What Happens When “Germs Don’t Get Killed and They Attack Again and Again”: Perceptions of Antimicrobial Resistance in the Context of Diarrheal Disease Treatment among Laypersons and Health-Care Providers in Karachi, Pakistan

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Abstract. In south Asia, where diarrhea is common and antibiotics are accessible without prescription, antimicrobial resistance is an emerging and serious problem. However, beliefs and behaviors related to antimicrobial resistance are poorly understood. We explored laypersons’ and health-care providers’ (HCP) awareness and perceptions of antimicrobial resistance in the context of treatment of adult diarrheal disease in Karachi, Pakistan. In-depth, open-ended interviews were conducted with 40 laypersons and 45 HCPs in a lower-middle-class urban neighborhood. Interviews conducted in Urdu were audiotaped, transcribed, translated, and coded using applied thematic analysis. Slightly over half of laypersons and two-thirds of HCPs were aware that antimicrobial medication could lose effectiveness, but misperceptions were common. Laypersons and HCPs often believed that “the body becomes immune” or “bacteria attack more strongly” if medications are taken “improperly.” Another prevalent theme was that causes and effects of antimicrobial resistance are limited to the individual taking the antimicrobial medication and to the specific diarrheal episode. Participants often attributed antimicrobial resistance to patient behaviors; HCP behavior was rarely discussed. Less than half of the HCPs were aware of treatment guidelines. To combat antimicrobial resistance in urban Pakistan, a health systems strategy and community-supported outreach campaigns on appropriate antimicrobial use are needed.

INTRODUCTION

Over the last 60 years, the use of antimicrobial drugs has become widespread, significantly reducing morbidity and mortality. The appropriate use of these drugs requires that patients receive medications suitable for their specific clinical needs, at the correct doses and for the correct duration, and at the lowest cost to the patient and community. It also requires that patients take the medications as prescribed. In practice, however, antimicrobial drugs have been extensively misused by humans and in agriculture, resulting in the selection and spread of resistant strains. Globally, half of all medicines may be inappropriately consumed, which can cause selection of antimicrobial-resistant pathogens among individual humans or animals treated with the antimicrobials.¹ Inadequate sanitation and hygiene, crowding, and travel facilitate transmission of such pathogens and contribute to the increased prevalence of antimicrobial-resistant pathogens globally.² Consequently, the supply of antimicrobial drugs has become less effective and sometimes ineffective. The seriousness of the situation is compounded by the historical trend of decreasing development of new antimicrobial drugs. The last new class of antimicrobial drugs to be developed was in the 1980s.³ Preserving the effectiveness of existing drugs by promoting responsible use and minimizing the spread of resistant strains is critical. Understanding both patient and provider perceptions of antimicrobial resistance is a logical starting point from which to develop effective, feasible, and acceptable education and communication strategies for enhancing the patient and provider stewardship of antimicrobials.

Approximately 2.1 billion diarrhea episodes occur annually among adults,⁴ and diarrhea morbidity in this age group has

remained stable for decades.⁵ Antimicrobials are often used inappropriately to treat diarrhea. This practice might be particularly common in south Asia. Antimicrobials are prescribed in 70% of patient encounters in Pakistan and may be prescribed more commonly for diarrhea patients.⁶ The average number of drugs prescribed per patient per encounter (for any condition) is three or more in Pakistan, which is higher than in other low- to middle-income countries.⁶ In India, 90% of ambulatory adults⁷ and 71% of children presenting to outpatient or inpatient settings⁸ with acute diarrhea were treated with antibiotics. A survey of public facilities in Pakistan found that the mean consultation time was 1.8 minutes, insufficient to obtain necessary history to diagnose a patient’s condition correctly and provide important information to educate the patient on how and why to take medicine properly.⁹

