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Household Animal and Human Medicine Use and Animal Husbandry Practices in Rural Bangladesh: Risk Factors for Emerging Zoonotic Disease and Antibiotic Resistance

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Impacts

- The use of antibiotics in livestock is an important risk factor for emerging antibiotic resistance.
- This paper describes household-level risk factors for emerging zoonotic diseases and antibiotic-resistant pathogens in rural Bangladesh and finds that 58% of household that own livestock report the use of medicines for their livestock.
- This is the first report to discuss household-level healthcare seeking and the use of antibiotics for livestock in a low-income country.

Keywords:
Livestock; animal husbandry; non-human antibiotic use; emerging zoonotic disease; antibiotic resistance; one health

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Summary

Animal antimicrobial use and husbandry practices increase risk of emerging zoonotic disease and antibiotic resistance. We surveyed 700 households to elicit information on human and animal medicine use and husbandry practices. Households that owned livestock (n = 265/459, 57.7%) reported using animal treatments 630 times during the previous 6 months; 57.6% obtained medicines, including antibiotics, from drug sellers. Government animal healthcare providers were rarely visited (9.7%), and respondents more often sought animal health care from pharmacies and village doctors (70.6% and 11.9%, respectively), citing the latter two as less costly and more successful based on past performance. Animal husbandry practices that could promote the transmission of microbes from animals to humans included the following: the proximity of chickens to humans (50.1% of households reported that the chickens slept in the bedroom); the shared use of natural bodies of water for human and animal bathing (78.3%); the use of livestock waste as fertilizer (60.9%); and gender roles that dictate that females are the primary caretakers of poultry and children (62.8%). In the absence of an effective animal healthcare system, villagers must depend on informal healthcare providers for treatment of their animals. Suboptimal use of antimicrobials coupled with unhygienic animal husbandry practices is an important risk factor for emerging zoonotic disease and resistant pathogens.

Introduction

Many factors contribute to the emergence of antibiotic resistance (See Fig. 1); antibiotic usage is considered the most important factor promoting the emergence, selection and dissemination of antibiotic-resistant microorganisms in both veterinary and human medicine (Marshall and Levy, 2011), and exposure to livestock is a risk factor for emerging zoonotic diseases, including antimicrobial-resistant pathogens, coronaviruses (SARS, MERS) and filoviruses (Ebola) (Morens et al., 2004). In the modern poultry industry, antimicrobials are used in high quantities – not only for therapy and prevention of bacterial disease but also as antimicrobial growth promoters (AMGPs) in animal feeds – which may constitute the greatest selection pressure for the emergence of resistance (Angulo et al., 2009; Marshall and Levy, 2011). The faecal flora of chickens, for example, contains a relatively high proportion of resistant bacteria. Studies from high-income countries have reported that poultry are a source of antibiotic resistance for poultry farm workers (van den Bogaard et al., 2002; Price et al., 2007). Studies from low- and middle-income countries (LMIC) have shown that poultry farm workers and their family members are at an increased risk for carriage of antibiotic-resistant bacteria and diarrhoeal pathogens than the general population (Al-Ghamdi et al., 1999; Raghunath, 2008; Donkor et al., 2012) (See Fig. 1). In LMIC, people generally live in closer contact with livestock than in high-income countries (HIC) and this is linked to increased risk for diarrhoeal diseases (Al-Ghamdi et al., 1999; Harvey et al., 2003) (See Fig. 1). Limited data are available on household-level antibiotic use for humans in Bangladesh, and no data exist on household-level antibiotic use for animals in Bangladesh or in other low-income countries (Hossain et al., 1982). One of the few published studies on human antibiotic use in Bangladesh suggested a high rate of medicine use; 189 individuals took 261 drugs, patients rarely obtained a full prescription, and about 95% of purchases were from private pharmacies (Hossain et al., 1982). According to this study, there was minimal antibiotic use in animals and none in animal feed in the early 1980s. An extensive literature review did not uncover any additional references on antibiotic use in Bangladesh.

Despite no active surveillance in Bangladesh, antimicrobial-resistant (AMR) strains of *Streptococcus pneumoniae*, gonorrhoea, enteric and other pathogens of public health importance have been reported (Saha et al., 2004, 2009). Reports of multidrug-resistant *S. pneumoniae, Haemophilus influenzae type B* and *Shigella* have also been increasing (Haq et al., 2005; Saha et al., 2009). Recently, antibiotic-resistant bacteria was reported on commercial poultry farms in Bangladesh (Akond et al., 2009).

