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Correlates of Antibiotic Diversion in the Philippines: Misconceptions and Community-Level Access to Nonmedical Sources of Antibiotics

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CORRELATES OF ANTIBIOTIC DIVERSION IN THE PHILIPPINES: MISCONCEPTIONS AND COMMUNITY-LEVEL ACCESS TO NONMEDICAL SOURCES OF ANTIBIOTICS

CAPSTONE PROJECT PAPER

A paper submitted in partial fulfillment of the requirements for the degree of
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Abstract

Aim: To identify sociodemographic, knowledge, and attitudinal correlates to antibiotic diversion among a community-based sample of adults (age 18 and older) in a low-income setting of the Philippines and to explore community-level data on informal antibiotic distribution in sari-sari stands.

Methods: Participants (n=307) completed self-administered surveys. Correlates to antibiotic diversion were assessed using logistic regression with Firth's bias-adjusted estimates. Availability and characteristics of antibiotics in the sari-sari stands (n=106) were observed through site visits.

Results: A majority (78%) had shared antibiotics in their lifetime, most often with family members. In multivariable analysis, agreement with the belief that it is safe to prematurely stop an antibiotic course (OR: 2.8, CI: 1.3-5.8) and concerns about antibiotic side effects (OR: 2.1, CI: 1.1-4.4) were significantly associated with increased odds of reported antibiotic diversion. Antibiotic diversion was not associated with sociodemographic characteristics or antibiotic knowledge. Antibiotics were widely available in sari-sari stores (60%), where antibiotic expiration dates were often unaccounted for (59%), and a full course of antibiotics was usually unavailable (68%).

Conclusions: Antibiotic diversion was common and was associated with misconceptions about proper antibiotic use. Antibiotics were widely available in sari-sari stands, but usually without expiration information or full dosages. Although more research is needed, it is clear that efforts to curb antibiotic resistance must include an understanding of location-specific antibiotic misconceptions and individual access to legitimate pharmaceutical outlets.

Introduction

Self-medication is defined as the use of medicinal products by an individual to treat self-diagnosed symptoms, or as the unsuitable administration of prescribed medicinal products, including intermittent or prolonged use of antibiotics and sharing of medications (i.e., drug diversion) [1]. Self-medication with antibiotics is particularly problematic, as it has been cited as a major contributor to antibiotic resistance [2-6]. Furthermore, self-medication with antibiotics can quadruple the odds of developing a drug resistant infection [6]. Recent meta-analyses have estimated that 38% of the world's population engages in self-medication with antibiotics [6, 7]. According to the World Health Organization (WHO), self-medication varies by location, with the highest prevalence in Southeast Asia and the Western Pacific Region—from 58-64% [7, 8]. In these same regions, the prevalence of resistance to many common antibiotics is on the rise [9].

Of the 27 member states in the Western Pacific Region participating in the WHO's 2015 evaluation of global antibiotic resistance, only one country, the Philippines, did not participate [10]. Thus, a critical gap exists in the present understanding of antibiotic misuse in the Philippines; this gap is especially concerning as the Philippines has a documented history of prevalent antibiotic misuse [11]. Compared to other countries, the Philippines has had the smallest percentage of prescriptions filled by doctors, with nonmedical sources being the most common source of antibiotics [12]. Furthermore, the Philippines has been reported to have one of the highest rates of antibiotic sharing [12]. The reported prevalence of antibiotic self-medication in the Philippines has ranged from 31-66% [13-17], with one study [13] reporting a greater overall prevalence than for Southeast Asia (range: 38-58%) [6, 7]. Antibiotic misuse in the Philippines has contributed to an increase in antibiotic-

resistant infections, including a 60% resistance of ciprofloxacin to *Staphylococcus aureus*, and 84% resistance of penicillin to *Neisseria gonorrhoeae*, among others [9].

To date, few studies have examined antibiotic self-medication in the Philippines [13-18]. With the exception of two studies that described prophylactic use of antibiotics by Filipino commercial sex workers (CSWs) to prevent sexually transmitted infections (STIs) [15, 18] and four studies that describe non-prescription access and use of antibiotics [13, 14, 16, 17], research on antibiotic misuse in the Philippines is scarce. Evidence from the Southeast Asian region more broadly has suggested that self-medication (inclusive of nonmedical use and diversion) may be associated with cultural misconceptions [11, 17, 19-21], premature termination of antibiotic courses [12], insufficient regulations and enforcement of pharmaceutical law [22], and antibiotic knowledge and/or attitudes [23-26]. Globally, education, age, sex, household size, severity of illness, former medical use, and poverty have been associated with antibiotic self-medication [7, 22].

A few studies have examined self-medication in Southeast Asia and the Philippines, but to my knowledge, none have examined characteristics or correlates related to antibiotic diversion, a fairly common form of self-medication globally and in the Philippines [7, 12]. A recent review by Radyowijati et al. (2003) highlighted the deficit in antibiotic diversion research; it revealed that the majority of studies on self-medication with antibiotics have examined antibiotic prescribing and the purchasing of antibiotics without a prescription rather than informal antibiotic dispensing within a community [19]. The present study addresses this gap in knowledge and extends antibiotic self-medication literature by triangulating individual-level data with community-level data on informal antibiotic distribution outlets. This study identifies sociodemographic, knowledge, attitudinal, and

community-level factors associated with antibiotic diversion in a low-income setting of the Philippines, a country with one of the highest rates of antibiotic sharing in the world [12].