Demand-side factors also contribute to this dynamic. In south Asia, desire for fast symptomatic relief leads consumers to choose allopathic medicines, which are simultaneously revered for their “strength,” yet also feared for their possible long-term consequences and considered an expensive investment.^{10–12} Consequently, individuals are compelled to seek these treatments and then discontinue them when symptoms subside. Economic considerations may also fuel self-medication, through consulting pharmacies instead of medical practitioners and saving unused pills for the next illness.^{11,12} It has been observed that approximately one-half of antimicrobials purchased in Indian pharmacies and chemist shops may be for self-care,^{11,13,14} a practice that has been associated with low education level, belief that medical consultation is expensive, and dissatisfaction with medical practitioners.^{12,15} Additional evidence confirms that self-administered antimicrobials are often taken in inadequate doses for too few days.^{12,13}

Unsurprisingly, high rates of multidrug-resistance have been detected among prevalent bacterial pathogens in India and Pakistan.^{16–19} However, few data currently exist to guide interventions to improve responsible antibiotic use among

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ambulatory patients.^{12,20} Provider education on antimicrobial prescribing guidelines can improve antimicrobial use²¹; however, such interventions are likely to be more effective when tailored to the local setting. Understanding the perspectives and practices of adult outpatients with diarrhea in south Asia and of the health care providers (HCPs) who treat them is critical to developing effective interventions to reduce the inappropriate antimicrobial use in this setting. Research that focuses on knowledge and perspectives on antimicrobial resistance among laypersons and HCPs in south Asia is limited, however.¹² Especially little is known about perspectives in Pakistan; we found no published research on this topic.

The purpose of this study was to understand layperson and HCP awareness and perceptions of antimicrobial resistance in Karachi, Pakistan, a geographic region with the high prevalence of diarrheal disease and antimicrobial resistance. We applied a qualitative methodology—in-depth interviews—to explore awareness of resistance, perceived causes, and potential solutions among a diverse sample of residents in a lower-middle-class community and a range of HCPs, including general practitioners, pharmacists and medical store owners, and unlicensed care providers.

METHODS

Setting. Health-Oriented Preventive Education (HOPE), a local nongovernmental organization that administers health clinics, schools, and community development programming, conducted the fieldwork between May and September 2013 in Karachi. The study was set in central Karachi among densely populated, low- to middle-income, multiethnic informal settlements. Approximately 31 settlements were targeted; these catchment areas comprise about 25% of the city's population. Typical professions include low-ranking government employees, factory workers, traders of petty goods, plumbers, tailors, masons, drivers, electricians, school teachers, and construction workers. Households generally own televisions and telephones. Drinking water is typically obtained from the tap, but is of poor microbiological quality.²²

In the study setting, antimicrobial medications are sold in medical stores and pharmacies, which are often open 24 hours a day. Medical stores are frequently run by individuals with no formal training in pharmacology. Despite Pakistani law requiring prescriptions for antimicrobials, enforcement is uncommon, and such medications are widely available over the counter (M. Agboatwalla, personal communication).

Study design and sampling. The research strategy was qualitative, featuring 85 semi-structured open-ended interviews with laypersons ($N = 40$) and HCPs ($N = 45$), including general practitioners in private care settings, unlicensed care

providers, as well as pharmacists and medical store keepers (persons who dispense medications in community retail environments, henceforth termed as “pharmacists”). The sample size was based on our estimation of saturation (i.e., the point at which no new information or themes are observed in the data), considering the breadth and depth of topics discussed in the interviews, as well as the practical implications of previous research on qualitative methods.²³ The study team aimed to recruit a diverse sample using a plan with geographic reach across the 31 settlements and quotas for key demographic characteristics. Table 1 displays quotas and eligibility criteria.

Laypersons were purposively recruited from over 30 target communities. The HOPE staff visited public community venues (e.g., markets and tea houses) and went door-to-door in target communities attempting to enroll and interview interested participants. To recruit HCPs, study staff generated a list of known practicing providers in the target communities. Given that the study took place in a time of sociopolitical unrest and low levels of trust, snowball sampling was used to enroll additional participants and providers. Respondents were asked to name up to five others who may be interested.

