children from selected low-income childcare centers. PPR low-cost flats are high density housing units for qualified individuals or families categorized as B40 with a total household income of less than RM 2,500 per month (RMK11 Speech Text, 2015). The Economic Planning Unit (EPU) indicated that 2.3% B40s in Kuala Lumpur, 12.3% in Selangor and 2.4% in Malacca (Data Asas Malaysia, 2015) comprising 2.7 million households survived on a mean monthly income of RM 2,537 (RMK11 Speech Text, 2015).

It should be noted that urban villages comprise original settlements, which were created from rapid urbanization and economic development of cities, within an urban boundary with its own organizations and nearest to a city center (Hao, 2015). The Welfare Department recorded 2.3 million children below 4 years of age with only 4,302 registered childcare centers and 3,173
caregivers certified (Shah, 2018). Therefore, children living in cramped spaces in selected orphanages and childcare centers were also included as part of this study cohort.

Residents from the PPR flats and other urban poor settlements were recruited from Kuala Lumpur (urbanization = 100%), Selangor (urbanization = 91.4%) and Malacca (urbanization = 86.5%) from October 2016 to February 2018 as in Table 1. All sampling sites were characterized with a tropical climate comprising high levels of humidity and temperature ranging between 30 °C and 36 °C plus periodic rainfall during the year.

Using questionnaires, residents were asked to provide details on socio-demographic, factors, environmental health, lifestyle habits and recent illnesses. Each individual was required to answer all questions prior to consent being obtained for stool collection. This study was approved by the Medical Ethics Committee of the University Malaya Medical Centre (UMMC), Malaysia (Reference number: MEDIC NO: 20143-40). All adults and childrens’ guardians were provided with written and informed consent to participate in the study.

Sample collection and screening

Following collection, stool samples were immediately preserved in 2.5% potassium dichromate to prevent parasite eggs /oocysts from disintegrating and maintained at 4 °C until required. For the formalin ethyl-acetate concentration technique, approximately 1-2 g of each faecal sample were mixed with 7 ml formalin and 3 ml ethyl acetate and centrifuged for 5 min at 2500 rpm. Following centrifugation, a drop of pellet was placed on a clean glass slide and stained with Lugol’s iodine. Slides were examined under a light microscope at 10x and 40x.
magnification for the presence of helminths/protozoans. A portion of pellet was smeared on a second slide and left to dry. Once dried, each slide was fixed in methanol for 5 minutes, flooded with strong carbol fuchsin for up to 10 minutes, rinsed under tap water and then decolourised in 3% acid alcohol before final rinsing. Each slide was counterstained with 0.25% malachite green for 30 seconds, rinsed and blotted dry prior to examination under oil immersion at 1000x.

Statistical analysis

Prevalence data are shown with 95% confidence limits (CL95) as described by Rohlf & Sokal (1995) using bespoke software. Prevalence’s were analyzed using maximum likelihood techniques based on log linear analysis of contingency tables using the software package SPSS (Version 22). Infection was considered a binary factor (presence/absence of parasites) and analyses were conducted using intrinsic factors such as host sex (2 levels: males and females), age (7 age classes: those<12 years old, 12–18 years old, 19–24 years old, 25–34 years old, 35-44 years old, 45-55 years old and those >55 years old) and ethnicity (3 ethnics: Malay, Chinese and Indian). Extrinsic factors included location (3 locations: Kuala Lumpur, Selangor and Malacca), settlements (2 categories: flats/ PPR house and others), education attainment (4 levels: primary school, secondary school, university and no formal schooling) and employment status (employed and unemployed).

Results

Socio-demographic factors
Stool samples from 206 participants were examined from Pantai Dalam, Kuala Lumpur (n=70; 34.0%), Bukit Bintang Kuala Lumpur (n=22; 10.7%), Bandar Tun Razak, Kuala Lumpur (n=9; 4.4%), Gombak, Selangor (n=76; 36.9%) and Alor Gajah, Malacca (n=29; 14.1%) as shown in Figure 1 and Table 1.

Demographic data of stool samples were obtained from 55.3% females and 44.7% males. The majority were children less than 12 years old (n=60; 29.1%) and predominantly Malay (n=176; 85.4%), followed by Indian (n=16; 7.8%) and Chinese (n=14; 6.8%). A large proportion of the population resided in Kuala Lumpur (n = 147; 71.4%) followed by Selangor (n=30; 14.6%) and Malacca (n=29; 14.1%) with the majority of the population residing in urban settlements (n=135; 65.5%) or low cost PPR flats (n=71; 34.5%).

Prevalence of intestinal parasitic infections

An overall infection value of 18.9% (n=39) was recorded on Table 2, with the roundworm, *Ascaris lumbricoides* being the most dominant helminth species (n=33; 16.0%), followed by the protozoans *Cryptosporidium* spp. (n=5; 2.4%) and *Giardia* sp. (n=1; 0.5%). Only one case of *Giardia* sp. was detected [0.5% (0.01–2.67)], from a female child below 12 years old.