Materials and Methods

Study Design and Sampling

From April to June 2015, 307 participants (age 18 or older) were recruited via convenience sampling in a low-income area of the Central Visayan region of the Philippines. This suburban area is adjacent to a large industrial metropolis and is fairly densely populated (17,000 people /sq mi). Based on survey information and informal conversations, the average wage-earner in this community brought home less than two US dollars per day. A local non-governmental organization (NGO) assisted in the recruitment of survey respondents by notifying and employing community leaders and health workers to inform the public about the study, prior to survey session dates; individuals were admitted to survey sessions based on a first-come, first-serve basis. Data were collected through an anonymous, self-administered, 46-item, cross-sectional survey. Participants could choose to take an English or Cebuano version. Translations of the consent form and survey were assessed for accuracy through back translation. Surveys were developed based on a review of previous antibiotic studies in Southeast Asia [23-28]. Surveys were administered in group sessions, held at churches, schools, health clinics, and public meeting spaces, with group sizes ranging from 29 to 88 participants. Participants were given hard copies of the consent form in either English or Cebuano and the consent form was read aloud in both languages. Documentation of consent was not obtained in order to protect individual identities. Participants were given the opportunity to decline participation, though none did. Following survey completion, participants were

compensated 100 pesos (~$2.13 USD) for their time and travel. The study protocol was approved by the University of Kentucky Institutional Review Board.

Survey Instrument and Data Measures

Antibiotic diversion, the dependent variable of interest in this study, was assessed with the question: "Have you ever shared antibiotics with any of the following (check all that apply): [children, spouses, elderly family members, other family members, friends, co-workers, neighbors, other, or 'I have never shared any antibiotic']." To determine correlates of antibiotic diversion, a dichotomous variable was created indicating whether individuals had ever shared antibiotics with anyone. The outcome was dichotomized in order to identify potential differences in sociodemographic, knowledge, and attitudinal factors between those having shared and never having shared their antibiotics with someone.

Sociodemographic characteristics (Table 1) addressed by the survey included age (years), household size (number of people living in household), sex (male, female, transgender), and education (elementary, high school, college, vocational, or graduate). For the analysis, educational attainment was dichotomized into elementary education or less versus more than an elementary education, due to small sample sizes in the vocational and graduate categories.

Questions regarding antibiotic knowledge included nine items (Table 2) related to proper antibiotic use (n=6), antibiotic safety (n=2), and bacterial resistance (n=1), that were developed from previous self-medication studies [23-26]. As in other studies [25, 26], knowledge questions were true/false with an additional option of 'I don't know.'

Knowledge was scored on a continuous scale comparing correct answers to incorrect or 'I don't know' responses.

Participants' perceptions and misconceptions about antibiotic use were measured by a set of 16 Likert-scale questions (response options: strongly agree, agree, disagree, and strongly disagree), as shown in Table 3. Perceptions were analyzed using dichotomized Likert-scales comparing strongly agree and agree to strongly disagree and disagree.

Analysis

Of the 307 respondents to complete a questionnaire only 278 were included for analysis. Participants were excluded due to failure to respond to at least one entire section of the survey (n=10), and missing data on the outcome measure of diversion (n=19). Those excluded from the analysis were not significantly different from those retained in the analysis in terms of sociodemographic characteristics. Data were entered using SPSS (version 22) [29] and analyses were completed in SAS version 9.4 for Windows [30].

To account for quasi-complete separation of data related to the sex variable (i.e., nearly ubiquitous antibiotic diversion among the 17 transgender participants), Firth logistic regression was used to assess correlations between respondent characteristics and diversion status. In essence, quasi-complete separation of the data results when covariates are associated with only one outcome, consequentially leading to an infinite parameter estimate [31]; this is a common phenomenon with logistic regression in small to medium data sets or in analyses with rare outcomes [31, 32]. In order to reduce this small sample bias, Firth recommends a modified score equation, which is related to a penalized log-likelihood function [33].

Covariates in the final model included age, education, sex, household size, knowledge, and six antibiotic perceptions related to access, safety, and proper use. Age, education, sex, household size, and knowledge were selected for the final model as they were previously examined for their association with self-medication in the literature [7, 25, 34-36]. Antibiotic perceptions were also included in the final model, based on correlations between perceptions and behaviors in the self-medication literature and observations within the local community. A confounding analysis was also used to help in the selection of covariates for the final model. Confounding was examined by assessing changes in the estimated, crude association between key independent variables (i.e., antibiotic knowledge and perceptions of access) and diversion in the presence versus absence of hypothesized confounders. Confounding was deemed present when the estimated odds ratio changed by greater than 15%. The analysis showed that education confounded the association between the perception that it is difficult for a person to obtain an antibiotic with a prescription and antibiotic diversion; thus, education was required in the final model.

Multicollinearity of the final model was assessed using the COLLIN macro for SAS [37]. Covariates did not exceed a conditional index of 20, indicating that multicollinearity was not an issue in the final model [38]. Of note, 47 participants had missing data on one or more covariates in the final model and were therefore excluded from the multivariable logistic regression. Participants excluded from the final model were not significantly different in terms of diversion and/or sociodemographic characteristics.

Characteristics and Availability of Antibiotics in Local Sari-Sari Stores

In addition to individual-level antibiotic data, information regarding informal antibiotic distribution channels was also collected. Research staff visited 106 local sari-sari stores (i.e., small roadside stands) from April 7 to April 15, 2015 and recorded information about antibiotic availability at the stands utilizing a geospatial data collection application, Fulcrum (version 2.6.0), installed on a smartphone [39]. Research staff recorded information on availability of antibiotics at the stands, names of antibiotics for sale, expiration date, storage conditions, and whether full courses of antibiotics could be filled.

Results

Respondent Characteristics

A total of 278 surveys were used for analysis, with mean participant age of 32 years (range: 18-74). Demographic, knowledge, and attitudinal characteristics are displayed in Table 1. Over half (57%) of respondents were female and 6% were transgender. Most participants had at least a high school education (69%). Many were unemployed (35%) with fisherman, housekeepers, and CSWs being the most common occupations (26%, 20%, and 7%, respectively).

Antibiotic Knowledge

Respondents' antibiotic knowledge was moderate (Table 2), with a median score of five on the knowledge scale (score range: 0-9, out of 9). Participants understood that antibiotics are useful against infections (88%), specifically those caused by bacteria (91%); however, most incorrectly believed that antibiotics are useful against a viral infection and/or common cold or cough (85% and 81%, respectively). Most knew that individuals

might be allergic to some types of antibiotics (77%). However, 55% did not know that antibiotics could have side effects. A slight majority (57%) thought someone should begin to take antibiotics as soon as they experienced a fever, and most (70%) did not understand the potential of developing antibiotic resistance from improper antibiotic use. Of note, nearly 40% of those who did not understand the potential of developing resistance marked 'I don't know' rather than a false response, possibly indicating unfamiliarity with the concept of antibiotic resistance.