Data collection. Separate interview guides were designed for laypersons and HCPs to elicit beliefs and practices related to diarrhea among adults. Interviews among laypersons aimed to explore definitions of diarrhea, self-management of diarrhea, perceptions about the role and utility of antibiotics in diarrhea treatment, awareness of antibiotic resistance, and where and how adults learn about diarrhea management. Interviews among HCPs explored beliefs and practices related to managing diarrhea among adults, antimicrobial resistance, and alternative treatment strategies. The interview guides were developed through extensive input from the HOPE staff, who have experience working in the study community on the prevention and treatment of diarrheal disease. Examples of the questions central to this analysis are presented in Table 2; analyses of other interview topics are presented separately.

After the English instruments were established, questions were translated into Urdu, checked for consistency and meaning, and then back translated. The instruments were also piloted among the HOPE staff and a small sample of laypersons and HCPs for linguistic accuracy and conceptual relevance.

HOPE staff served as interviewers and received intensive training in qualitative data collection and interviewing techniques. Female respondents were interviewed by female staff, and male respondents were interviewed by male or female staff. Interviews were conducted face-to-face in homes, public venues, or workplaces (for HCPs); attempts were made to administer the interviews in a private setting. The interviews,

TABLE 1
Eligibility criteria and sampling quotas

	Laypersons ($N = 40$)	General practitioners ($N = 15$)	Pharmacists ($N = 15$)	Unlicensed care providers ($N = 15$)
Eligibility criteria	18–60 years old Speak Urdu or English —	≥ 22 years old Speak Urdu or English Been in practice for at least 6 months	≥ 22 years old Speak Urdu or English Been in practice for at least 6 months	≥ 22 years old Speak Urdu or English Been in practice for at least 6 months
Sampling quotas	50% female 50% under 40 years of age	≥ 30% female —	— —	≥ 30% female —

Because of the paucity of female pharmacists in Karachi, there was no gender sampling quota for this group. Laypersons were not practicing health-care providers (HCPs), and only one participant per household could be enrolled. Household members of participant HCPs were excluded.

TABLE 2

Example interview questions about antimicrobial resistance

Laypersons	Do you think there are any problems with using antibiotics for diarrhea? What are the problems?
	Have you heard about antibiotics not working or being ineffective because of not using the drugs properly?
	How serious of a problem is this?
	What can be done to prevent it?
Health-care providers	Have you heard the term "antibiotic resistance"? What does it mean to you?
	How does it occur?
	Is it a problem in Karachi? In Pakistan?
	Does antibiotic resistance affect the way you practice? How so?
	Have you heard about antibiotics not being effective because of inappropriate use of the drug?

averaging 90 minutes, were conducted in Urdu and digitally recorded. A second interviewer took detailed handwritten notes simultaneously. All respondents received a small incentive (a meal and handwashing supplies for laypersons and a wallet-keychain set for providers).

The audio files were transcribed in Urdu and then translated into English by other team members. To ensure high data quality, routine spot checks were conducted for both transcription and translation fidelity.

Analysis. Transcribed English interviews were coded using qualitative analysis software *NVivo* version 10 (QSR International, Doncaster, Australia). We used applied thematic analyses to identify and describe both implicit and explicit ideas within the data. These themes were detected by applying and linking codes in the raw data as summary markers for later analysis.²⁴ A combination of inductive and deductive coding was used. The coding system involved two stages and was implemented by a three-person analysis team. First, an a priori codebook, consisting of both structural and thematic codes, was developed after an initial review of randomly selected transcripts. To enhance the validity and reliability, analysts independently coded a random selection of transcripts, and then the team compared results, discussed coding decisions, and resolved differences. During this process, emergent codes were added to the codebook. Once the pre-established benchmark (80% of the codes achieving a kappa statistic of at least 0.8) was reached (double coding and comparing approximately 30 transcripts), all transcripts were coded. In the second stage, the analysis team defined the scope for this report (perceptions of antimicrobial resistance) and conducted a second round of more detailed coding and subcoding, as well as axial coding. We performed the reliability testing using the same procedures (double coding and comparing approximately 20 transcripts to reach a benchmark of 80% of the codes achieving a kappa statistic of at least 0.8). At this point, the remaining transcripts were coded by a single coder, who created extensive memos on emerging themes related to perceptions of antimicrobial resistance that were iteratively discussed with the team throughout the analysis process. We explored the differences by the type of HCP; such instances are reported in the Results section. Finally, HOPE staff reviewed and provided substantive feedback on interpretations and provided insights about community context.

