

# Fecal Carriage Rate of Extended-Spectrum Beta-Lactamase-Producing *Enterobacteriaceae* as a Proxy Composite Indicator of Antimicrobial Resistance in a Community in Thailand

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**Background.** Increasing awareness of and understanding about antimicrobial resistance (AMR), promoting changes in behavior, and monitoring of AMR in the community are challenging, as AMR is associated with many contributing factors that are difficult to assess individually. This study aimed to determine the effectiveness of a community-based AMR campaign for improving awareness, understanding, and behavior relating to antibiotic use and AMR in Thailand and to assess if fecal carriage of extended-spectrum beta-lactamase (ESBL)-producing *Enterobacteriaceae* could be a proxy composite indicator of AMR in the community.

**Methods.** This study was conducted in 4 communities that are home to approximately 400 000 people. A self-administered questionnaire on awareness, understanding, and behavior relating to antibiotic use and AMR was responded to by 20 521 and 19 634 adults before and immediately after the AMR campaign, respectively, at the household level. Fecal samples were collected from 534 adults before the AMR campaign and from 709 adults at 18 months after the AMR campaign to determine presence of ESBL-producing *Enterobacteriaceae*.

**Results.** Awareness, understanding, and behavior relating to antibiotic use and AMR, as assessed by a self-administered questionnaire, were significantly improved after the AMR campaign. The fecal carriage rate of ESBL-producing *Enterobacteriaceae* decreased from 66.5% before to 44.6% after the AMR campaign ( $P < .01$ ).

**Conclusions.** Our AMR campaign was effective for improving awareness, understanding, and behavior relating to antibiotic use and AMR among people in the community at the household level, and the prevalence of fecal carriage of ESBL-producing *Enterobacteriaceae* seemed to be decreased after the AMR campaign. Fecal carriage rate of ESBL-producing *Enterobacteriaceae* may be a proxy composite indicator of AMR in the community.

**Keywords.** antimicrobial resistance; community; extended-spectrum beta-lactamase-producing *Enterobacteriaceae*; fecal carriage; indicator.

Antimicrobial resistance (AMR) has an enormous adverse impact on humankind in terms of morbidity, mortality, and economic loss [1]. It also unfavorably influences animal health, food security, environmental well-being, and socioeconomic development, which together threaten delivery of the 2030 Agenda for Sustainable Development [2]. Several reports on AMR burden in human health in Thailand also revealed a vast health and economic burden [3–6]. The World Health

Organization (WHO), the World Organisation for Animal Health (OIE), and the Food and Agriculture Organization of the United Nations (FAO) all endorsed a global action plan on AMR in 2015 [7]. The global action plan on AMR includes 5 strategic objectives aimed at ensuring the world's continued ability to treat and prevent infections with effective and safe medicines that are quality-assured, that are used in a responsible way, and that are accessible to all who need them. The first strategic objective in the global action plan on AMR was to raise awareness and understanding of AMR and to promote behavior change through effective communication, education, and training programs that target different audiences, including the general public and relevant personnel in human health, animal health, and agricultural practice.

Extended-spectrum beta-lactamase (ESBL)-producing *Enterobacteriaceae* is the most common antibiotic-resistant bacteria causing community-acquired infection in Thailand, and the prevalence of infection caused by this type of multidrug-resistant bacteria has been increasing in Thailand [8–10].

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Fecal carriage of ESBL-producing *Enterobacteriaceae* is a risk factor associated with infection caused by ESBL-producing *Enterobacteriaceae* [11–13]. The prevalence of fecal carriage of ESBL-producing *Enterobacteriaceae* has been found to be much higher in Southeast Asia than in other regions of the world [14]. The prevalence of fecal carriage of ESBL-producing *Enterobacteriaceae* in Thai people in many communities is higher than 50% [15–18]. Fecal carriage of ESBL-producing *Enterobacteriaceae* in these people has been associated with consumption of antibiotics and consumption of food contaminated with ESBL-producing *Enterobacteriaceae*. These factors may also be contributing to a high prevalence of fecal carriage of ESBL-producing *Enterobacteriaceae* among travelers after visiting Southeast Asia [19–26]. The carriers of ESBL-producing *Enterobacteriaceae* can transmit these multidrug-resistant bacteria to others, and they are at risk for developing ESBL-producing *Enterobacteriaceae* infection that is difficult to treat and has higher mortality than non-ESBL-producing *Enterobacteriaceae* infection [11, 12]. Fecal carriage of ESBL-producing *Enterobacteriaceae* is reversible. ESBL-producing *Enterobacteriaceae* in the gut of most travelers who acquired ESBL-producing *Enterobacteriaceae* disappeared within 1 year after they returned to their home country [21, 23, 25–28] where antibiotics cannot be given without a prescription, the foods contain no antibiotic residue and no contamination with ESBL-producing *Enterobacteriaceae*, and the levels of personal sanitation and hygiene are high.

