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Comparison of two methods for collecting antibiotic use data on small dairy farms

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Abstract

Antibiotics are commonly used in animal agriculture; they can improve animal health and productivity, but their use may also represent a public health threat. Very little is known about antibiotic use on small farms in lower/middle income countries. To understand antibiotic use on these farms and promote the judicious use of these drugs, pharmacoepidemiologic data are necessary. However, acquiring such data can be difficult, as farmers are often illiterate (and therefore cannot participate in written surveys or keep treatment records), antibiotics can be obtained over-the-counter (in which case no prescriptions are generated) and monitoring and surveillance systems for drug use are often non-existent. The goal of this study was to compare two methods of acquiring pharmacoepidemiologic data pertaining to antibiotics that are well-adapted to farms in lower-middle income countries: self-report and the collection of discarded drug packaging. A convenience sample of 20 farmers in Cajamarca, Peru, participated in the study. Farmers placed discarded antibiotic packaging in bins for six months. At the end of the six-month period, farmers were interviewed and asked to recall the antibiotic usage that occurred on their farm over the past month and past six months; these self-reported data were quantitatively and qualitatively compared to the bin contents collected in the last month and previous six months. We found that the agreement between the bins and self-report was relatively poor for both the quantity and types of antibiotics used. The bins appeared to perform better than self-report when bottles and mLs of antibiotics were measured, while self-report appeared to perform better for intra-mammary infusions. The bins also appeared to perform better when data pertaining to an extended time period (six months) were collected. The results of this study will provide guidance to investigators seeking to collect pharmacoepidemiologic data in similar environments.

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Keywords

Antibiotic use; Dairy Farms; Lower-Middle Income Countries

1. INTRODUCTION

Antibiotics are commonly used in animal agriculture for growth promotion, the treatment of sick animals and the prophylactic and/or metaphylactic treatment of healthy animals during periods of increased risk of infection. These uses can improve animal health and productivity (Mathew et al., 2007), but they may also promote antibiotic resistance among bacteria isolated from animals and humans, which can lead to infections with limited treatment options, greater mortality, and increased healthcare costs (Walsh and Fanning, 2008). The US Centers for Disease Control and Prevention (CDC) reported that the widespread use of antibiotics in agriculture has resulted in increased resistance in infections in humans (CDC, 2013), and the propagation of resistant bacteria in animals and animal food products can increase the likelihood of the transmission of these bacteria to humans via food, the environment or direct contact with animals (Turnidge, 2004).

The misuse of antibiotics in human medicine in lower/middle income (LMI) countries has been extensively documented (Radyowijati and Haak, 2003; Kristiansson et al., 2009; WHO, 2009; Haak and Radyowijati, 2010; Okeke, 2010). It is highly likely that antibiotics are also used inappropriately in animal agriculture in LMI countries.

To understand the public health risk associated with antibiotic use in animal agriculture, pharmacoepidemiologic data on antibiotic use in livestock are necessary. Despite recommendations from the World Health Organization (WHO, 2003) to implement national surveillance programs for assessing antimicrobial usage in food animals, very little is known about the use of antibiotics in food animals in LMI countries. Furthermore, in LMI countries where sales records and on-farm treatment records are rarely kept, it can be difficult to collect accurate data of this type.

In general, data on antibiotic use in livestock have been collected at the national, regional, local and farm level from a variety of sources, including pharmaceutical companies, distributors, feed stores, pharmacies, over-the-counter retailers, veterinary clinics or farmers (Singer et al., 2006). Examples of the different methods/sources used to collect information on drug use in both human medicine and veterinary medicine in previous studies are shown in Table 1.

Each source of data can be more or less accessible, especially in LMI countries where record-keeping and regulatory oversight may be limited. Data collected from the final user of the drug (or from the guardian or owner of the user – i.e., in this case, the farmer) are ideally suited for investigations on patterns of drug use (Singer et al., 2006). However, the ascertainment of drug use data from the users of the drug is subject to misclassification of drug exposure due to recall bias, reporting bias or social desirability bias (West et al., 2013). Using data from prescriptions or sales records can also be unreliable, as such data do not take into account the adherence of the patient (or, in the case of a farm, the adherence of the farmer purchasing the drug) or the possibility of obtaining drugs from other sources (over-the-counter drugs, drugs sold on the black market, etc.) (West et al., 2013). Enhancing the validity of pharmacoepidemiologic data obtained at the farm level is vital for using antibiotic-use data to make inferences or design interventions aimed at promoting the judicious use of these drugs.

Few of the methods used in veterinary medicine can be applied in LMI countries where farmers are often illiterate, few (if any) treatment records or sales receipts are kept and national monitoring programs are nonexistent; as a result, the two methods most suited to small farms in LMI countries are in-person interviews with farmers and the collection of discarded drug packaging. The goal of this study was to compare the results obtained with these two methods on a sample of farms in a rural area of Cajamarca, a major dairy-producing region of Peru characterized by small peri-urban and rural farms (<15 cows/farm) with 30,000 registered milk producers (Garcia and Gomez, 2006) producing an estimated 307,187 kg of milk per day (Gerz and Boucher, 2006). The farms encountered in Cajamarca are typical of small dairy farms in many other LMI countries, especially in Latin America.

2. MATERIALS AND METHODS

2.1 Farms

The field research team (first and second author) approached a convenience sample of owners of mid-sized farms in and around the city of Cajamarca to participate in the study. The purpose of the study was explained to the farmers, a consent form was read and farmers who agreed to participate provided verbal consent. Approval for this study was granted by the Institutional Review Boards of the University of Pennsylvania and the Universidad Peruana Cayetano-Heredia in Lima.