TABLE 3

Characteristics of layperson participants in Karachi, Pakistan, 2013

	N = 40	%
Demographics		
Male	20	50
Age in years, median (range)	33.5 (24–55)	
Family characteristics		
Married	37	93
Any children at home	28	70
No. of children at home (among those with any), median (range)	2 (1–6)	
Language		
Speak Urdu at home	40	100
Speak Urdu and ≥ 1 other languages at home	22	55
Education		
Completed secondary school	38	95
Completed university degree	25	63
Completed Master's degree	7	18
Material wealth		
Own television	39	98
Own mobile phone	38	95
Own car or motorcycle	32	82

Ethics. The protocol was approved by the institutional review boards at the U.S. Centers for Disease Control and Prevention and HOPE. All respondents provided verbal informed consent.

RESULTS

The sampling strategy yielded a diverse sample, in terms of gender and age, among the layperson participants (Table 3), as well as age and duration of practice among HCPs (Table 4). Respondents were drawn from 31 communities; a median of two respondents was enrolled per settlement area (range = 1–8). Laypersons in our sample were highly educated for this setting. Among the pharmacists in this study, none reported formal pharmacological training; eight had 4-year university degrees, six finished 2 years of university, and one finished tenth grade (high school equivalent).

Table 5 presents a summary of the major findings and themes, along with illustrative quotes, segmented by domain and group.

TABLE 4

Characteristics of health-care provider participants in Karachi, Pakistan, 2013

	General practitioners N = 15	Pharmacists N = 15	Unlicensed care providers N = 15
Demographics			
Male	9	15	9
Age in years, median (range)	30 (25–58)	30 (22–48)	35 (24–59)
Practice			
No. of years in practice, median (range)	3 (2–32)	7 (2–18)	10 (2–32)
Provides outpatient care	15	15	15
Provides some inpatient care	1	NA	2
Dispenses medications*	2	15†	9
Provides daytime care	14	15	13
Provides evening care	11	15	11

NA = not applicable.

*Questions were not asked of all providers.

†Most pharmacists (12/15) provided antimicrobial medications with no prescription (two specified that they only do this rarely, such as when no doctor is available or the patient refuses to go to a medical clinic).

TABLE 5
Summary findings, themes, and quotes about antimicrobial resistance (AR), segmented by domain and group

Domain	Group	Summary findings and themes	Reflective quotes
Awareness, definitions, and perceived seriousness	Laypersons	Approximately one-half were aware of AR Framed both as treatment not working and germ becoming more pathogenic Considered a serious problem for the individual	<i>The viruses or bacteria become more harmful. Bacteria attack more strongly.</i>
	HCPs	Approximately two-thirds aware of AR Awareness varied by HCP type Understanding of AR was basic Most felt AR is a serious problem, though varied by HCP type	<i>Most of the time patients use antibiotics again and again due to which the medicine stops being effective. And in some patients, it happens that their bodies start generating antibodies which binds with the medicine and render it ineffective. The body of the patient gets immune by using the antibiotics again and again. It's a serious issue. In our country, people have this attitude of using a lot of self-medication.</i>
Causes and implications	Laypersons	Most commonly mentioned cause was not following doctor's instructions, particularly not completing the prescribed course of antimicrobials, followed by self-medication Effects were described in terms of the individual and often referred to the particular episode of diarrhea	<i>If you don't complete the course and don't follow the doctor's prescription, then the disease that you are using antibiotics for can occur again because the germs don't get killed and they attack again and again.</i>
	HCPs	Most commonly mentioned cause was self-medication, followed by not taking drug according to doctor's instructions Some mentioned HCP prescribing practices Misunderstanding were common; many attributed AR to the body becoming immune to antimicrobials	<i>People are misusing antibiotics. They don't take its doses properly and that's why antibiotics become ineffective. Sometimes, they don't complete the course as prescribed by the doctor. For example, if it's a 5 day course and the patient takes it for a day and feels better, then he stops taking it.</i>
Prevention	Laypersons	Most commonly mentioned strategy was for persons to take antimicrobials as directed by an HCP, particularly completing the course as prescribed Some suggested taking antimicrobials less often Some mentioned taking a drug only with a prescription	<i>The patient should complete the course as prescribed by the doctor. I also think the doctor should ensure that patients understand how essential it is to complete the course. The doctor should explain the adverse impact that not completing the course can have on the patient, basically scare them into following the prescription and instructions.</i>
	HCPs	Prioritized patient education via interactions with HCPs and social marketing campaigns Some supported reducing usage of antimicrobials While most general practitioners were aware of treatment guidelines, this was less common among unlicensed providers	<i>There are some steps which can be taken to address antibiotic resistance. People should be informed and educated regarding the drawbacks and disadvantages of excessive use of antibiotics. We should also tell them that they should use antibiotics when they have absolute need of the drug. Blind usage of antibiotic is not going to help out the patient, rather it is going to do more harm than good.</i>