Increasing awareness of and understanding about AMR, promoting changes in behavior among the general public, and monitoring of AMR in the community are challenging due to the fact that AMR is associated with many contributing factors that are difficult to assess individually. The aim of this study was to investigate the effectiveness of a community-based AMR campaign for improving awareness, understanding, and behavior relating to antibiotic use and AMR in Thailand and to assess if fecal carriage of ESBL-producing *Enterobacteriaceae* could be a proxy composite indicator of AMR in the community.

## METHODS

This study was approved by the Siriraj Institutional Review Board of the Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand.

### Study Communities

Four district-level communities within 1 northern province or 1 eastern province in Thailand were studied, and approximately 400 000 people living in 100 000 households were included. These communities had all levels of health care facilities (from drugstores to general hospitals), food animal farms, public water sources, and agricultural practices. These communities had 7933 village health volunteers (VHVs). A VHV was defined as an individual living in a community that is chosen by the

people of that community to communicate information about health promotion and disease prevention and control to people in that community. Each VHV was responsible for overseeing approximately 10 to 20 households.

### Development of the AMR Campaign Package

The AMR campaign package for improving awareness of and understanding about AMR and for promoting behavior change among people living in the community was developed based on information the research team received from in-depth interviews with local people, VHVs, and health personnel in all study communities. Such an AMR campaign package was developed, validated, and tested during January to December 2014. The AMR campaign package contained the key issues relating to the awareness, understanding, and behavior of people in the community relative to antibiotic use and prevention and containment of AMR, as shown in [Box 1](#).

The AMR campaign package media contained all appropriate and necessary information relating to the aforementioned key issues on antibiotic use and AMR. The communication material included (1) a 21-page flip sheet; (2) 4 brochures on the clinical features and management of the common cold, acute diarrhea, simple fresh traumatic wounds, and what the carrier of antibiotic-resistant bacteria should do; and 3) short video clips that illustrate the development, transmission, and consequence of antibiotic-resistant bacteria and that describe the true story of a patient who survived infection caused by antibiotic-resistant bacteria related to consumption of several courses of antibiotics purchased from a drugstore.

### Implementation of AMR Campaign

VHVs were the media persons that communicated AMR campaign information in the community according to the suggestions of people in the community. Each VHV asked 3 adults who were members of the households under his/her oversight to voluntarily respond to self-administered questionnaire 1 on awareness, understanding, and behavior relating to antibiotic use and AMR before implementing the AMR campaign during January to June 2015. Adults aged  $\geq 18$  years living in the study communities were invited to voluntarily collect their stool samples using Cary-Blair transport media to determine fecal carriage of ESBL-producing *Enterobacteriaceae* and to respond to the questionnaire designed to assess their risk of being an ESBL-producing *Enterobacteriaceae* carrier before implementing the AMR campaign during January to June 2015.

The research team organized intensive training on appropriate antibiotic use and AMR prevention and containment, as well as how to use the aforementioned media for the selected 72 VHVs who had good communication skills during July and October 2015. These well-trained VHVs then provided small group training sessions for their VHV peers (approximately 6300 VHVs) using the same media provided by the research

**Box 1. Key Issues Relating to the Awareness, Understanding, and Behavior of People in the Community on Antibiotic use and Prevention and Containment of AMR in the AMR Campaign Package**

Antibiotic is not an anti-inflammatory drug.

Antibiotic is a drug that can inhibit or kill bacteria, and it is classified by the Thailand Food and Drug Administration as a dangerous drug.

Antibiotic is not effective for alleviating pain.

Antibiotic cannot kill viruses, and it should not be used to treat the common cold, which is a viral condition.

Antibiotic is usually not necessary for the common cold, acute diarrhea, or simple fresh traumatic wounds.