Perceptions of antibiotic access and common misconceptions

There were four questions pertaining to individuals' perceived access to antibiotics (Table 3). When asked about the difficulty for people in the community to get a prescription for antibiotics, 62% agreed that it was difficult to obtain a prescription. Most (65%) also indicated that it was still difficult to obtain an antibiotic even with a prescription. Over half disagreed (55%) that it was easy to access antibiotics without a prescription from a healthcare worker. However, when asked whether people in their communities used antibiotics without instructions from a healthcare worker, 57% agreed. Most participants stated it was not safe to take antibiotics without instructions from a healthcare worker or pharmacist and most worried about side effects when using antibiotics (62% and 65%, respectively).

Misconceptions and indications of improper antibiotic use were also common (Table 3). When asked whether it was good for a person to save extra antibiotics for use at another time when sick, 52% thought this behavior acceptable. A majority (62%) agreed that when sick, it was better to take a small dose of antibiotics than to take none at all.

Nearly half (45%) agreed that it was acceptable to stop taking antibiotics when they felt better even if there were still antibiotics left to take. Among other misconceptions, two-thirds (66%) believed that a skin injury could be cured by putting crushed antibiotic powder into the wound. A majority (82%) expected to receive antibiotics from a healthcare worker when sick with a cold. Lastly, a substantial minority (42%) agreed that regular administration of antibiotics could prevent HIV, but a large majority (71%) disagreed that when used before or after sex, antibiotics could prevent a STI.

Characteristics of antibiotics in roadside stands

Among the 106 roadside stands visited, 64 (60%) sold antibiotics. A total of 95 packages of antibiotics (single doses and/or full courses) were found in these stands, representing nine unique antibiotic varieties (Table 4). Of the 95 antibiotics, 56 (59%) lacked an expiration date and, among those with an expiration date, 4 (10%) were expired. In many instances expiration dates had been removed from the blister packs or pills had been removed from blister packs and individually wrapped in plastic. Only two of the 95 antibiotics (both reconstitutable) were improperly stored, in terms of protection from light, moisture, and/or heat. Of the 95 packages of antibiotics for sale, 65 packages (68%) did not have enough pills for a full course of proper treatment.

Antibiotic diversion and correlates

Of the 278 participants included in this analysis, 60 (22%) indicated they had never shared antibiotics in their lifetime. Participants who reported sharing antibiotics most often shared them with ‘other family members’ (37%) and children (33%), followed by

neighbors (18%), elderly family members (18%), spouse or sex partner (16%), friends (14%), and others (4%). Among those employed at the time of the survey (65%), a small percent indicated that they shared antibiotics with coworkers (7%).

Table 1 presents results from univariate logistic regression models, and shows the estimated, unadjusted associations between covariates and reported antibiotic diversion. None of the sociodemographic characteristics were significantly associated with antibiotic diversion. For each unit increase in knowledge score, the odds of antibiotic diversion decreased 20% (CI: 0.7, 1.0). The perception that it is safe to take antibiotics without instructions from a healthcare worker was associated with a 2.4 increase in the odds of diversion (CI: 1.2, 4.5). The perception that it is acceptable to save antibiotics for later use was associated with a 2.6 increase in the odds of diversion (CI: 1.4, 4.7). Participants who perceived it is safe to prematurely terminate a course of antibiotics had 3.3 higher odds of reporting diversion (CI: 1.7, 6.4). Lastly, the perception that it is better to take a small dose of antibiotics when sick compared to no dose at all was associated with a 2.4-fold increase in the odds of diversion (CI: 1.4, 4.4). All covariates examined in the univariate analysis were included in the final multivariable logistic regression.

Table 5 presents results from the final multiple logistic regression model (N=231). After controlling for other variables, covariates significantly associated with antibiotic diversion included the belief that it is safe to prematurely terminate a course of antibiotics, and concerns about side effects when taking antibiotics. More specifically, when holding all other covariates constant, agreement that it is safe to stop the course of antibiotics was associated with odds of reporting diversion 2.8 (CI: 1.3, 5.8) times higher than those who disagree. Fear of antibiotic side effects was associated with an estimated odds of diversion

2.1 times higher than those who do not worry about side effects when taking antibiotics (CI: 1.1, 4.4).

Discussion

To my knowledge, this is the first study of its kind to examine correlates of antibiotic diversion in Southeast Asia or the Philippines, and the first to examine the availability and condition of antibiotics in sari-sari stores. The purpose of this study was to identify sociodemographic, knowledge, and attitudinal characteristics associated with antibiotic diversion in the Philippines and to examine community-level data on informal antibiotic distribution channels. Notably, most respondents (78%) indicated they had shared antibiotics in their lifetime. Data from the sari-sari stores revealed that antibiotics were readily available without prescription in the surveyed communities (60%). Furthermore, a full course of antibiotics was rarely available for purchase (68%), and expiration dates had often been removed or were indiscernible (59%). Overall, this study found both the perception that it is safe to prematurely discontinue an antibiotic course, and fear of antibiotic side effects, to be associated with an increase in the odds of antibiotic diversion. Interestingly, sociodemographic characteristics and knowledge were not significantly associated with diversion.

The findings from this study demonstrate that misconceptions were more strongly associated with antibiotic diversion than were sociodemographic characteristics, which have commonly been cited as correlates to antibiotic self-medication and the diversion of other prescription drugs. A recent, global meta-analysis found a number of socioeconomic factors associated with antibiotic self-medication, including: low level of education, female

gender, age, and middle income [7]. In addition, among non-antibiotic prescription drug diversion studies, having a prescription [34], lacking medical insurance [34], age [34, 35], and female sex [36], have been found to be associated with prescription drug diversion.