AR = antimicrobial resistance; HCPs = health-care providers.

Awareness, definitions, and perceived seriousness of antimicrobial resistance. Laypersons were generally less aware of antimicrobial resistance compared with HCPs. However, awareness varied by HCP type; general practitioners were more frequently aware of antimicrobial resistance compared with unlicensed providers and pharmacists. Among almost all participants, definitions were offered in basic terms. Most who were aware of antimicrobial resistance seemed to consider it a serious problem, although this perception varied by HCP type.

Laypersons. Approximately half the laypersons reported that they had “heard about antibiotics not working or being ineffective because of not using the drugs properly” and were able to describe it with general accuracy (22/40). We further probed on how they personally defined it; many answered that “medicines are ineffective” or the “medicine won’t work on you.” Others framed the problem as “the

viruses or bacteria become more harmful,” or “bacteria attack more strongly.” Those who were aware of antimicrobial resistance seemed to consider it a serious problem. However, respondents often viewed it as problematic for the individual patient, rather than the larger society. For example, one respondent said “It’s a very serious issue, there is a chance that the patient can die due to this,” and another explained “It’s a very important issue, if antibiotics become ineffective then it’s difficult to get cured, and the condition can even get worse after some time.”

Health-care providers. Overall, two-thirds (30/45) of the HCPs reported that they had heard the term “antibiotic resistance.” All of the general practitioners, most of the unlicensed providers (12/15), and about half of the pharmacists (8/15) were aware of it. Most providers defined it using basic nonspecific terms, such as the antibiotic “not working” or being “ineffective.” Among those who were asked, most

(22/26) felt that resistance was a serious problem in Pakistan. While all general practitioners indicated this (12/12), fewer unlicensed providers shared this belief (5/8).

Causes and implications of antimicrobial resistance. Laypersons and HCPs were asked to describe the causes of antimicrobial resistance; both groups often used the individual patient as the frame of reference. Consequently, predominant themes were individual medication-taking behavior, including disregard for HCP instructions or self-medicating with antibiotics, and a relative lack of focus on HCP behavior regarding overprescribing antibiotics. Themes among HCPs were similar and responses revealed pervasive misunderstanding about antimicrobial resistance.

Laypersons. In general, laypersons focused on the individual's behavior as the cause of antimicrobial resistance. Among those aware of antimicrobial resistance, most (16/22) attributed it to not taking the medication "properly." More specifically, laypersons described "not following the doctor's prescription on completing the course." One respondent offered "If you don't complete the course and don't follow the doctor's prescription, then the disease that you are using antibiotics for can occur again because the germs don't get killed and they attack again and again." Some also attributed it to patients "taking antibiotics themselves" or "without the doctor's advice" (5). Only two respondents cited generalized antibiotic overuse. Though HCPs were often regarded as authoritative experts, no respondents discussed the role of HCPs or factors related to the broader health-care system.