Purchasing antibiotic or anti-inflammatory drugs from grocery stores, retail shops, and drugstores should be avoided.

Do not ask for antibiotic when seeking medical care from a health care facility.

If antibiotic is really needed and it is prescribed by a physician, the full course of the antibiotic should be taken.

Do not keep leftover antibiotic for future ailments.

Do not share antibiotic with others.

Antibiotic can induce antibiotic-susceptible bacteria in the gut of an individual who has taken antibiotic to become antibiotic-resistant bacteria that reside in the gut, and antibiotic-resistant bacteria can cause difficult-to-treat infection or fatal infection later on.

Antibiotic has side effects that can be fatal.

Antibiotic is also used in animals, and antibiotic-resistant bacteria can develop in animals that receive antibiotic.

Antibiotic residue is present in meat and other animal products if the withdrawal period of antibiotic use in animals is not sufficient.

An individual who consumes food contaminated with antibiotic-resistant bacteria or food containing antibiotic residue could become a carrier of antibiotic-resistant bacteria.

A measure to stop the production of antibiotic-resistant bacteria is avoidance of unnecessary use of antibiotic in humans and animals.

Measures to stop the acquisition and transmission of antibiotic-resistant bacteria are consumption of clean and cooked foods and good personal sanitation and hygiene, such as handwashing after contact with contaminated materials and before eating food.

Abbreviation: AMR, antimicrobial resistance.

team during November 2015 to March 2016. Each trained VHV then visited family members of the households under his/her oversight to communicate information about antibiotic use and AMR using the aforementioned media provided by the

research team. Each VHV asked 3 adults who were members of the households under his/her oversight to voluntarily respond to self-administered questionnaire 2 on awareness, understanding, and behavior relating to antibiotic use and AMR immediately after receiving AMR campaign information from the VHV during April to August 2016. Questionnaire 2 contained some content identical to that contained in questionnaire 1.

From November 2017 to February 2018 (~18 months after the AMR campaign in 2016), adults aged  $\geq 18$  years living in the study communities who had received communication on awareness, understanding, and behavior relating to antibiotic use and AMR from VHVs in 2016 were invited to voluntarily respond to self-administered questionnaire 3 on awareness, understanding, and behavior relating to antibiotic use and AMR. Questionnaire 3 contained some content identical to that contained in questionnaire 2. Adults aged  $\geq 18$  years living in the study communities were invited to voluntarily collect their stool samples using Cary-Blair transport media to determine fecal carriage of ESBL-producing *Enterobacteriaceae* and to respond to the questionnaire to assess their risk of being an ESBL-producing *Enterobacteriaceae* carrier at 18 months after AMR campaign.

None of the 3 questionnaires to assess awareness, understanding, and behavior relating to antibiotic use and AMR contained respondent identification information. However, the questionnaire to assess the respondent's risk of being an ESBL-producing *Enterobacteriaceae* carrier and the collected stool sample from each volunteer contained the same alpha-numeric code so that the volunteer could be notified of the culture result. The results of the stool cultures were sent to the same health promotion hospitals to which the volunteers initially brought their stool samples. The volunteers picked up the stool culture results that were kept in a sealed envelope labeled with each volunteer's code. The result of stool culture was accompanied by a brochure containing information on ESBL-producing *Enterobacteriaceae*, how to avoid acquiring it for the volunteer without ESBL-producing *Enterobacteriaceae*, and what to do to eliminate it for volunteers with ESBL-producing *Enterobacteriaceae*.

#### Stool Culture

Each fecal swab sample from Cary-Blair transport media was streaked on MacConkey agar supplemented with ceftriaxone 4 mg/L. The bacteria grown on the agar were identified up to the species level for *Enterobacteriaceae* (*Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter* spp., *Citrobacter freundii*, or *Edwardsiella tarda*). Determination of ESBL-producing *Enterobacteriaceae* was performed by double-disk synergy test using a ceftriaxone disk (30  $\mu$ g), ceftazidime disk (30  $\mu$ g), and amoxicillin/clavulanic acid disk (2:1 30  $\mu$ g) [29].