Although this study deviates from other studies in terms of the association between self-medication and sociodemographic characteristics, findings related to the association of antibiotic misconceptions and diversion are consistent with the antibiotic self-medication literature [7, 11, 12, 15, 40, 41]. In the present study, fear of antibiotic side effects and the premature termination of antibiotic courses were significantly associated with antibiotic diversion. Though the two-fold increase in the odds of diversion from worrying about side effects is somewhat counterintuitive, it is plausible that individuals who are fearful of antibiotics may refrain from taking the antibiotics, stockpiling them within their home, and potentially diverting them at a later time to friends or family. Similarly, if individuals prematurely terminate their antibiotic course, they will have antibiotics leftover to store within their homes for later personal use and/or to share with others. These possibilities are largely speculative; however, the connection between antibiotic leftovers and diversion have been suggested by others. In a global survey of antibiotic use (antibiotics obtained with or without a prescription), Kardas et al. (2007) reported that antibiotic leftovers were present in about half of all sample populations that had recently used antibiotics. Among those having antibiotic leftovers, 77% were saving them for later use, 5% reported sharing them with someone else, and only 18% threw them away [12]. Kardas et al. identified two major predictors of saving and diverting the antibiotics, including: pack-based dispensing systems and patients' misconceptions. Integrating the findings and implications from Kardas' study with this study, these data

suggest that interventions aimed at decreasing antibiotic diversion should consider identifying and addressing community-specific misconceptions around completing antibiotic courses and the stockpiling of extra antibiotics.

Antibiotic self-medication literature has established that antibiotics are commonly available from nonmedical sources in low income countries, including countries in Southeast Asia, but very few of these studies have examined the availability of antibiotics in roadside stands [7, 19]. The present study was among the first to directly assess antibiotic availability in nonmedical, community-level outlets in Southeast Asia. The descriptive, observational data regarding antibiotic characteristics and availability in sari-sari stands provide insight into the epidemiology of antibiotic misuse and adverse health consequences, such as the development of an antibiotic-resistant infection. For example, beta-lactam antibiotics (i.e., amoxicillin, cephalexin, and penicillin) were the most common types of antibiotics found for purchase in the surveyed sari-sari stores. Given the high prevalence of reported antibiotic self-medication and diversion present in the Philippines (58% [13], and 78%, respectively), antibiotic availability in sari-sari stands may have been associated with the extensive development of beta-lactam resistant *N. gonorrhoeae* and *Escherichia coli* in the Philippines (84% and 92% resistance, respectively) [9]. Although the association in the aforementioned example is speculative, data from this study showed that many sari-sari stores in the community stocked a number of expired antibiotics and were deficient in the availability of a legitimate course of antibiotics. Thus, if the conditions of antibiotics in these sari-sari stands are representative of that in the broader community, there exists a number of risk factors that could have

major implications on the health of individuals in the community, as well as the development of antibiotic resistance.

In an attempt to curb the illicit access to potentially harmful antibiotics and to increase antibiotic affordability in poorer communities, the Philippines has rapidly expanded three major government-affiliated programs, including: Botika ng Barangay (BnB), Botik ng Bayan (BNB), and PHP100 Treatment Pack (P100) [42]. These programs originated from the Cheaper Medicines Program (CMP) in conjunction with a series of governmental policies beginning in the late 1980s, including the Generics Act of 1988. The BnB and BNB programs serve the same purpose – to provide cheaper and more convenient locations of pharmaceutical drugs – but, BnBs are managed on a local scale, whereas BNBs are supervised by either the federal government or NGOs. The PHP100 program provides pre-packaged, individualized medication regimens for under 100 pesos to individuals who use medicines on more of a daily basis; the government believes the PHP100 program has dropped the cost of pharmaceutical drugs and increased patient compliance with drug regimens. Although these programs have benefitted many communities in the Philippines, a recent analysis of the CMP found these programs to lack effectiveness, efficiency, and sustainability [42]. The sheer number of sari-sari stores selling antibiotics, as identified in this study, supports previous findings [42], suggesting that the government may need to direct additional monetary subsidies to these programs or build more accessible locations for individuals to purchase safe and legitimately-obtained antibiotics.

Compared to other studies in Southeast Asia, this study's participants had a similar level of antibiotic knowledge. Knowledge related to the use of antibiotics for coughs/colds, viruses, fevers, and potential allergic reactions or side effects from antibiotics, was nearly

identical to that reported in other studies [23, 25, 26, 43]. Knowledge on the benefits of using antibiotics against bacteria was better in this study than in other studies, but levels of knowledge about antibiotic resistance were lower [23, 26, 27, 43]. Nevertheless, participants' scores on the knowledge questions were not significantly associated with reported antibiotic diversion.

Although this study addresses an important gap in the literature about antibiotic diversion, it is not without limitations. The use of a convenience sample and self-report data could have led to sampling and information biases, respectively. The self-selection of oneself into the study could have introduced a sampling bias that would hamper the generalization of these results to other Filipino or Southeast Asian populations. The self-reported nature of data may have led to an under-reporting of antibiotic diversion; if under-reporting was present then the results of the analysis would be biased away from the null. Due to small sample size, it is possible the analysis lacked statistical power to detect small differences in some of the other covariates, increasing the probability of a Type II error.

Despite these limitations, this study builds upon the literature of self-medication in Southeast Asia and the Philippines by allowing for an assessment of socioeconomic, knowledge, and attitudinal correlates related to antibiotic diversion. Furthermore, this study extends beyond previous self-medication research by focusing on the informal distribution and dispensing of antibiotics within community outlets, rather than the purchasing of antibiotics without a prescription in pharmaceutical stores. More studies of this kind should be utilized in the Philippines in order to understand risk factors for antibiotic self-medication and diversion, as the Philippines has historically had the smallest percentage of prescriptions filled by doctors and one of the highest rates of antibiotic

sharing [12]. In agreement with portions of the self-medication literature, the findings of this study suggest that antibiotic misconceptions among individuals are equally or more important to antibiotic diversion than sociodemographic or knowledge factors. Additionally, data from sari-sari stores indicate that antibiotics diverted throughout this community may present significant health concerns, as the antibiotics were sold in ineffective dose sizes, often expired, or occasionally improperly stored. In order to better understand the relationship between sari-sari stands and antibiotic diversion in the communities, future studies may benefit from using geospatial techniques to gauge individual access to pharmacies versus roadside stands selling antibiotics. Although more research is needed to understand the individual and community-level factors involved with antibiotic diversion, it is clear that efforts to curb the epidemic of antibiotic resistance must include an understanding of location-specific antibiotic misconceptions and individual access to legitimate pharmaceutical outlets.