Even with the increasing evidence for the emergence of zoonotic diseases and the transference of antibiotic resistance determinants from livestock to farm workers and their family members, there are few studies that examine this phenomenon or its risk factors, at the household level in LMIC where the vulnerability to resistant infectious diseases may be greatest. In Bangladesh, specifically, there are no published data available on animal healthcare practices at the household level. This study was conducted

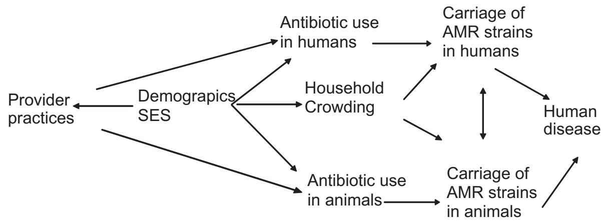

Fig. 1. Study framework of factors that influence the emergence of antibiotic resistance. There is a direct relationship between carriage of resistant bacteria and disease caused by that bacteria. An association between animal carriage and human carriage of AMR has been shown. Antibiotic use in humans and animals is associated with carriage of resistant bacteria. Known risk factors for the spread of AMR include household-level variables (crowding, travel, proximity to clinics). Socio-economic status (SES) is associated with these household variables and with antibiotic use. Provider practices influence antibiotic use, but SES can also influence providers' practices. This research was designed to obtain information on human- and animal-level antibiotic use, related HH and SES variables and provider practices.

to (i) quantify animal health treatment practices at the household level, specifically antibiotic use, animal healthcare provider utilization and animal medicine sources; (ii) quantify animal husbandry practices that increase the risk for the potential transmission of antibiotic resistance determinants from animals to humans in the study area; and (iii) compare healthcare seeking and treatment trends for household members and animals.

Methods

Sampling and interviews

This descriptive, cross-sectional study of human and agricultural antibiotic use and resistance in households in rural Bangladesh (Sylhet district) was conducted between July 2002 and December 2004 in the comparison arm of the Project to Advance the Health of Neonates and their Mothers (Projahnmo). Projahnmo was a 3-year trial to evaluate the impact of a package of obstetric and neonatal care that includes community health education, clean delivery, essential newborn care and management of neonatal infections in north-east Bangladesh. The methods and data collection procedures for Projahnmo have been described elsewhere (Baqui et al., 2008). The study area is characterized by a weak health system and high neonatal and child mortality.

To be eligible for participation, women had to reside in the comparison arm of the Projahnmo site for the 6 months prior to interview, be 18 years of age or older, be married or divorced or widowed and have a baby <18 months old. A list of households that met these eligibility criteria was generated from a census carried out by Projahnmo (Baqui et al., 2008). From this list, an equal number of households were randomly selected from low (≤1 USD/day), medium (1.01–3.99 USD/day) and high socio-economic status (SES) groups (>4 USD/day) to identify differences in animal husbandry practices by SES using cut-off values previously defined (Baqui et al., 2008). An equal number of women with young children from each of the SES strata were then randomly selected because they were believed to be a good source for information on both human and animal medicine use and care and were most likely to be at home during the day when interviews were conducted.

The development of the structured questionnaire used for this study was informed by the results of qualitative research (Roess, 2006). The qualitative research uncovered important themes related to antibiotic use that this study quantified (Roess et al., 2013). The qualitative research uncovered local language terminology for animal husbandry practices including types of treatments (antibiotics and feed additives) given to livestock and animal health problems (poor growth, diarrhoea). These terms were used in the questionnaire. The questionnaire was designed to elicit information on and quantify (i) human and animal medicine use at the household level, (ii) animal husbandry practices and (iii) human and animal healthcare provider utilization in rural Bangladesh. The dependent variable of interest was reported recent animal treatment (animal treatment was defined as seeking advice for addressing an animal health concern) within the 6 months prior to the survey. Possible factors associated with recent animal treatment were recorded, including socio-economic and demographic factors, specifically household structure, drinking water source and education status; type of animal healthcare provider (homoeopath, drug seller, village doctor, veterinarian); ownership of animals (type of animal, number of animals); type of animal illness; characteristics of the use of medicine for household members (type of medicine, source of medicine, purpose of medicine use); and household member farm worker status (any member working on a farm, any poultry farm workers, any dairy farm workers, any agricultural farm workers). Each of these factors has been shown to have an association with human medicine use variables (Radyowijati and Haak, 2001). Because limited literature is available on household-level animal medicine use and because literature has described animals as an important investment, we hypothesized that some of the same socio-economic factors influencing household-level human antibiotic use would also influence animal antibiotic use.

Interviewers were trained during a 1-week workshop to administer the survey and to record information from all animal and human medicine products and prescriptions (the latter was used to confirm that the terms uncovered to mean antibiotics during the qualitative research were in fact antibiotics). We surveyed 700 households because this was the sample size required to meet the objectives of the larger study (Roess, 2006). At the end of the survey, interviewers inquired whether a male animal caretaker was available to answer animal health questions, and in 117 households, we were able to collect animal healthcare data from both male and female members of the household for data triangulation.