#### Sample Size and Data Analysis

The number of people who responded to the questionnaires on awareness, understanding, and behavior relating to antibiotic

use and AMR before and immediately after the AMR campaign was expected to be approximately 20 000 based on the suggestion that each participating VHV recruit 3 adult family members from the households under his/her oversight to voluntarily respond to the questionnaires. The number of people who provided stool samples for determination of ESBL-producing *Enterobacteriaceae* and who responded to the questionnaire to assess their risk of being an ESBL-producing *Enterobacteriaceae* carrier was at least 100 for each community, or at least 400 for 4 communities to detect a fecal carriage rate of ESBL-producing *Enterobacteriaceae* of 50%±10%.

Questionnaire response and ESBL-producing *Enterobacteriaceae* data were analyzed by descriptive statistics (mean, SD, percentage) and by inferential statistics for comparison of variables by the chi-square statistic or Fisher exact test. SPSS Statistics, version 16.0 (SPSS, Inc., Chicago, IL), was used to perform all data analyses. A *P* value ≤.05 was considered statistically significant.

## RESULTS

### Responses to Questionnaire on Awareness, Understanding, and Behavior Relating to Antibiotic Use and AMR

The responses to questionnaire on awareness, understanding, and behavior relating to antibiotic use and AMR from 20 521 adults before the AMR campaign and from 19 634 adults immediately after receiving AMR campaign information from VHVs are shown in Table 1. The characteristics of questionnaire respondents in terms of gender, age, marital status, and occupation were comparable between the before and after groups. Most respondents before the AMR campaign (73.1%–93.3%) believed that antibiotic and anti-inflammatory drugs were the same, and that belief was markedly decreased after the AMR campaign (12.1%–29.3%). Most respondents before the AMR campaign (91.1%) misunderstood that tetracycline, which is one of the most commonly used antibiotics in many communities in Thailand, is an anti-inflammatory drug, and this misunderstanding was much decreased after the AMR campaign (29.2%). Most respondents did not understand how AMR develops and is transmitted before the AMR campaign; however, most respondents understood this information after the AMR campaign. Most respondents were not aware that antibiotic-resistant infection is a fatal disease, that they could have antibiotic-resistant infection, that they could be contributing to the increase in prevalence of AMR, and that AMR is one of the major health problems in Thailand before the AMR campaign. After the AMR campaign, understanding about all of these important issues was substantially increased. After the AMR campaign, most respondents stated that they would stop their AMR-producing behaviors and their behaviors that lead to the acquisition and transmission of AMR. They also agreed that antibiotics should not be available for sale in grocery stores, retail shops, and drugstores; that people should not ask health personnel to provide unnecessary antibiotics; and that only antibiotics prescribed by a physician should be taken. After the AMR

campaign, most respondents thought that their awareness, understanding, and behavior relating to antibiotic use and AMR were much improved.

The responses to the questionnaire on awareness, understanding, and behavior relating to antibiotic use and AMR from 709 adults at 18 months after the AMR campaign are also shown in Table 1. The characteristics of the questionnaire respondents in terms of gender, age, marital status, and occupation were comparable to those of respondents surveyed immediately after the AMR campaign. The responses relating to awareness, understanding, and behavior of antibiotic use and AMR were also comparable to those given immediately after the AMR campaign. At 18 months after the AMR campaign, 82.7% of respondents stated that they avoided behaviors that were associated with AMR (eg, did not purchase antibiotics, did not ask health personnel to provide antibiotics, tried to consume clean and cooked food) over the past year, and 75.9% said that they informed and advised surrounding people to avoid using unnecessary antibiotics over the past year. However, some respondents at 18 months after the AMR campaign (16.4%–20.0%) admitted that they still purchased antibiotics from the grocery store, retail shop, or drugstore, and/or they asked health personnel to provide them with antibiotics over the past year.

### Prevalence of ESBL-Producing *Enterobacteriaceae* in Stool Samples

Baseline characteristics, such as gender, age, marital status, and occupation, of 534 adults before the AMR campaign and of 709 adults at 18 months after the AMR campaign who provided their stool samples for determination of ESBL-producing *Enterobacteriaceae* were similar. ESBL-producing *Enterobacteriaceae* were detected in 355 stool samples collected from 534 adults before the AMR campaign, for a prevalence of ESBL-producing *Enterobacteriaceae* in stool samples of 66.5% (95% confidence interval [CI], 62.5%–70.5%). ESBL-producing *Enterobacteriaceae* were detected in 316 stool samples collected from 709 adults at 18 months after the AMR campaign, for a prevalence of ESBL-producing *Enterobacteriaceae* in stool samples of 44.6% (95% CI, 40.9%–48.2%). The prevalence of ESBL-producing *Enterobacteriaceae* in stool samples after the AMR campaign was significantly lower than before the AMR campaign (32.9% decrease; *P* < .01). ESBL-producing *Enterobacteriaceae* isolated from all stool samples were *E. coli* (85.4%–87.1%), *K. pneumoniae* (2.6%–7.6%), *E. tarda* (6.4%–7.6%), *Enterobacter* spp. (0.2%–1.7%), and *C. freundii* (0.2%–1.5%).