Intrinsic / extrinsic factors and parasitic infections

Infections with *A. lumbricoides* and *Cryptosporidium* spp. were analyzed using the minimum sufficient model and the backwards stepwise selection, relative to intrinsic factors such
as host age, sex and ethnicity in Table 2. In the case of *A. lumbricoides*, ethnicity ($X^2_4 = 7.005, P = 0.030$) was the only factor found to be significant, although this might be attributed to disproportionate group sampling. Host age ($X^2_4 = 12.642, P = 0.049$) appeared to be the only significant risk factor in *Cryptosporidium* spp. infections.

Of four extrinsic factors considered such as location, living settlement, education attainment and employment status, none were found to significantly influence the prevalence of *A. lumbricoides*. On the other hand, a significant increase in *Cryptosporidium* spp. infections was associated with the lack of both education attainment ($X^2_1 = 12.642, P = 0.005$) and the status of employment ($X^2_1 = 4.067, P = 0.044$).

**Lifestyle factors and parasitic infections**

Of the six lifestyle factors considered in Table 2, including preferred types of drinking water, waste disposal method, preferred cooking of meat, eating styles, frequency of hand washing and pet keeping, only waste disposal and filtration of drinking water showed significant higher prevalences of *A. lumbricoides* ($X^2_1 = 3.848, P = 0.050$) and *Cryptosporidium* spp. ($X^2_1 = 4.182, P = 0.041$) respectively.

**Discussion**

Intestinal parasitic infections (IPI) occur primarily in populations from low income countries lacking proper facilities for sanitation. Human infections usually occur via the oral
faecal route and from contaminated food and water supplies. In Malaysia, the occurrence of IPI have declined from 52.4% in the 1970’s to 1.0% in 2012, largely due to a 96% and 98.2% improvement in access to sanitation facilities and drinking water sources respectively and in both urban and rural areas (CIA, 2019). However, IPI continues to persist with moderate infections (18.9%) occurring in the urban poor population. PPR flat dwellers showed an increase in prevalence from 8.1% (Sinniah et al., 2002) to 22.5% (present study). On the other hand, the prevalence of infection among other urban poor settlements was 17.0% (present study) which demonstrated a dramatic decline compared with 90.9% in 1978 (Chia et al., 1978). PPR was initially established by the Ministry of Housing & Local Government in Malaysia to fulfill the need for low cost housing, following demolition of squatter dwellings. Through a “zero slum” settlement program by the year 2020, local authorities successfully relocated slum dwellers through an affordable housing scheme to own a modest unit in a multi-storey low cost flat equipped with clean water supply, sanitation and electricity. But the majority of PPR flat developments in Kuala Lumpur are vastly overcrowded with indiscriminate methods of waste disposal and this situation is reflected in the relatively high prevalence (22.5%) of parasitic infections in residents of PPR flats in the present study compared with previous studies (Kan, 1983; Sinniah et al., 2002; Sinniah et al., 2014).

The three parasite species identified in the present study included the ascarid nematode *Ascaris lumbricoides* and two protozoan species *Cryptosporidium* spp. and *Giardia* sp. Previously, 6 parasite species were reported by Sinniah et al. (2014) from urban areas including *A. lumbricoides, Trichuris trichiura, Blastocystis hominis, Giardia* sp., *Entamoeba histolytica*
and *E. coli* and up to 4 species from flat dwellers including *A. lumbricoides*, *T. trichiura*, *B. hominis* and *E. coli*. The trichurid nematode, *Trichuris trichura* rather than *A. lumbricoides* appeared to be the most prevalent species reported by Sinniah *et al.* (2014) but the present results concur with global findings highlighting *A. lumbricoides* as the most common helminth occurring in underprivileged communities (WHO, 2018). High numbers of *A. lumbricoides* eggs have also been recently reported as contaminating public parks in Peninsular Malaysia (Rahman *et al.*, 2015).

In the present study, the significant relationship between the prevalence of *A. lumbricoides* and host ethnicity ($X^2_a = 7.005, P < 0.030$) amongst urban poor dwellers was likely to be attributed to disproportionate group sampling rather than racial susceptibility or resistance to infection. In the time frame available for this study it was not possible to assess more subjects as many refused to co-operate for understandable reasons, but nevertheless the transmission of *A. lumbricoides* among urban poor dwellers appears to be related to poor waste management. Indiscriminate garbage disposal, which is particularly rampant in PPR low-cost flats, is not only a matter of poor civic consciousness, but is also attributed to the lack of maintenance of functioning elevators. Without such a facility, residents tend to dispose rubbish directly and indiscriminately at the ground level. This poor attitude then attracts stray animals and pests to scavenge for food, litter and contaminate the environment with *A. lumbricoides* eggs. Both poor hygiene practices and behavior in turn facilitate the transmission of roundworm infections especially to children in the community.
The presence of intestinal protozoan infections in this study cohort is predominantly dependent on human behavior, particularly during ingestion and defecation, personal hygiene, and cleanliness. Low prevalences of Cryptosporidium spp. were recorded among the urban poor, although prevalences do vary among different cohort groups (Sahimin et al., 2018). In the present study, Cryptosporidium spp. was particularly evident in children below 12 years old and those with no formal education and unemployed. Food and water-borne illnesses due to Giardia sp. and Cryptosporidium spp. is uncommon in Malaysia (Sahimin et al., 2018), but the present findings confirm that transmission of these parasitic protozoan occurs through contaminated water supplies, particularly through the consumption of filtered rather than boiled water. Minute oocysts of Cryptosporidium sp., 2-6µm in size, not only readily pass through filtration mechanisms within water dispensers but also resists most chemical disinfectants and chlorination. Oocysts on the other hand are susceptible to drying and ultraviolet sunlight but can be eradicated by boiling drinking water.