Data management and analysis

To ensure data quality, the study investigators made periodic field visits to observe data collection by the field staff. All survey and data forms were reviewed for accuracy, consistency and completeness. Whenever necessary and feasible, additional field visits to clarify inconsistencies or collect missing information were made. Data were entered in a database using online custom-designed FoxPro data entry software programs.

Bivariate associations between each independent factor and the dependent outcome, animal treatment event, were determined by two-tailed chi-square tests. Continuous data were assessed using *t*-tests, and nonparametric tests (i.e. Kruskal–Wallis) as appropriate. Following the recommendation of Hosmer and Lemeshow (Hosmer et al., 2013), independent factors that were statistically significant with the outcome at the 0.25 level were included in the multiple logistic regression analysis (Hosmer et al., 2013). Associations between the dependent variable and each of the potential associated independent variables are reported as odds ratio (OR) and the 95% confidence interval (CI) (Hosmer et al., 2013). The analysis was restricted to those reporting ownership of at least one chicken and/or 1 or more cattle.

Ethical approval

This study was approved by the Johns Hopkins University Bloomberg School of Public Health Institutional Review Board and the Ethical Review Committee of the International Centre for Diarrheal Disease Research, Bangladesh. Informed written consent was obtained from all participants prior to the start of the interview.

Results

Socio-economic and demographic profile of respondents

Surveys were administered in 700 households. The majority reported that they did not have electricity (67.3%; n = 471), did not have access to piped water (100%) and made part of their living from agriculture (90%; n = 630). The main source of drinking water for the majority of the population was tube well water (60.9%; n = 426), followed by surface water (37.5%; n = 262) (Table 1). The majority of respondents were using a pit latrine (63.9%; n = 447), and half of houses were made of natural materials (54.3%; n = 385). About 42.1% (n = 295) of mothers had no education, and about half (52.3%; n = 366) of respondents had a household member who was a remittance worker. In terms of educational status and economic status, the population of women who had recently given birth and was sampled *is generally representative* of the population in Sylhet – based on the results of the 1999–2000 Bangladesh Demographic and Health Surveys (BDHS, 2000) data, the Bangladesh Maternal Health Services and Maternal Mortality Survey data (BMMS, 2002) – and the Projahnmo population (Baqui et al., 2008). Approximately 84% of households reported having human medicines in stock, and almost 38% of households reported recent animal treatment (Table 1).

Animal treatment characteristics

Animal treatment was defined as seeking advice for addressing an animal health concern. Of 700 households, 521 (74.4%) reported owning at least one chicken and/or at least one cattle (cow, oxen, 'bull' or 'buffalo'). The statistical analysis was restricted to these 521 households because the question about animal treatment in the last 6 months was thought to be relevant to them and not to households that did not own any livestock. Households owned between 1 and 16 cattle and between 1 and 40 poultry. Of the 521 households, 278 (53.4%) reported at least one animal treatment in the 6 months prior to the survey. Using multiple logistic regression, we found no statistically significant association between socio-economic and demographic factors and having an animal treatment event after controlling for the number of poultry owned and ownership of cattle, although a number of variables were marginally associated with the use of medicine (data not shown). There were no statistically significant ($P < 0.05$) differences between animal treatment event and the number of poultry owned and ownership of cattle.

Owning three or more poultry was associated with a recent animal treatment (OR = 1.87 95% CL: 1.15–3.05), and there was a positive association between having a household member who was a poultry farm worker and recent animal treatment (OR = 2.68 95% CL: 0.72–10.00) although this was not statistically significant. The majority of treatments were recommended by a fellow household member (61.6%) (Fig. 1). Additives, medicines

Table 1. Descriptive characteristics of study population and their association with recent animal treatment

		Animal medicine use (n = 521)	
	Total n* (%)	Yes	No
Total	700	278 (53.4)	243 (46.6)
Own land other than homestead land†			
Yes	303 (43.3)	126 (45.3)	123 (50.6)
Electricity‡			
Yes	229 (32.7)	98 (38.7)	78 (29.1)
Source of drinking water			
Tube well/filtered	426 (60.9)	188 (67.6)	154 (63.4)
Surface water	262 (37.5)	90 (32.4)	86 (36.6)
Sanitation facility			
Septic tank, modern	110 (15.7)	45 (16.2)	37 (15.2)
Pit latrine/water sealed	279 (39.9)	103 (37.1)	113 (46.5)
Pit latrine/not water sealed	168 (24)	72 (25.9)	46 (18.9)
Open latrine/no facility	144 (20.3)	58 (20.9)	47 (19.3)
House type			
Natural materials – full katcha§	81 (11.5)	25 (9.0)	25 (12.3)
Mostly katcha	304 (42.8)	111 (39.9)	77 (31.7)
Semi-pucca¶	238 (33.5)	120 (43.2)	108 (44.4)
Full pucca	77 (10.8)	22 (7.9)	28 (11.5)
Ownership of cattle			
Yes	533 (74.2)	96 (34.5)	71 (29.2)