### Responses to Questionnaire Designed to Assess a Respondent's Risk of Being an ESBL-Producing *Enterobacteriaceae* Carrier

Comparison of people with and without ESBL-producing *Enterobacteriaceae* in stool samples among 534 adults before the AMR campaign and among 709 adults after the AMR campaign is shown in Table 2. The factors significantly associated with being an ESBL-producing *Enterobacteriaceae* carrier included presence

**Table 1. Questionnaire Responses Compared Before, Immediately After, and 18 Months After the Antimicrobial Resistance Campaign**

Characteristics of Questionnaire Respondents and Questionnaire Topics	Questionnaire 1 Responses Before AMR Campaign (n = 20 521)	Questionnaire 2 Responses Immediately After AMR Campaign (n = 19 634)	Questionnaire 3 Responses at 18 Months After AMR Campaign (n = 709)
Female gender	58.2%	61.4%	62.4%
Mean age (SD), y	53.6 (12.4)	51.3 (11.9)	52.4 (13.2)
Married	63.3%	61.1%	66.2%
Farmer	28.8%	25.2%	24.1%
Had common cold, sore throat, diarrhea, dysuria, traumatic wound, fever, myalgia, or joint/back pain, within the previous year	11.5%–64.4%		
Received treatment at a health care facility	48.3%–49.7%		
Took antibiotic or anti-inflammatory drug	63.6%–77.9%		
Regular or frequent consumption of undercooked foods	36.6%		
Regular or frequent handwashing before eating food	31.7%		
Regular or frequent handwashing after toilet use	65.1%		
Regular or frequent consumption of water from open public water sources	21.6%		
Having any awareness about antibiotic-resistant organism	31.7%		
Understand the meaning of antibiotic-resistant organism	32.1%	88.9%	83.2%
Understand that antibiotic-resistant organism is antibiotic-resistant bacteria	27.3%	85.7%	83.4%
Understand the meaning of antibiotic	31.4%	88.6%	87.0%
Understand that antibiotic is anti-inflammatory drug	73.1%	12.1%	9.6%
Understand that antibiotic is antibacterial drug	28.6%	87.2%	86.5%
Understand that anti-inflammatory drug is antibiotic	93.3%	29.3%	20.7%
Know of the drug named Gano or TC-mycin	80.2%	83.2%	88.2%
Understand that Gano or TC-mycin is anti-inflammatory drug	91.1%	29.2%	20.0%
Understand that AMR is associated with consumption of anti-inflammatory drug	47.2%	22.4%	21.2%
Understand that AMR is associated with consumption of antibiotic	30.2%	82.2%	79.4%
Understand that AMR is associated with using anti-inflammatory drug in food animals	24.8%	9.2%	11.4%
Understand that AMR is associated with using antibiotic in food animals	16.2%	88.6%	87.1%
Understand that AMR is associated with consumption of foods containing antibiotic residue	20.4%	89.3%	79.5%
Understand that AMR is associated with consumption of foods contaminated with antibiotic-resistant bacteria	24.2%	91.8%	89.9%
Having previously seen a patient with antibiotic-resistant infection	24.3%		
Aware that antibiotic-resistant infection is a fatal disease	33.3%	94.6%	96.0%
Aware that he/she could have antibiotic-resistant infection	34.1%	89.2%	81.1%
Aware that he/she could be contributing to the increasing prevalence of AMR	14.2%	82.1%	78.6%
Aware that AMR is one of the major health problems in Thailand	25.2%	94.7%	91.4%
If he/she has behavior that is associated with increasing the prevalence of AMR (eg, purchasing antibiotic from drugstore, asking health personnel to provide unnecessary antibiotic), he/she will stop such behavior		93.6%	
After learning that antibiotic can induce antibiotic-resistant bacteria that can cause fatal infection, he/she will tell relatives and friends to avoid using unnecessary antibiotic		96.3%	
Willing to avoid acquiring antibiotic-resistant bacteria by consuming clean and cooked foods and by complying with acceptable standards of personal sanitation and hygiene		92.2%	
After learning that antibiotic can induce antibiotic-resistant bacteria that can cause fatal infection, he/she understands that nobody should purchase antibiotic from any source without a physician's prescription		95.3%	
After learning that antibiotic can induce antibiotic-resistant bacteria that can cause fatal infection, he/she understands that grocery stores and retail shops must not be authorized to sell antibiotic		92.4%	