Paralleling the causes, the perceived effects of antimicrobial resistance were also centered on the individual and often referred to the particular episode of diarrhea for which the person was seeking treatment. For example, one respondent stated, "Usually people start using antibiotics without the doctor's prescription; they don't know the duration of the course and dosage. Obviously if they use it without the doctor's advice, they will have to bear the drawbacks and side-effects."

Health-care providers. Among all HCPs, antimicrobial resistance was commonly attributed to persons using antimicrobial medications without a prescription or not taking them according to the provider's instructions (21/22). The following statement reflects a common perception: "People are misusing antibiotics. They don't take its doses properly and that's why antibiotics become ineffective. Sometimes, they don't complete the course as prescribed by the doctor. For example, if it's a 5-day course and the patient takes it for a day and feels better, then he stops taking it. This causes antibiotic resistance."

Only four HCPs discussed antimicrobial overprescribing practices by fellow providers as a source of antimicrobial resistance and often ascribed prescribing errors to unlicensed care providers. One offered, "Because there are so many quacks or unlicensed health care providers practicing in Pakistan, they are usually unaware about the proper dosage and side-effects of antibiotics. So many patients come to me with the prescriptions of the quacks, and I have seen that in most of the cases, they were given the wrong medicines or dosage." Several HCPs discussed issues related to the production of antimicrobial medication as a source of antimicrobial resistance (4); "Sometimes antibiotics are light. That is the reason their antibiotics don't work. (What do you mean by light?) Light as in they have low quality. The bigger the company would be, the more effective is the antibiotics."

Misunderstanding was common. Often, HCPs attributed resistance to the patient's body developing immunity to the antibiotics (9). Comments included "The body gets immune and thus it resists the treatment" and "if a patient uses antibiotics excessively, then in a while, the body becomes immune to it." Slightly less often, HCPs associated antimicrobial resistance with adverse drug effects (7). For example, one HCP stated that, "Resistance means when the patients use antibiotics without the prescription of doctors, they get side effects affecting their body organs like liver, eyes, and arteries. They may also get the same diseases again for which antibiotics were previously taken."

Prevention of antimicrobial resistance. Both laypersons and HCPs were able to discuss ways to prevent antimicrobial resistance, and they referred to similar strategies of enhancing patient education about adhering to prescriptions and using antimicrobial medication less often. In both groups, restriction of antibiotic dispensing to prescription-only was mentioned repeatedly. However, adherence to treatment guidelines was not discussed by HCPs in the context of antimicrobial resistance.

Laypersons. Among those asked how to prevent resistance, the most common response was to take antibiotics as directed by the HCP (10/22), followed by using these medicines less often (7), and not taking antibiotics without a prescription (5). The HCPs' role was rarely discussed. A layperson commented: "The patient should complete the course as prescribed by the doctor. I also think the doctor should ensure that patients understand how essential it is to complete the course. The doctor should explain the adverse impact that not completing the course can have on the patient, basically scare them into following the prescription and instructions." Another mentioned, "People should avoid antibiotics as much as they can and shouldn't use them without a doctor's prescription. They should try to get better with other medicines other than antibiotics."

Health-care providers. Most HCPs were able to describe some prevention strategies (except unlicensed providers, who felt that nothing could be done [3/4]). The most common recommendations were to educate patients via social campaigns and during office visits (21). One respondent said, "I think medical care providers should give the awareness to their patients about the dosage of the antibiotic and pharmacists should also give details of the medication according to the doctor's prescription."

Some HCPs (16) discussed the need to limit the prescription of antimicrobials: "There are some steps which can be taken to address antibiotic resistance; for instance, common people should be informed and educated regarding the drawbacks and disadvantages of excessive use of antibiotics and should also tell them that they should use antibiotics, when they have absolute need of the drug. Moreover, blind usage of antibiotic is not going to help out the patient; rather, it is going to do more harm than good." This sentiment was most prevalent among licensed HCPs (8/15) and least among unlicensed HCPs (1/15). Many of them (15) also discussed the role of medical shop owners, "Medical stores should only give out antibiotics when the patient shows the doctor's prescription. I think doctors should also be well-versed in the impact of incorrect antibiotic usage and they should take extreme care when prescribing them."