*Totals do not always add up to 521 due to missing data.
†A total of 98.4% of the respondents reported owning the land that they live on, and 43.3% reported owning additional land.
‡In this population, having electricity does not necessarily mean that households pay for it. Electricity is often 'borrowed' from power lines.
§Katcha-bamboo/thatch.
¶Pucca-cement/concrete/tiled.

and injections were the most common treatments reported (39%, 23.3% and 18.1%, respectively). Based on the results of the preceding qualitative study, we determined that the term 'additive' referred to commercial feed which contained grains and sometimes antimicrobials and 'medicines' referred to antibiotics in the majority of instances [we also compared terms reported for medicine to the packages presented in those same households in subsample]; homoeopathic treatments or other substances obtained from a healthcare provider (Roess, 2006; Roess et al., 2013). The most common animal illness reported was poor general health and slow growth (Roess, 2006). Respondents sought treatment for this from household members more often than from other healthcare providers (350/469 versus 119/469, respectively) (Table 2), and additives were almost exclusively used for treatment (245/246) (Table 3). For diarrhoea and fever, respondents visited village doctors more than government doctors or drug sellers (Table 2), where the medicines that were purchased differed significantly according to who recommended the medicines. For instance, village doctors sold what they recommended in more than half of cases (73/135); household members recommended treatments that were most often obtained from pharmacies (331/388); and drug sellers sold what they recommended (30/33). In this context, drug sellers were generally in the informal sector and may or may not have formal training as pharmacists. They generally travelled with their products or had small stalls in a market. Pharmacies on the other hand were well stocked and generally run by pharmacists who had formal training. They were generally larger stalls in market places or small stand alone building.

Household spending on animal health care

Total household spending on animal treatments was available for 173 of the 294 households that reported an animal treatment event (missing data were a result of the respondent not knowing or not wanting to disclose the information). Total household expenditure was almost twice as much for animal medicines compared to medicines for people (average US$ 2.49 versus 1.49 for animals versus humans, respectively) (Table 2). The amount a household spent on treatment for cows was significantly greater than

Table 2. Mean and median household expenditure on human and animal treatments

	n	Mean (Median) cost U$	Mean (Median) [58Taka = 1 USD]
Human healthcare total	451	1.49 (1.03)	86.41 (60)
Animal health care*			
Total	173	2.49 (0.71)	144.53 (41)
Only chickens owned	114	1.14 (0.34)	66.07 (20)
Only cows owned	12	9.59 (2.41)	556.05 (140)
Both cows and chickens owned	44	4.01 (1.72)	232.70 (100)
Individual treatment event spending for animals by characteristics†			
Type of treatment/product*			
Food	59	0.73 (1.35)	42.17 (78.47)
Additives	142	2.69 (5.68)	156.07 (329.59)
Vitamins	8	1.39 (2.93)	80.63 (169.84)
Medicine	57	0.86 (1.71)	49.98 (98.97)
Injection	59	0.78 (1.25)	45.07 (72.59)
Drug source*			
Pharmacy/drug seller	233	1.44 (2.62)	83.49 (152.08)
Government source	11	3.16 (2.70)	183.00 (156.35)
Village doctor	39	0.89 (1.69)	51.54 (97.93)
Homoeopath	2	0.34 (0.17)	20 (20)
Purpose			
Diarrhoea	17	0.82 (0.68)	47.71 (39.52)
Newcastle disease	42	0.30 (0.48)	17.45 (27.98)
Fever	21	0.33 (0.31)	19.14 (17.79)
Malaise	247	2.02 (4.55)	116.91 (263.73)
Type of healthcare provider*			
Village doctor	61	0.75 (1.39)	43.38 (80.87)
Government doctor	21	2.05 (2.58)	119.10 (149.78)
Drug seller	17	0.49 (0.58)	28.35 (33.50)
Household member	221	1.96 (4.72)	113.77 (273.54)

*Nonparametric test (Kruskal–Wallis $P < 0.001$).
†Details were available for 317 animal treatment events, and multiple responses were possible.

Table 3. Animal husbandry practices and related domestic hygiene factors

Factor	n (%)
Use of the closest body of water (N = 700)	
Drinking	270 (38.6)
Clothes washing	582 (83.1)
Cooking	472 (67.4)
Bathing	548 (78.3)
Fishing	338 (48.3)
Children and livestock same use	373 (53.3)
Livestock use	117 (16.7)
Female household member raising chicken (N = 700)	
Yes	440 (62.8)
Chicken waste use (N = 700)	
Fertilizer	280 (40.0)
Livestock waste use* (N = 700)	
Fertilizer	426 (60.9)
Where poultry slept (N = 700)	
Special house	143 (20.4)
Underbed	296 (42.3)

*Even though not all respondents owned livestock, they reported using livestock waste products from their neighbours' livestock.

that for chickens (US$ 9.59 versus 1.15, respectively). Cost information was available for 327 of 630 individual animal treatment events. Cost of treatment significantly differed by type of product, with additives as the most expensive form of animal treatment followed by vitamins and medicines. Treatments obtained from government animal healthcare providers were more than twice as expensive compared to those obtained from pharmacies and village doctors (US$ 3.16 compared to 1.44 and 0.89, respectively). Households spent the most on treatments for malaise, followed by diarrhoea, US$ 2.02 versus 0.82, respectively. There were no statistically significant differences between demographic and socio-economic characteristics of households that provided cost data and those that did not.