**Table 1. Continued**

Characteristics of Questionnaire Respondents and Questionnaire Topics	Questionnaire 1 Responses Before AMR Campaign (n = 20 521)	Questionnaire 2 Responses Immediately After AMR Campaign (n = 19 634)	Questionnaire 3 Responses at 18 Months After AMR Campaign (n = 709)
After learning that antibiotic can induce antibiotic-resistant bacteria that can cause fatal infection, he/she understands that drugstores should not be authorized to sell antibiotic		89.3%	
After learning that antibiotic can induce antibiotic-resistant bacteria that can cause fatal infection, he/she understands that people should take antibiotic prescribed by physician if needed		87.4%	
After learning that antibiotic can induce antibiotic-resistant bacteria that can cause fatal infection, he/she understands that patients should not ask health personnel to provide unnecessary antibiotic		84.2%	
Thinks that the media that are used by the VHVs to communicate AMR information are very useful		91.2%	
Thinks that his/her awareness and understanding of antibiotic use and AMR are much improved after receiving communication on antibiotic use and AMR from VHVs		89.4%	
Thinks that his/her behaviors relating to antibiotic use and AMR are much improved after receiving communication on antibiotic use and AMR from VHVs		89.2%	

Gano and TC-mycin are tetracycline formulations that are commonly sold in grocery stores, retail shops, and drugstores in many communities in Thailand. Abbreviations: AMR, antimicrobial resistance; VHVs, village health volunteers.

of chronic underlying diseases, chicken or pig farmer, health care personnel, regular or frequent consumption of undercooked foods or water from open public water sources, receipt of antibiotic or anti-inflammatory drugs within 90 days of stool collection, and hospital visit or hospitalization within 90 days of stool collection.

**DISCUSSION**

Increasing awareness of and understanding about AMR and promoting changes in behavior among the general public are

very important for prevention and containment of AMR, especially in low- and middle-income countries with a higher risk of AMR and greater magnitude of AMR burden than developed countries [30]. Antibiotics can be purchased without prescription, and they are available via unofficial distributors (grocery stores and retail shops) and official distributors (drugstores and hospitals) in many low- and middle-income countries. Although antibiotics are classified as dangerous drugs by the Thailand Food and Drug Administration and they should be available only in hospitals and drugstores under the supervision of pharmacists,

**Table 2. Questionnaire Responses Significantly Associated With *Enterobacteriaceae* Carriage Compared Before and After the Antimicrobial Resistance Campaign**

Questionnaire Response	534 Adults Before AMR Campaign				709 Adults at 18 Months After AMR Campaign			
	Total	Presence of ESBL-Producing <i>Enterobacteriaceae</i> (n = 355)	Absence of ESBL-Producing <i>Enterobacteriaceae</i> (n = 179)	P	Total	Presence of ESBL-Producing <i>Enterobacteriaceae</i> (n = 316)	Absence of ESBL-Producing <i>Enterobacteriaceae</i> (n = 393)	P
Presence of chronic underlying diseases	186	135 (38.0%)	51 (28.5%)	<b>.03</b>	240	140 (44.3%)	100 (25.4%)	<b>&lt;.01</b>
Chicken or pig farmer	69	55 (15.5%)	14 (7.8%)	<b>.02</b>	71	52 (17.7%)	19 (4.8%)	<b>&lt;.01</b>
Health personnel	27	24 (6.8%)	3 (1.7%)	<b>.02</b>	28	20 (6.3%)	8 (2.0%)	<b>.01</b>
Regular or frequent consumption of undercooked foods and/or water from open public water sources	164	123 (34.6%)	41 (22.9%)	<b>.01</b>	177	100 (31.6%)	77 (19.6%)	<b>&lt;.01</b>
Receipt of antibiotic or anti-inflammatory drug within 90 d of stool collection	148	110 (31.0%)	38 (21.2%)	<b>.02</b>	142	78 (24.7%)	64 (16.3%)	<b>&lt;.01</b>
Hospital visit or hospitalization within 90 d of stool collection	107	81 (22.8%)	26 (14.5%)	<b>.03</b>	120	68 (21.5%)	52 (13.2%)	<b>&lt;.01</b>
Presence of >1 associated factor	146	114 (32.1%)	32 (17.9%)	<b>&lt;.01</b>	156	86 (27.2%)	70 (17.8%)	<b>&lt;.01</b>