An examination of larger numbers of stool samples from the three selected geographical sites in Malaysia would have been desirable but barriers shown by the urban poor population including embarrassment, fear of results, concerns relating to hygiene and contamination, discretion and privacy are difficult to overcome. Personal gain must be highlighted as the main incentive for sampling and returning a stool sample (Lecky et al., 2014) together with the provision of an information leaflet on stool collection.

**Conclusion**
Overall prevalences of infection amongst urban poor communities in parts of Kuala Lumpur, Selangor and Malacca mainly fluctuate in line with both the downward trend of poverty and acceleration of urbanization. Infection values recorded in the present investigation are indicative of the Malaysian Government’s successful efforts to improve health through the provision of clean water supplies and good sanitation facilities to the general public. However, intestinal parasitic infections continue to persist particularly amongst occupants of low cost PPR flats (22.5%) and according to World Health Organization (WHO), deworming treatment should be given once a year when the baseline prevalence of soil-transmitted helminth infections in the community is over 20%. This intervention should be included among the study cohort in addition to programs encouraging healthy behaviors. In addition, overall improvements are still required for better public services such as regular rubbish collection and maintenance of lifts in these developments.

Acknowledgments. The authors wish to extend their grateful thanks to the Ministry of Health, Malaysia for their co-operation and support in this study. Special thanks are also extended to all medical staff from the University Malaya Medical Centre for their technical assistance. This research work was funded by University of Malaya (GPF 012B-2018).

REFERENCES


Figure 1: Location of study sites from urban poor communities in Peninsular Malaysia.
Table 1: Study locations with GPS coordinates and number of participants

<table>
<thead>
<tr>
<th>Area</th>
<th>Coordinates</th>
<th>Number of participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alor Gajah, Malacca</td>
<td>2.373966, 102.211406</td>
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<tr>
<td>Gombak, Selangor</td>
<td>3.283647, 101.607723</td>
<td>76</td>
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<tr>
<td>Bandar Tun Razak, Kuala Lumpur</td>
<td>3.091852, 101.721012</td>
<td>9</td>
</tr>
<tr>
<td>Bukit Bintang, Kuala Lumpur</td>
<td>3.146838, 101.709775</td>
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<td>Pantai Dalam, Kuala Lumpur</td>
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<td><strong>Total</strong></td>
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Table 2: Prevalence’s of intestinal parasitic infections amongst selected urban communities in Peninsular Malaysia, relative to socio-economic and lifestyle factors; *significant at 0.05

<table>
<thead>
<tr>
<th>Factors</th>
<th>Helminth</th>
<th></th>
<th>Protozoa</th>
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<td></td>
<td></td>
<td>[% 95% CI]</td>
<td>P-value</td>
<td>[% 95% CI]</td>
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<tr>
<td>Age</td>
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<tr>
<td>&lt;12 (n=60)</td>
<td>11.6[4.8-22.5]</td>
<td>0.661</td>
<td>8.3[2.7-18.4]</td>
<td><strong>0.049</strong> *</td>
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<td>18-24 (n=12)</td>
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<td>35-44 (n=26)</td>
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<td>45-55 (n=27)</td>
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<td>&gt;55 (n=55)</td>
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<td>Ethnicity</td>
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<td>Malay (n=176)</td>
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<td><strong>Extrinsic Factors</strong></td>
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<td>No formal education (n=60)</td>
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<td>8.3[2.7-18.3]</td>
<td><strong>0.005</strong> *</td>
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<tr>
<td>Preferred type of drinking water</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boil (n=132)</td>
<td>15.9[10.1-23.2]</td>
<td>0.954</td>
<td>0.7[0.0-4.1]</td>
<td><strong>0.041</strong> *</td>
</tr>
<tr>
<td>Filter (n=74)</td>
<td>16.2[8.6-26.6]</td>
<td></td>
<td>5.4[1.4-13.2]</td>
<td></td>
</tr>
<tr>
<td>Waste management method</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local municipality (n=107)</td>
<td>11.2[5.9-18.7]</td>
<td><strong>0.05</strong> *</td>
<td>1.8[0.2-6.5]</td>
<td>0.739</td>
</tr>
<tr>
<td>Unsatisfactory method (n=99)</td>
<td>21.2[13.6-30.5]</td>
<td></td>
<td>3.0[0.6-8.6]</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: n, total number of participants; CI, confidence interval.