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Table 1. Sociodemographic, knowledge, and attitudinal characteristics and univariate associations with diversion

	Total N=278 (%)	**Diversion N= 218 (78.4%)**	**No Diversion N= 60 (21.6%)**	**OR**	**95% CI**	**p-value**
Demographics	-	-	-	-	-	-
Age years (N=277) - median (IQR)	32 (20.0)	31 (20.0)	32 (17.0)	1.0	1.0, 1.0	0.957
Sex (N=277)	-	-	-	-	-	-
Female	157 (56.7)	118 (75.2)	39 (24.8)	ref.	ref.	ref.
Male	103 (37.2)	84 (81.6)	19 (18.4)	1.4	0.8, 2.7	0.239
Transgender	17 (6.1)	15 (88.2)	2 (11.8)	2.1	0.5, 8.6	0.317
Education (N=269)	-	-	-	-	-	-
High school or more	186 (69.1)	143 (76.9)	43 (23.1)	ref.	ref.	ref.
Elementary	83 (30.9)	69 (83.1)	14 (16.9)	1.5	0.7, 2.8	0.269
Household size (N=264) - median (IQR)	6 (3.0)	6 (3.0)	4 (3.0)	1.1	1.0, 1.2	0.107
Knowledge Score (N=278) - median (IQR)	5 (3.0)	5 (3.0)	5 (2.5)	0.8	0.7, 1.0	0.011
Perceptions (agree, ref=disagree)*	-	-	-	-	-	-
With prescription, difficult to get abx. (N=272)	177 (65.1)	145 (81.9)	32 (18.1)	1.7	0.9, 3.1	0.076
Safe to use abx without instructions (N=273)	104 (38.1)	90 (86.5)	14 (13.5)	2.4	1.2, 4.5	0.010
Good to save abx for later (N=273)	143 (52.4)	123 (86.0)	20 (14.0)	2.6	1.4, 4.7	0.002
Small abx dose is better than no dose (N=274)	170 (62.0)	143 (84.1)	27 (15.9)	2.4	1.4, 4.4	0.003
Can stop abx when feeling better (N=274)	123 (44.9)	109 (88.6)	14 (11.4)	3.3	1.7, 6.4	<0.001
On abx., worry about side effects (N=273)	177 (64.8)	143 (80.8)	34 (19.2)	1.6	0.9, 2.8	0.133

OR: Estimated odds ratio, ref: reference, abx: antibiotic, IQR: Interquartile range. *Full questions pertaining to these perceptions are located in Table 3. The odds of diversion were estimated in comparison to those who disagreed with these statements.

Table 2. Participants' knowledge of antibiotics

Question (correct response)	Correct n (%)
1. Antibiotics are used for treating infection (true) (n=274)	241 (88.0)
2. Antibiotics are useful against all types of common cold and cough (false) (n=264)	51 (19.3)
3. Antibiotics can help someone who is infected with bacteria (true) (n=272)	247 (90.8)
4. Antibiotics can help someone who is infected with a virus (false) (n=267)	41 (15.4)
5. A person should start antibiotics as soon as they have a fever (false) (n=268)	115 (42.9)
6. Some people are allergic to antibiotics (true) (n=268)	206 (76.9)
7. Antibiotics can cause bad side effects (true) (n=270)	121 (44.8)
8. Antibiotics are like vitamins (false) (n=269)	171 (63.6)
9. When someone takes antibiotics very frequently, it can become more difficult to cure their future infections with antibiotics (true) (n=273)	81 (29.7)

Table 3. Participants' perceptions and misconceptions of antibiotic access and behaviors.

Question	Agree (%)*
Access	
1. It is difficult for people in the community to get a prescription for antibiotics. (n=248)	154 (62.1)
2. It is easy to access antibiotics without a prescription from a healthcare worker. (n=269)	121 (45.0)
3. Even with a prescription, it is difficult to get an antibiotic. (n=272)	177 (65.1)
4. There are people in my community who use antibiotics without instruction from a healthcare worker. (n=274)	157 (57.3)
Misconceptions	
5. It is safe to take antibiotics without instructions from a healthcare worker. (n=273)	104 (38.1)
6. When I need antibiotics, I usually get them without a prescription. (n=275)	92 (33.5)
7. It is good for a person to save antibiotics so that they can be used later for similar symptoms without needing to see a doctor. (n=273)	143 (52.4)
8. It is better to take a small dose of antibiotics than not take any dose. (n=274)	170 (62.0)
9. When a person starts feeling better, they can safely stop taking their antibiotics even when there are still antibiotics left to take. (n=274)	123 (44.9)
10. A skin injury can be cured quickly by putting crushed antibiotic powder onto the injury. (n=273)	180 (65.9)
11. Taking antibiotics regularly can prevent HIV, the virus causing AIDS. (n=274)	114 (41.6)
12. Taking antibiotics before or after sex can prevent sexually transmitted infections. (n=272)	78 (28.7)
13. When I use antibiotics, I worry about the side effects. (n=273)	177 (64.8)
14. If I were to experience a side effect from using an antibiotic, I would visit a doctor. (n=275)	259 (94.2)
15. When I am very sick with a cold and visit a healthcare worker, I usually expect a prescription for antibiotics. (n=274)	225 (82.1)
16. When I have a common cold or cough I normally use antibiotics. (n=274)	181 (66.1)

*Agree represents those who strongly agree or agree.