A P value <.05, shown in bold formatting, indicates statistical significance. Abbreviation: ESBL, extended-spectrum beta-lactamase.

many commonly used antibiotics, such as tetracycline, amoxicillin, and norfloxacin, are commonly available in grocery stores and retail shops in many communities, even though it is illegal for grocery stores and retail shops to sell antibiotics. People in remote communities usually seek primary care by purchasing drugs from grocery stores, retail shops, or drugstores when they are sick, and they will go to a health care facility only if they do not get better after taking the purchased medications. Patients usually ask for antibiotics from health personnel when they have illnesses related to inflammation (eg, back pain, joint pain, sore throat) or when they have an infection for which antibiotics are not normally indicated (eg, common cold, acute diarrhea). Analysis of the drugs purchased from grocery stores and retail shops in the study communities using simulated patients with common complaints, such as sore throat, backache, common cold, or acute diarrhea, revealed that most of them were antibiotics [18]. Therefore, most of the anti-inflammatory drugs that were reported by the questionnaire respondents before the AMR campaign (Table 1) were likely to have been antibiotics, because the people, drug sellers, and health personnel always referred to antibiotics as anti-inflammatory drugs, and these drugs were given for inflammatory conditions and infections. Easy access to antibiotics and unnecessary usage of antibiotics result in production of antibiotic-resistant bacteria. Moreover, water, sanitation, and hygiene in many areas of low- and middle-income countries are poor, which leads to acquisition and transmission of antibiotic-resistant bacteria.

It is clear from the questionnaire responses from adults in the study communities before the AMR campaign that most of general public was unaware, misunderstood, and had inappropriate behavior relating to antibiotic use and AMR and that these deficits require urgent correction. The AMR campaign package that was used to improve the awareness, understanding, and behavior of antibiotic use and AMR for the general public in these communities was developed from information derived from the residents in these communities in a local context, including the communication of all intended messages via the VHV, who was the media person for this campaign. Media for the AMR campaign, including a 21-page flip sheet, brochures, and video clips provided by the research team to each VHV, were conveniently carried by the VHV to each of their assigned households within their respective study community to facilitate communication with the individuals in each household. Most respondents who received communications from a VHV via these media felt that these media were very useful, and their awareness, understanding, and behavior related to antibiotic use and AMR were much improved after receiving communication on antibiotic use and AMR from the VHV. The awareness, understanding, and behavior regarding antibiotic use and AMR of respondents after the AMR campaign were improved more than 100% when compared with those parameters before the AMR campaign. Therefore, this

locally developed AMR campaign was effective for improving awareness, understanding, and behavior related to antibiotic use and AMR among the general public when assessed by self-administered questionnaire. However, the fact that improvement in awareness, understanding, and behavior related to antibiotic use and AMR immediately after the AMR campaign was not observed in 100% of respondents (improvement was observed in 80%–90% of respondents) may be explained by the following reasons. First, some VHVs had limited capacity to understand the contents of the media from the well-trained VHVs, and their communications with individuals at the household level might not have been sufficiently effective. Second, some individuals living in those households, such as elderly family members, who received communications on antibiotic use and AMR from the VHV may have had a limited ability to understand the provided information. The awareness, understanding, and behavior related to antibiotic use and AMR of respondents at 18 months after the AMR campaign were somewhat similar to those measured immediately after the AMR campaign. These findings suggest that the awareness, understanding, and behavior of antibiotic use and AMR of respondents who had received communications from a VHV were maintained for up to 18 months after the AMR campaign. However, some respondents at 18 months after the AMR campaign (16.4%–20.0%) admitted that they did not comply with some measures for AMR containment, as they still purchased antibiotics from a grocery store, retail shop, or drugstore, and/or they asked health personnel to provide them with antibiotics over the past year.