Husbandry practices as risk factors for emerging zoonotic disease and antibiotic resistance

The most commonly reported risk factor for acquisition of emerging zoonotic disease and antibiotic resistance was the multiple use of water from the same source; for example, 78.3% (548/700) of households that owned livestock reported that their children and cattle swam in the same water (Table 3). Assigned gender roles were also common; 62.8% (440/700) of women took care of both poultry and children. Housing of animals in confined spaces with people at night was the next most common factor (during the day, poultry were free-ranging); poultry were housed in a basket and placed under the bed or in the same room where household members slept in 42.3% (296/700) of households.

Poultry and other livestock waste was used as fertilizer in 40% and 60.9% of households, respectively (Table 3).

Discussion

There is evidence that the use of antibiotics for growth promotion in animal husbandry leads to the emergence and spread of antibiotic resistance. While some have estimated it to contribute more to the overall burden of drug resistance than human use of antibiotics; the attributable fraction of this practice on the burden of antibiotic resistance in clinically important pathogens to humans is unknown (Angulo et al., 2009; Marshall and Levy, 2011). The prevalence of antibiotic-resistant pathogens has increased steadily in LMIC since the introduction of antibiotics (Radyowijati and Haak, 2003). Despite the recognized importance of examining both animal and human antibiotic use at the household level in a LMIC setting, no other studies have been published that report this information. We report frequent animal medicine use at the household level in rural Bangladesh (Sylhet district) and frequent treatment purchase from pharmacies which are indicative of non-human antibiotic use. Respondents reported using medicines in almost a quarter of animal treatment events specifically for diarrhoea and fever more than other treatments, and medicines were recommended and obtained from trained healthcare providers and drug sellers. We conducted qualitative interviews with drug sellers and village doctors to triangulate the findings of this study, and we found that the terms that respondents used for medicines were used by drug sellers and village doctors for antimicrobials (most commonly referring to oxytetracycline and metronidazole). The reported use of medicines may be a proxy for antibiotic use, yet information on the extent of non-human antibiotic use is lacking (Roess, 2006; Roess et al., 2013). Additives were most often recommended by household members and were a common treatment. As described, additives referred to grain and commercial animal feed that included antimicrobials and were used primarily to treat animals that were in general poor health or were not growing (Roess, 2006). Living with a household member who was working on a poultry farm or another type of farm was associated with using animal medicines and additives. We previously reported that commercial poultry farms in Bangladesh use prepared animal feed and antibiotics and that poultry farm workers reported applying these techniques for their personal livestock holdings (Roess, 2006; Roess et al., 2013).

Our findings complement the few previously documented studies showing that in LMIC settings, lay people are an important source for advice and knowledge for animal treatments (Peeling and Holden, 2004). This is also the case for human treatment (Schorling et al., 1991; Dua et al., 1994; Calva and Bojalil, 1996). Other important animal healthcare providers that emerged in our studies included government veterinarians, livestock office doctors (*poshudaktar*) and 'locals who know about animals' (Roess, 2006). The lack of infrastructure was perceived by the household respondents and by the veterinarians interviewed as an obstacle to seeking adequate health care for themselves and their livestock when it is needed (Roess, 2006). Livestock are important culturally: in establishing the status of the farmer as providers of employment to the farmer and family members; as a store of wealth; and as a form of insurance (Riethmuller, Chai et al. 1999). Livestock provide an opportunity for low-income farmers to accumulate capital, which in turn helps reduce hunger (Riethmuller, Chai et al. 1999; Peeling and Holden, 2004). The loss of an animal for a small farmer can have severe consequences, such as the loss of a source of income or social standing in the community. These are important justifications for spending a significant portion of household income on animal medicines, health care and other means of protecting livestock.

The primary reason for providing animal health care to rural small-scale farmers is to improve animal health and output, thereby reducing starvation and poverty.

One of the few peer-reviewed studies documenting rural agricultural practices in Kenya found that lay people, such as farmers and their neighbours, were the main sources of animal healthcare treatment (Machila et al., 2003). However, compared to the 6.3% of government animal health specialists that were sought for advice and treatment in our study, over one-quarter (29.4%) of government animal health assistants (AHAs) were sought out in the Kenya study (Machila et al., 2003), illustrating the lack of concerted efforts in Bangladesh to promote the use of AHAs. Our study population and similar ones would benefit greatly from provision of similar interventions.