Table 4. Antibiotic characteristics and diversity in roadside stands

Stand Characteristics	n (%)
Selling antibiotics (N=106)	
Yes	64 (60.4)
No	42 (39.6)
Antibiotics sold (N=95)*	
Amoxicillin	57 (60.0)
Cephalexin	20 (21.1)
Tetracycline	7 (7.4)
Cotrimoxazole	5 (5.3)
Metronidazole	2 (2.1)
Antibiotics expired^	
Yes	4 (4.2)
No	35 (36.8)
Unable to determine	56 (59.0)
Full course available	
Yes	25 (26.3)
No	65 (68.4)
Unable to determine	5 (5.3)
Properly Stored	
Yes	93 (97.9)
No	2 (2.1)

*A total of 95 antibiotics were found in the 64 roadside stands selling antibiotics. Of these 64 roadside stands, there were only 9 unique antibiotic types, the top 5 are displayed in this table. Other antibiotics included: clarithromycin, levofloxacin, penicillin, and tigecycline. ^Among antibiotics that presented with an expiration date, only 10% were expired (4/39).

Table 5. Multivariable, Estimated OR's for Correlates of Antibiotic Diversion (N=231)

	Adjusted OR	95% CI	p-value
Demographics	-	-	-
Age (years)	1.0	1.0, 1.0	0.942
Sex	-	-	-
Female	ref.	ref.	ref.
Male	1.0	0.5, 2.1	0.960
Transgender	5.7	0.3, 107.3	0.248
Education	-	-	-
High school or more	ref.	ref.	ref.
Elementary	1.3	0.6, 3.3	0.514
Household size	1.0	0.9, 1.1	0.850
Knowledge Score (N=278)	0.8	0.7, 1.0	0.066
Perceptions (agree, ref=disagree)	-	-	-
With prescription, difficult to get abx.	1.3	0.7, 2.7	0.423
Safe to use abx without instructions	1.4	0.6, 3.2	0.385
Good to save abx for later	1.9	0.9, 4.0	0.090
Small abx dose is better than no dose	1.9	0.9, 3.9	0.098
Can stop abx when feeling better	2.8	1.3, 5.8	0.008
On abx., worry about side effects	2.1	1.1, 4.4	0.035

OR: Estimated odds ratio, CI: confidence interval, ref: reference, abx: antibiotic

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Biosketch

Daniel Barber was born and raised in Frankfort, Kentucky. He earned his Bachelor of Arts degree in Chemistry from Transylvania University. Currently, he is completing his MPH degree with a primary concentration in epidemiology and a graduate certificate in global health. He has been working as a graduate research assistant under Drs. James Holsinger and David Mannino.

The research presented in this capstone is based on a project that Daniel has been working on since the fall of 2014 in collaboration with Dr. April Young. The overall project involved the collection of survey data and a basic intervention with community members during a brief trip to the Philippines in the summer of 2015. The results of this study and intervention will be presented in New Haven, CT, at the 2016 Global Health & Innovations Conference. Following graduation, Daniel will begin an internship with the Department of Health and Human Services in Washington, DC.

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Correlates of Antibiotic Diversion in the Philippines:

Misconceptions and community-level antibiotic access to nonmedical sources of antibiotics

Daniel A. Barber
MPH Candidate, Epidemiology

February 16, 2016
Capstone Presentation

Purpose

A. To identify sociodemographic, knowledge, and attitudinal correlates to antibiotic diversion (sharing) among a community-based sample of adults in a low-income setting of the Philippines.

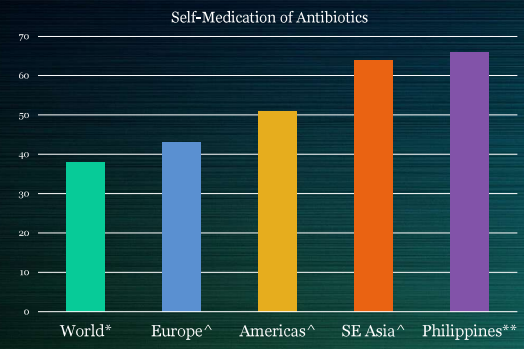
B. To explore community-level data on informal antibiotic distribution in sari-sari stands.

Background

Epidemiology of antibiotic self-medication, diversion

Background

- Antibiotic self-medication:
  - "The use of medicinal products… to treat self-diagnosed symptoms or unsuitable administration of prescribed medicinal products, including intermittent use…and sharing of medications." (World Health Organization 2000)

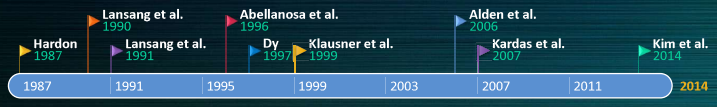


*Morgan, Okeke et al. 2011; *Ocan, Obuku et al. 2015; ^World Health Organization 2015; **Lansang, Lucas-Aquino et al. 1990

Background

- In 2015 evaluation of global antibiotic resistance, no participation from Philippines (World Health Organization 2015)
- In Philippines, 60% resistance of *Staphylococcus aureus* to ciprofloxacin and 84% resistance of *Neisseria gonorrhoeae* to penicillin (Lestari, Severin et al. 2012)
- Few studies have examined self-medication in the Philippines

Background



1997: "Clinically and economically inappropriate use of antibiotics is a major problem in the Philippines." (Dy 1997)

2007: Philippines had the smallest percentage of prescriptions filled by a doctor; greatest source of antibiotics coming from a non-medical professional; highest rate of antibiotic sharing. (Kardas, Pechere et al. 2007)

Background

Risk Factors for Self-Medication

(Dy 1997, Hardon 1987, Radyowijati and Haak 2003, Nelster 1989, Kardas, Pechere et al. 2007, Lim and Teh 2012, You, Yau et al. 2008, Widayati, Suryowati et al. 2012, Ngadimen, Islahudin et al. 2015)

Background

The majority of studies on self-medication with antibiotics have examined antibiotic prescribing and the purchasing of antibiotics without a prescription rather than informal antibiotic dispensing within a community. (Radyowijati and Haak 2003)

Aim: Addresses this gap in knowledge and extend antibiotic self-medication literature by triangulating individual-level data with community-level data on informal antibiotic distribution outlets.