Assessment of the effectiveness of the AMR campaign by self-administered questionnaire might not be valid, as the responses to the questionnaire were very subjective. A self-administered questionnaire can measure awareness, but assessment of understanding might need examination, and assessment of behavioral change might need direct observations. The aforementioned assessment tools to measure understanding and behavioral change were not feasible for complex health problems like AMR in the community, as there were many contributing factors related to development, acquisition, and transmission of AMR. Hence, it would be extremely difficult or impossible to assess all those factors using objective tools.

This study attempted to assess whether fecal carriage of ESBL-producing *Enterobacteriaceae* could be a proxy composite indicator of AMR in the community because it was a combination of the factors contributing to the development, acquisition, and transmission of antibiotic-resistant bacteria, and it should reflect behavior related to antibiotic use and AMR. The prevalence of fecal carriage of ESBL-producing *Enterobacteriaceae* of individuals in the study communities was significantly decreased by 32.9% at 18 months after the AMR campaign when compared with before the AMR campaign. The magnitude of such a decrease observed from objective

measurement was much less than that from the responses to the questionnaire items related to the respondents' behavior. Therefore, the magnitude of behavioral change on antibiotic use and AMR assessed by a self-administered questionnaire may have been overestimated when compared with the magnitude of difference in fecal carriage rate of ESBL-producing *Enterobacteriaceae* before and after the AMR campaign. It should be noted that the fecal carriage rate of ESBL-producing *Enterobacteriaceae* at 18 months after the AMR campaign was still high at 44.6%, even in individuals who participated in the AMR campaign. This observation could be due to noncompliance with the measures for prevention of development, acquisition, and transmission of AMR in individuals with fecal carriage of ESBL-producing *Enterobacteriaceae* and/or that the measures for prevention of development, acquisition, and transmission of AMR could not be avoided as the prevalence of foods and environment contaminated with ESBL-producing *Enterobacteriaceae* in the study communities was high [17, 18]. This observation was confirmed by the results from the responses to the questionnaire designed to estimate a volunteer's risk of being a fecal carrier of ESBL-producing *Enterobacteriaceae*, that presence of chronic underlying diseases, chicken or pig farmer, health personnel, regular or frequent consumption of undercooked foods or water from open public water sources, receipt of antibiotic or anti-inflammatory drugs within 90 days of stool collection, and hospital visit or hospitalization within 90 days of stool collection were significantly associated with having ESBL-producing *Enterobacteriaceae* in the gut, similar to previous reports [15, 16, 20–28, 31–35]. Therefore, additional interventions are needed to minimize the fecal carriage rate of ESBL-producing *Enterobacteriaceae* in the community. These interventions include eradication of antibiotic sale without prescription and avoidance of contamination of ESBL-producing *Enterobacteriaceae* and containment of antibiotic residue in foods and the environment.

The main limitation of this study was that the responses to the questionnaire for assessment of awareness, understanding, and behavior of antibiotic use and AMR, the stool samples, and the responses to the questionnaire for the risk factor of being a carrier of ESBL-producing *Enterobacteriaceae* were done by anonymous adult volunteers. Therefore, we did not know how many respondents to the questionnaire before the AMR campaign, immediately after the AMR campaign, and 18 months after the AMR campaign, as well as the people who provided their stool samples before the AMR campaign and 18 months after the AMR campaign, were the same individuals. The decrease in the fecal carriage rate of ESBL-producing *Enterobacteriaceae* observed in this study may have been due to sampling bias in favor of people who provided their stool samples at 18 months after the AMR campaign. However, volunteer characteristic data of the people in both groups do not support this assumption.

## CONCLUSIONS

The AMR campaign in the community at the household level was effective for improving awareness, understanding, and behavior related to antibiotic use and AMR assessed by self-administered questionnaire and for decreasing the prevalence of fecal carriage of ESBL-producing *Enterobacteriaceae*. Fecal carriage of ESBL-producing *Enterobacteriaceae* may be a proxy composite indicator of AMR in the community.

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**Author contributions.** V.T. contributed to the conception and design of the study, data collection, data analysis, and preparation of the manuscript. T.T. and C.S. performed stool culture, analyzed the culture results, and reviewed the manuscript. All authors read and approved the final manuscript.

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