Qualitative interviews uncovered that farm owners and household members raising animals preferred pharmacists and local village doctors to government veterinarians, citing that the latter would charge them more for treatments (Roess, 2006; Roess et al., 2013). This same sentiment has been expressed in human antibiotic use studies (Dua et al., 1994; Duong et al., 1997). Respondents reported that treatments obtained from a government source were on average almost twice as expensive as those obtained from pharmacies (Roess, 2006; Roess et al., 2013). Although these treatments are officially free of charge, various factors may contribute to this. For example, because there is often a lack of paved roads and other infrastructure deficits, employees incur costs to reach their posts that they then pass on to their customers (Roess, 2006; Roess et al., 2013). Efforts to improve infrastructure (roads, clinics, communication networks) would help government workers reach remote populations, thus driving down costs.

The average cost of a treatment event was greatest for cattle followed by poultry and then humans. Other studies have reported similar findings that households often spend a greater amount of their income on protecting their livelihood than on food or health care (Catley, 1999).

Several similarities between human and animal disease management and healthcare seeking emerged in our study. For both animal and human treatments, pharmacies were the most common source of treatment, government healthcare providers were the least popular source of treatment, and cost associated with seeking care was a perceived obstacle for accessing health care from a government source. Our findings complement and expand upon similar findings from the studies of human antibiotic use in India and Vietnam (Dua et al., 1994; Morgan et al., 2011). In addition, our study confirms prior findings that farmers in areas with no or poor access to government animal health care obtain treatments from pharmacies more than any other source (Peeling and Holden, 2004; Rubyogo et al., 2005).

Drug-resistant bacteria and genetic material can be transferred from poultry treated with antimicrobials to poultry farm workers and their family members and from people treated with antibiotics to livestock (van den Bogaard et al., 2002; Price et al., 2007), and suboptimal animal husbandry practices and poor hygiene practices lead to an increase of diarrhoeal pathogens in household members (McLennan, 2000; Oberhelman et al., 2003). We report the use of antibiotics for both livestock at the household level in rural Bangladesh and suboptimal animal husbandry and hygienic practices – a combination that may place families at increased risk for the emergence of zoonotic diseases and antibiotic resistance.

An important limitation of our study is that in general, respondents were unable to identify the chemical compounds in the treatments given to their animals. Respondents provided local terms to describe the products used. To address this limitation and potential source of misclassification bias, we applied the results of our qualitative research to the development of the survey and to the interpretation of our results. In addition to the respondents' use of the same terms for medicines as the healthcare providers used for antibiotics, we found that villagers who reported using animal medicine presented medicine packages or pills that were for antibiotics (Roess, 2006; Roess et al., 2013). The use of additives (39%) may be indicative of commercial animal feed that may contain antibiotics as previously described. In-depth interviews with personnel of pharmaceutical distribution centres uncovered frequent animal pharmaceutical sales to drug sellers in rural markets during the study period, and more than 50% of animal products sold in any reporting period were antibiotics (Roess, 2006; Roess et al., 2013). Rationale for animal antibiotic use in rural Bangladesh is similar to that of American farmers in the 1950s and 1960s when agricultural antibiotic use was beginning (McEwen and Fedorka-Cray, 2002) – specifically respondents report that it is an effective way to protect herds of animals who lived in closed quarters from diseases and thus appears to be economically sound. Future studies should examine the prevalence and emergence of antibiotic-resistant microbes in similar settings in the context of household-level antibiotic use for humans and animals. Due to logistic constraints and the lack of financial resources, we were unable to do so. Nevertheless, the emergence of antibiotic-resistant pathogens is quickly outweighing the perceived benefits of animal agricultural antimicrobial use. Several European countries and the European Commission banned avoparcin in animal feed, and this led to a decrease in human cases of vancomycin-resistant enterococcus (Angulo et al., 2009); similar interventions may be useful in Bangladesh. Another limitation in our study is that it was nested in the comparison arm of an impact evaluation and participants had to meet the inclusion criteria which included the following: be married or divorced or widowed and have a baby <18 months old. It can be argued that families that do not have infants may behave differently with regard to the use of animal household products.

Considering the increasing body of evidence that links animal agricultural antibiotic use and suboptimal animal husbandry practices to the emergence of resistant pathogens and the transmission of zoonotic diseases, it is important to adopt measures to prevent such emergence in LMIC settings where a weak health system would not be able to cope with emerging epidemics. Environmental health impacts of agricultural antibiotic use, including the observation of antibiotic-resistant bacteria of animal origin in areas surrounding livestock operations, could also be mitigated by such measures (Landers et al., 2012). Globalization and the documented epidemics during the study period, most notably severe acute respiratory syndrome (SARS), Nipah-like virus and H5N1, are evidence for the need to strengthen surveillance of emerging diseases, including resistant strains in even remote areas of the world (Xing et al., 2010; Kerkhove, 2013). In May 2005, the World Health Organization passed an amendment mandating the reporting of seven diseases in member countries (Steiger, 2005). Although none of these reportable diseases include antibiotic resistance, this important step can be a platform on which surveillance programs can be built to monitor the emergence of resistance in the environment in remote areas. Information gathering of agricultural antibiotic use is necessary to inform treatment recommendations for people in affected areas. Improvement of government animal health services to strengthen outreach to the remote populations is needed to assist them to protect their livelihood, monitor animal health and prevent emergence of resistant bacteria in such populations.