No HCPs mentioned the existence or use of treatment guidelines in relation to antimicrobial resistance. However,

we specifically asked the general practitioners and unlicensed practitioners at the end of the interview about their awareness and use of national or international diarrhea treatment guidelines. Most general practitioners were aware of the guidelines (9/15); however, this was less common among unlicensed HCPs (2/15). Almost all reported that these could be found on the Internet, but HCPs frequently suggested the guidelines would be more effective if publicized further (8) and were available in additional languages (4).

DISCUSSION

We conducted this qualitative study to gather insight about how laypersons and HCPs perceive the problem of antimicrobial resistance in the context of adult diarrhea to help inform community-level interventions that rely on the changes in knowledge, beliefs, and behavior. We focused on adult diarrhea, which is usually self-limited and typically only requires rehydration therapy, because of its high prevalence in these communities and frequent use of antimicrobials for treatment. Antimicrobial misuse is a complicated and evolving public health problem due to a lack of global therapy standards and varying national regulations, policies, and systems. In addition, developing and evaluating impactful behavior change interventions for health consumers and providers is challenging, complicated by varying social, cultural, and economic circumstances.^{25,26} We focused on three primary areas of understanding: awareness, perceived causes and implications, and community-identified solutions for antimicrobial resistance. Considered in combination with other research, our findings support several potential strategies to combat antimicrobial resistance.

Although laypersons enrolled in this study were highly educated, only half were aware of the concept of antimicrobial resistance, suggesting that efforts are needed to increase consumer knowledge. Among those who did report a basic understanding, many perceived antimicrobial resistance to be an individual problem. That is, if a person did not use antimicrobial medication properly, the drugs would not work for that specific person's bout of illness. Drug-resistant pathogens, however, are communicable and are a societal problem as well as an individual one. Educational messages on the emergence of antimicrobial resistance even among those who have not personally "misused" antibiotics should be considered. A social good motivation to use antimicrobial medication responsibly may be harnessed; in places where the collective is prioritized over the individual, this notion may be especially resonant. Although no evidence demonstrates that social motivation messaging has been effective in the United States, different outcomes may be observed in other settings.²⁷ Fundamentally, behavior change is unlikely unless people believe in its importance and in their ability to achieve it through feasible action.^{28–31} Additional research should measure the effectiveness of messaging that emphasizes the importance of the problem to individuals, families, and communities and provides specific behavioral alternatives. However, evidence of effective consumer education campaigns regarding antimicrobial resistance in developing countries is inconclusive, partially due to limited research. We found only a few modestly effective community education interventions described in the literature.^{32,33}

There is an opportunity to increase awareness and understanding of antimicrobial misuse and resistance among HCPs, especially pharmacists. HCPs may not have a common and correct understanding of "antibiotic resistance," even if familiar with the term. Many HCPs, across all three provider types, believed that resistance was a result of "the body" becoming resistant to the effects of antibiotics. Blame was most often attributed to patient behavior, rather than provider practice. Furthermore, although HCPs were most concerned about the individual-level effects of antimicrobial misuse, none mentioned the individual's increased risk of infection due to microbiota disruption, which may have equal, if not more, significant consequences than antimicrobial resistance for the individual. By disrupting the host microbiota, antibiotics likely increase susceptibility to infection including diarrhea, fungal overgrowth, clostridial infections, and sepsis.^{34,35} Fewer than half of the HCPs in this study were aware of existing diarrhea treatment guidelines, with a notable difference between general practitioners and unlicensed HCPs. Furthermore, no pharmacists in the present study reported formal pharmacological training. Other have noted similar gaps in awareness of treatment guidelines and formal training. One survey in Pakistan found that only 12% of dispensers were pharmacologically trained, and 35% had secondary school qualification.³⁶ Only 24% knew proper administration of oral rehydration solution and 60% knew the proper dose of amoxicillin for adults with pneumonia.