Methods

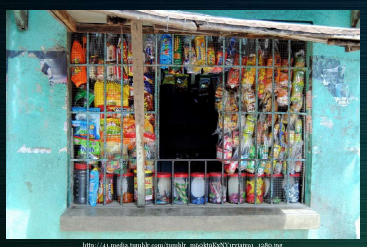
Sample, protocol, measures, and model selection

Sample

- Five barangays from Central Visayas
- Community-based research assistants
- April to May 2015
- Convenience and purposive sampling
  - Individual-level Data:
    - Sample size: 307 (age 18 or older)
  - Sari-Sari antibiotic characteristics:
    - Sample size: 106

http://www.worldatlas.com/r/w425/img/maps/philippines.jpg

Sari Sari Stand



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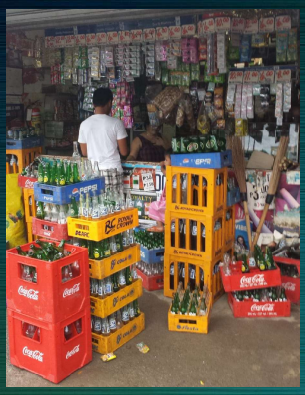
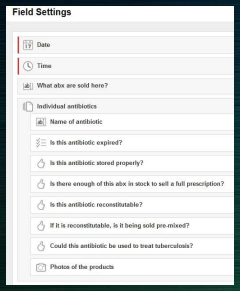


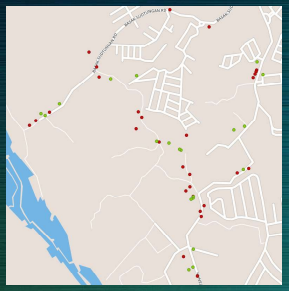
Procedures

- Anonymous, self-administered, cross-sectional survey*
- Recruited for group survey sessions (range: 29-88)
- Study Information Sheets
- Choice of Cebuano or English Study Materials
- Reimbursed ₱100 (Philippine peso), or $2.10 USD
- Visited sari-sari stores, asked to see antibiotics for sale
  - Use of Fulcrum Mobile Solutions
- All study protocol approved by UK IRB

*Informed by: (Hadi, Duerink et al. 2008), (You, Yau et al. 2008),(Widayati, Suryawati et al. 2011),(Widayati, Suryawati et al. 2012),(Lim and Teh 2012),(Ngadimon, Islahudin et al. 2015)

Fulcrum Application





Measures

- Independent Variables:
  - Sociodemographic
  - Knowledge (9 items, continuous)
  - Attitudinal (16 items, 4-point Likert-scale)
  - Community-level
    - Selling abx., name, expiration, full course, storage, geospatial data

Note: Abx. - Antibiotics

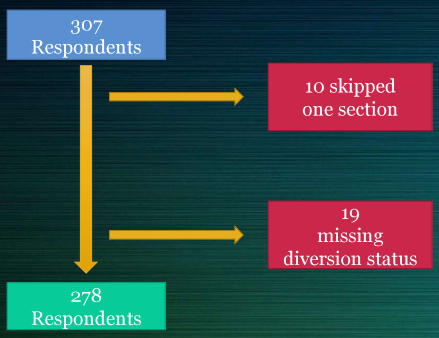
Measures

- Outcome Variable
  - Antibiotic Diversion
    - "Have you ever shared antibiotics with any of the following (check all that apply):"
      - Children, spouses, elderly family members, other family members, friends, co-workers, neighbors, other
      - I have never shared any antibiotic

Data Analysis

- Outcome Variable was dichotomized
- Likert-scale items dichotomized (agree vs. disagree)
- Descriptive Analysis of Sari-Sari Stores
- Univariate Associations
- Firth Logistic Regression
  - Test assumption of multicolliearity

Sample size



Model Selection

- Literature review* and community observations
- Missingness
- Confounding analysis
- Sample size limitations on number of covariates

Rank	Covariate
1	Knowledge – 9
2	Save abx. for later
3	Premature Termination
4	Take small dose vs. no dose
5	Perceived Community Access
6	~~Individual Access Barriers~~
7	Household Size
8	Sex
9	No Instructions
10	Perceived Side Effects
11	Age
12	Education (SES)
13	Relationship Status
14	Insurance
15	Site
16	Crushed Antibiotic
17	HIV/STI

*Informed by: (Morgan, Okeke et al. 2011),(Ocan, Obuku et al. 2015),(Widayati, Suryawati et al. 2012),(Harris, Nikulina et al. 2015),(Boyd, McCabe et al. 2007)

Results

Descriptive and Univariate Analysis

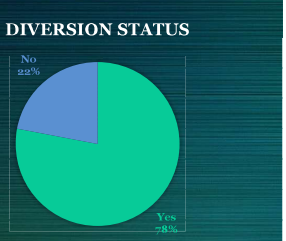
Results: Sample Description

- Median age – 32 (IQR: 20)
- Female (57%), male (37%), transgender (6%)
- ≥ High school education (69%), Elementary (31%)
- Median household size - 6 (IQR: 3)

Note: IQR: Interquartile Range, n=278, response rate: 95-100%

Results: Diversion

Reported diversion categories	Percent*
Other family member	37
Children	33
Neighbor	18
Elderly family member	18
Spouse or sex partner	16
Friend	14
Co-worker	8
Other	4
Never shared	22



*Percent's do not add to 100 as individuals could select multiple categories. 61% of respondents selected only 1 or 2 categories, with a range of 0 (never shared) to 8 (all categories but never shared).