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References

Akond, M. A., S. Hassan, S. Alam, and M. Shirin, 2009: Antibiotic resistance of *Escherichia coli* isolated from poultry and poultry environment of Bangladesh. *Am. J. Environ. Sci.* 5, 47–52.

Al-Ghamdi, M. S., F. El-Morsy, Z. H. Al-Mustafa, M. Al-Ramadhan, and M. Hanif, 1999: Antibiotic resistance of *Escherichia coli* isolated from poultry workers, patients and chicken in the eastern province of Saudi Arabia. *Trop. Med. Int. Health* 4, 278–283.

Angulo, F. J., P. Collignon, J. H. Powers, T. M. Chiller, A. Aidara-Kane, and F. M. Aarestrup, 2009: World Health Organization ranking of antimicrobials according to their importance in human medicine: a critical step for developing risk management strategies for the use of antimicrobials in food production animals. *Clin. Infect. Dis.* 49, 132–141.

Baqui, A. H., S. El-Arifeen, G. L. Darmstadt, S. Ahmed, E. K. Williams, H. R. Seraji, I. Mannan, S. M. Rahman, R. Shah, S. K. Saha, U. Syed, P. J. Winch, A. Lefevre, M. Santosham, and R. E. Black, 2008: Effect of community-based newborn-care intervention package implemented through two service-delivery strategies in Sylhet district, Bangladesh: a cluster-randomised controlled trial. *Lancet* 371, 1936–1944.

BDHS, 2000: Bangladesh Demographic and Health Survey.

BMMS, 2002: Bangladesh Maternal Mortality Survey.

van den Bogaard, A. E., R. Willems, N. London, J. Top, and E. E. Stobberingh, 2002: Antibiotic resistance of faecal enterococci