In terms of previously evaluated interventions, those targeted to HCPs may be more effective than those for consumers. Evidence supports educational programs for HCPs, with outcomes such as more appropriate diagnostic procedures, more accurate perceptions about patient preferences, and more appropriate use of antimicrobial treatments.^{37–40} Further evidence suggests that coaching clinicians to educate patients about symptomatic care might decrease antibiotic prescribing but preserve patient satisfaction.⁴¹ Effective educational interventions may require repeated and frequent interaction with participants, including refresher courses and sustained outreach efforts.^{27,42–44} In the present study, layperson respondents were receptive to information from physicians, who were frequently regarded as authoritative experts. Thus, counseling by HCPs may be particularly effective in altering patient behavior in this setting. However, HCPs will first require increased access to and awareness of treatment guidelines, which would recommend rehydration and symptomatic care, rather than antimicrobial medications, for most diarrhea patients. In addition, office visits may need to be extended to accommodate additional health education.⁹ Efforts to increase knowledge of antimicrobial resistance among both HCPs and laypersons may need to include social marketing campaigns and directed government outreach on the local level, both of which were supported by participants in this study. Community pharmacies and medical stores play a significant role in consumers' access to antimicrobials. Pakistan has one of the highest numbers of drug outlets (45,000–50,000) in low- to middle-income countries, making regulatory monitoring difficult.⁴⁵ Although Pakistan law requires that antimicrobial medication be dispensed by physician prescription, more than three-quarters of pharmacists in this study acknowledged dispensing without a prescription. Furthermore, antimicrobial medications are generally sold in set quantities rather than as the specific number of doses called for in a prescription; thus,

patients may purchase only the portion of a prescription that they can afford, or they may receive excess pills that are saved for later use (M. Agboatwalla, personal communication). However, HCPs—including pharmacists—commonly proposed that all antimicrobial medication be dispensed only with a prescription. While requiring a prescription may be a logical response in developed countries with adequate infrastructure and where dispensers are officially registered, such regulations are difficult to implement where there is limited enforcement but strong demand among consumers and economic incentives among HCPs to dispense antimicrobial medications.⁴⁶ Alternatively, pharmacists may be trained to offer non-antimicrobial medications for symptomatic care, so that patients are satisfied and pharmacists do not incur economic penalties for being good stewards.⁴¹

This study has several limitations. First, the sample was created via a snowball recruitment, which may have reduced diversity. The laypersons had relatively high educational attainment for the study setting. However, sampling quotas partially limited the sample from being weighted too heavily by any one gender or age group. Also, the samples of specific HCP types were small; any differences noted between HCP types should be considered suggestive pending further research. Since the interviews were conducted with semi-structured guides, interviewers somewhat varied in the degree to which they probed for follow-up responses. Finally, the interviews were transcribed and translated, processes that inevitably include some error. However, the interviews were audio recorded, and our quality assurance protocols likely reduced transcription and translation error rate.

Much of the accumulating research on interventions to control antimicrobial resistance has been conducted in resource-rich countries and focused on reducing transmission in health-care facilities rather than the drivers of antimicrobial resistance in the community. Improving basic water, sanitation, and hygiene in resource-poor settings would reduce illness and thus inappropriate prescriptions and self-treatment with antimicrobials and consequently would likely have substantial impact on the prevalence of drug-resistant pathogens both within and beyond the region.^{47,48} However, other complementary strategies are also needed and should be informed by an understanding of local perceptions.⁴⁶ Though not the focus of this report, additional attention is warranted for the behavioral economics that compel laypersons with limited resources to self-medicate and use antimicrobial medications in ways that may facilitate the development of antimicrobial resistance. HCP and pharmacists' prescribing and selling practices are likely affected by similar forces. This research highlights important perspectives from the targets of future interventions. In this study, both HCPs and laypersons considered antimicrobial resistance to be an individual problem resulting from the very fine point of a patient's medication-taking behavior for a particular illness. Reframing this collective problem will necessarily be an effort that engages multiple strategies and stakeholders, including governments, pharmaceutical firms, HCPs, dispensers, and consumers.

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