Results: Knowledge

- Moderate Knowledge – Median of 5 (IQR: 3)
- Most Missed Questions*
  - Antibiotics can help someone who is infected with a virus – (85%)
  - Antibiotics are useful against all types of common cold/ cough – (81%)
  - When someone takes antibiotics very frequently, it can become more difficult to cure their future infections with antibiotics – (70%)

*Derived from (Hadi, Duerink et al. 2008), (You, Yau et al. 2008),(Widayati, Suryawati et al. 2011),(Widayati, Suryawati et al. 2012),(Lim and Teh 2012),(Ngadimon, Islahuddin et al. 2015)

Results: Perceptions of Access

- It is difficult for people in the community to get a prescription for antibiotics – (62%)
- It is easy to access antibiotics without a prescription from a healthcare worker – (45%)
- Even with a prescription, it is difficult to get an antibiotic (65%)
- There are people in my community who use antibiotics without instructions from a healthcare worker – (57%)

Results: Misconceptions

- It is safe to take antibiotics without instructions from a healthcare worker – (38%)
- It is good for a person to save antibiotics so that they can be used later for similar symptoms without needing to see a doctor – (52%)
- It is better to take a small dose of antibiotics than not take any dose – (62%)
- When a person starts feeling better, they can safely stop taking their antibiotics even when there are still antibiotics left to take – (45%)
- When I use antibiotics, I worry about the side effects – (65%)

Note: All questions used in the final multivariate model

Results

Univariate Associations	OR	95% CI	p-value
Demographics	-	-	-
Age years (n=277) - median (IQR)	1.0	1.0, 1.0	0.957
Sex (n=277)	-	-	-
Female	ref.	ref.	ref.
Male	1.4	0.8, 2.7	0.239
Transgender	2.1	0.5, 8.6	0.317
Education (n=269)	-	-	-
High school or more	ref.	ref.	ref.
Elementary	1.5	0.7, 2.8	0.269
Household size (n=264) - median (IQR)	1.1	1.0, 1.2	0.107

OR: estimated odds ratio, ref: reference, CI: confidence interval, abx.: antibiotic, IQR: interquartile range.

* vs. disagree; Agree = Strongly Agree + Agree

Results

Univariate Associations	OR	95% CI	p-value
Knowledge Score (n=278) - median (IQR)	0.8	0.7, 1.0	0.011
Perceptions (agree, ref=disagree)*	-	-	-
With prescription, difficult to get abx. (n=272)	1.7	0.9, 3.1	0.076
Safe to use abx. without instructions (n=273)	2.4	1.2, 4.5	0.010
Good to save abx. for later (n=273)	2.6	1.4, 4.7	0.002
Small abx. dose is better than no dose (n=274)	2.4	1.4, 4.4	0.003
Can stop abx. when feeling better (n=274)	3.3	1.7, 6.4	<0.001
On abx., worry about side effects (n=273)	1.6	0.9, 2.8	0.133

OR: Estimated odds ratio, ref: reference, CI: confidence interval, abx.: antibiotic, IQR: interquartile range. *The odds of diversion were estimated in comparison to those who disagreed with these statements.

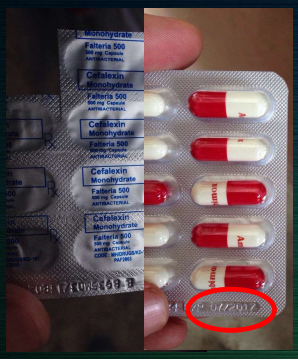
Results

Stand Characteristics	n (%)
Selling antibiotics (n=106)	
Yes	64 (60.4)
No	42 (39.6)
Antibiotics sold (n=95)*	
Amoxicillin	57 (60.0)
Cephalexin	20 (21.1)
Tetracycline	7 (7.4)
Cotrimoxazole	5 (5.3)
Metronidazole	2 (2.1)

Stand Characteristics	n (%)
Antibiotics expired	
Yes	4 (4.2)
No	35 (36.8)
Unable to determine	56 (59.0)
Full course available	
Yes	25 (26.3)
No	65 (68.4)
Unable to determine	5 (5.3)
Properly Stored	
Yes	93 (97.9)
No	2 (2.1)

*A total of 95 antibiotics were found in the 64 roadside stands selling antibiotics. Other antibiotics included: clarithromycin, levofloxacin, penicillin, and tigecycline.

Results



Stand Characteristics	n (%)
Antibiotics expired	
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Unable to determine	56 (59.0)
Full course available	
Yes	25 (26.3)
No	65 (68.4)
Unable to determine	5 (5.3)
Properly Stored	
Yes	93 (97.9)
No	2 (2.1)

Multivariate Results

Firth Logistic Regression

Multivariate Results

Multivariate Firth logistic regression (n=231)

	Adjusted OR	95% CI	p-value
Demographics	-	-	-
Age (years)	1.0	1.0, 1.0	0.942
Sex	-	-	-
Female	ref.	ref.	ref.
Male	1.0	0.5, 2.1	0.960
Transgender	5.7	0.3, 107.3	0.248
Education	-	-	-
High school or more	ref.	ref.	ref.
Elementary	1.3	0.6, 3.3	0.514
Household size	1.0	0.9, 1.1	0.850

OR: Estimated odds ratio, CI: confidence interval, ref: reference, abx.: antibiotic

Multivariate Results

	Adjusted OR	95% CI	p-value
Knowledge Score (n=278)	0.8	0.7, 1.0	0.066
Perceptions (agree, ref=disagree)	-	-	-
With prescription, difficult to get abx.	1.3	0.7, 2.7	0.423
Safe to use abx. without instructions	1.4	0.6, 3.2	0.385
Good to save abx. for later	1.9	0.9, 4.0	0.090
Small abx. dose is better than no dose	1.9	0.9, 3.9	0.098
Can stop abx. when feeling better	2.8	1.3, 5.8	0.008
On abx., worry about side effects	2.1	1.1, 4.4	0.035

OR: Estimated odds ratio, CI: confidence interval, ref: reference, abx.: antibiotic

Limitations

- Convenience sample
- Self-Report
- Small sample size
- Lack of spatial consensus for sari-sari stands
- Analysis
  - Missingness on covariates of interest

Conclusions/Recommendations

- Prevalence of reported antibiotic diversion is high – (78%)
- Diversion most common among family members
- Antibiotic misconceptions are equally or more important to antibiotic diversion than sociodemographic characteristics or knowledge factors
- Data from sari-sari stores indicate that antibiotics diverted throughout this community may present significant health concerns
- In order to curb the epidemic of antibiotic resistance, interventions must target location-specific antibiotic misconceptions and issues of access to legitimate pharmaceutical outlets

Acknowledgements

Capstone Committee

Dr. April Young, Chair

Dr. Jay Christian

Dr. Wayne Sanderson

Research Personnel

Joshua Tiller and April Ballard

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Island Ventures, Inc.

Aimee Hilliard

Barangay captains and health workers

Dr. Rudolfo Berame