in poultry, poultry farmers and poultry slaughterers. *J. Antimicrob. Chemother.* 49, 497–505.
Calva, J., and R. Bojalil, 1996: Antibiotic use in a periurban community in Mexico: a household and drugstore survey. *Soc. Sci. Med.* 42, 1121–1128.
Catley, A., 1999: Community-Based Animal Health Care in Somali Areas of Africa: A Review. Organization of African Unity/Interafrican Bureau for Animal Resources, London.
Donkor, E. S., M. J. Newman, and D. Yeboah-Manu, 2012: Epidemiological aspects of non-human antibiotic usage and resistance: implications for the control of antibiotic resistance in Ghana. *Tropical Med. Int. Health* 17, 462–468.
Dua, V., C. M. Kunin, and L. V. White, 1994: The use of antimicrobial drugs in Nagpur, India. A window on medical care in a developing country. *Soc. Sci. Med.* 38, 717–724.
Duong, D. V., C. W. Binns, and T. V. Le, 1997: Availability of antibiotics as over-the-counter drugs in pharmacies: a threat to public health in Vietnam. *Trop. Med. Int. Health* 2, 1133–1139.
Haq, J. A., M. M. Rahman, S. M. Asna, M. A. Hossain, I. Ahmed, T. Haq, and M. A. Morshed, 2005: Methicillin-resistant *Staphylococcus aureus* in Bangladesh–a multicentre study. *Int. J. Antimicrob. Agents* 25, 276–277.
Harvey, S. A., P. J. Winch, E. Leontsini, C. Torres Gayoso, S. Lopez Romero, R. H. Gilman, and R. A. Oberhelman, 2003: Domestic poultry-raising practices in a Peruvian shantytown: implications for control of *Campylobacter jejuni*-associated diarrhea. *Acta Trop.* 86, 41–54.
Hosmer, D. W. Jr, S. Lemeshow, and R. X. Sturdivant, 2013: *Applied logistic regression*. Wiley. com.
Hossain, M. M., R. I. Glass, and M. R. Khan, 1982: Antibiotic use in a rural community in Bangladesh. *Int. J. Epidemiol.* 11, 402–405.
Kerkhove, M. D., 2013: Brief literature review for the WHO global influenza research agenda–highly pathogenic avian influenza H5N1 risk in humans. *Influenza Other Respir. Viruses* 7, 26–33.
Landers, T. F., B. Cohen, T. E. Wittum, and E. L. Larson, 2012: A review of antibiotic use in food animals: perspective, policy, and potential. *Public Health Rep.* 127, 4–22.
Machila, N., S. W. Wanyangu, J. McDermott, S. C. Welburn, I. Maudlin, and M. C. Eisler, 2003: Cattle owners' perceptions of African bovine trypanosomiasis and its control in Busia and Kwale Districts of Kenya. *Acta Trop.* 86, 25–34.
Marshall, B. M., and S. B. Levy, 2011: Food animals and antimicrobials: impacts on human health. *Clin. Microbiol. Rev.* 24, 718–733.
McEwen, S. A., and P. J. Fedorka-Cray, 2002: Antimicrobial use and resistance in animals. *Clin. Infect. Dis.* 34(Suppl 3), S93–S106.
McLennan, J. D., 2000: Prevention of diarrhoea in a poor District of Santo Domingo, Dominican Republic: practices, knowledge, and barriers. *J. Health. Popul. Nutr.* 18, 15–22.
Morens, D. M., G. K. Folkers, and A. S. Fauci, 2004: The challenge of emerging and re-emerging infectious diseases. *Nature* 430, 242–249.
Morgan, D. J., I. N. Okeke, R. Laxminarayan, E. N. Perencevich, and S. Weisenberg, 2011: Non-prescription antimicrobial use worldwide: a systematic review. *Lancet Infect. Dis.* 11, 692–701.
Oberhelman, R. A., R. H. Gilman, P. Sheen, J. Cordova, D. N. Taylor, M. Zimic, R. Meza, J. Perez, C. LeBron, L. Cabrera, F. G. Rodgers, D. L. Woodward, and L. J. Price, 2003: Campylobacter transmission in a Peruvian shantytown: a longitudinal study using strain typing of campylobacter isolates from chickens and humans in household clusters. *J. Infect. Dis.* 187, 260–269.
Peeling, D., and S. Holden, 2004: The effectiveness of community-based animal health workers, for the poor, for communities and for public safety. *Rev. Sci. Tech.* 23, 253–276; discussion 391–401.
Price, L. B., J. P. Graham, L. G. Lackey, A. Roess, R. Vailes, and E. Silbergeld, 2007: Elevated risk of carrying gentamicin-resistant *Escherichia coli* among US poultry workers. *Environ. Health Perspect.* 115, 1738.
Radyowijati, A., and H. Haak, 2001: Determinants of antimicrobial use in the developing world. Child health research project special report. Geneva.
Radyowijati, A., and H. Haak, 2003: Improving antibiotic use in low-income countries: an overview of evidence on determinants. *Soc. Sci. Med.* 57, 733–744.
Raghunath, D., 2008: Emerging antibiotic resistance in bacteria with special reference to India. *J. Biosci.* 33, 593–603.
Riethmuller, P., J. Chai, D. Smith, B. Hutabarat, B. Sayaka, and Y. Yusda, 1999: The mixing ratio in the Indonesian dairy industry. *Agric. Econ.* 20, 51–56.
Roess, A. A., 2006: Risk Factors for Antibiotic Resistant Infections in a Rural Developing Country Setting: Human and Animal Agricultural Antibiotic Use and Animal Husbandry Practices in Rural Bangladesh. Johns Hopkins University, Baltimore, MD.
Roess, A. A., P. J. Winch, N. A. Ali, A. Akhter, D. Afroz, S. El Arifeen, G. L. Darmstadt, and A. H. Baqui, 2013: Animal husbandry practices in rural Bangladesh: potential risk factors for antimicrobial drug resistance and emerging diseases. *Am. J. Trop. Med. Hyg.* 89, 965–970.
Rubyogo, J. C., P. M. Murithii, G. J. Agumbah, and G. Obhai, 2005: Sustainability of a privatized community-based animal health worker system in Mwingi District, Kenya. *Trop. Anim. Health Prod.* 37, 253–266.
Saha, U. R., M. A. Khan, M. Begum, and R. Bairagi, 2004: Determinants of pill failure in rural Bangladesh. *J. Biosoc. Sci.* 36, 39–50.
Saha, S. K., A. Naheed, S. El Arifeen, M. Islam, H. Al-Emran, R. Amin, K. Fatima, W. A. Brooks, R. F. Breiman, and D. A. Sack, 2009: Surveillance for invasive *Streptococcus pneumoniae*

disease among hospitalized children in Bangladesh: antimicrobial susceptibility and serotype distribution. *Clin. Infect. Dis.* 48, S75–S81.

Schorling, J. B., M. A. De Souza, and R. L. Guerrant, 1991: Patterns of antibiotic use among children in an urban Brazilian slum. *Int. J. Epidemiol.* 20, 293–299.

Steiger, W. R., 2005: Revisions to the international health regulations. *Lancet* 365, 381.

Xing, W., G. Hejblum, G. M. Leung, and A.-J. Valleron, 2010: Anatomy of the epidemiological literature on the 2003 SARS outbreaks in Hong Kong and Toronto: a time-stratified review. *PLoS Med.* 7, e1000272.