2.2 Demographic data collection and distribution of bins

Farmers who agreed to participate in the study were asked a series of questions to obtain demographic data and information on their farm and animals. Farmers were then provided with a 10-L plastic bin with a swinging lid labeled “Antibiotic packaging”. Farmers were instructed to place discarded packaging (bottles, boxes, empty infusion tubes) of any antibiotics (and antibiotics only) used on the farm (whether administered by the farmer or veterinarian) into the bin throughout the month.

2.3 Collection of bins and tallying of bin contents

At the end of each month, all of the farmers were visited and asked if they had used any antibiotic products in the previous month. Farmers who stated “Yes” and had items in the bin or who stated “No” and had no items in the bins were considered adherent to the study protocol. Farmers who reported “Yes” but had no items in the bins were considered non-adherent. The bin contents from each farm were emptied into a plastic bag labeled with the farmer’s unique ID number. The bin items were then tallied and the following information was recorded for each month: 1) number of bottles of antibiotic, 2) number of milliliters of antibiotic, 3) number of intra-mammary infusions, 4) names/active ingredients of all antibiotics, 5) names of any other type of (non-antibiotic) drug placed in the bin. Bin contents were collected at the end of each month during the six-month study period.

2.4 Final interview

At the end of the six-month period, the farmers or attendants-in-charge were interviewed by the research team to obtain self-reported drug use measurements. In particular, while being shown photos of antibiotics currently available on the market, farmers or attendants were asked the following questions:

1. How many bottles of antibiotics did you use in the past month?
2. How many milliliters of antibiotics did you use in the past month?
3. How many antibiotic intra-mammary infusions did you use in the past month?
4. What types of antibiotics did you use in the past month?

The same series of questions was then repeated, replacing “the past month” with “the past six months”. Half of the farmers/assistants were randomly assigned to answer the last-month series of questions first and the six-month series last; the second half of the sample was asked the questions in the opposite order.

2.5 Statistical analyses

Cohen’s kappas and McNemar odd ratios were calculated for the bin and self-report measures of categorical outcomes (presence/absence and reporting/non-reporting of specific drug types). Intraclass correlation coefficients for the bin and self-report measures of the continuous outcomes (bottles and mLs of antibiotics and infusions) were calculated.

Bland-Altman plots consisting of the mean number ((bin measure+self-report measure)/2) of continuous measures plotted against the difference between measures (bin measure minus self-report measure) were constructed. The mean difference $\bar{d}$ between the number of bottles placed in bins and the number of bottles reported by the farmer represents the bias or lack of agreement between methods. The standard deviation of the difference $\bar{d}$ represents the variability of the differences and is used to calculate 95% limits of agreement between the methods. The 95% limits of agreement represent the range within which 95% of observations (i.e., differences between bin measures and self-report measures) fall. They do not represent confidence limits but function rather as a reference interval (Bland and Altman, 1999). If the values of the differences within the range are considered “clinically acceptable”, then the two methods could be used interchangeably. The mean bias of the methods and the standard deviation of the bias were calculated, and the biases for the six-month and last-month period were compared with a Wilcoxon rank sum test. Ninety-five percent limits of agreement, calculated as the mean difference in drug measures ±1.96*SD, were calculated and labeled on the Bland-Altman plots. A horizontal line at y=0 was added to the plot to indicate the line of equality upon which all points would lie if both methods yielded the same results. Plots were then examined visually to identify any patterns in the data.

To investigate the potential for bias that is not constant across the range of values (proportional bias), linear regression models were fit for each measure of antibiotic (bottles, mLs, infusions) for each time period, with self-reported measures as the outcome variable and bin measures as the independent variable. The slope of the regression line was used to evaluate the extent of systematic bias between the two types of measurements. A Wald test was used to determine whether the slope of the regression line was significantly different from one.

Ratios of six-month drug use to last-month drug use were calculated to examine the consistency of reported drug use by month. Ratios were compared for the two methods with the Wilcoxon rank sum test. P-values<0.05 were considered to indicate statistical significance. All analyses were conducted in Stata, v.11 (StataCorp. College Station, TX).

3. RESULTS

3.1 Farm and farmer characteristics

Twenty-two farmers were approached to participate in the study. One farmer declined to participate (participation rate of 95.5%) and one farmer, citing that the process was "too complicated", dropped out of the study in the first month, resulting in a completion rate of 95.2%. Demographic data were collected on all farm owners at the beginning of the study (Table 2). The final interviews were conducted with six farm owners and 14 attendants-in-charge. Farms had an average of 33 lactating cows producing a total of 392 L of milk per day (12.4 L/cow/day). Farm owners had a mean age of 50.2 years and 60% of farm owners had completed university-level studies. Attendants-in-charge had a mean age of 40.6 years and, in general, were less educated than farm owners. Milk was sold to either large dairy processing companies (Nestlé or Gloria) or to local cheesemakers. On average, 3.2 men and 3.0 women worked on the farm in various capacities, including caring for the animals and the facilities, tending the fields or milking the animals (6.8 cows/worker).

3.2 Adherence to study protocol

Seventeen (85%) farmers were adherent to the study protocol (i.e., placed antibiotic packaging in the bins after having used antibiotics during the previous month) for the entire study period. Three farmers were non-adherent for one, two and three months, respectively.

3.3 Bin contents and self-reported data

The counts for the number of bottles, mLs and infusions of antibiotics used on each farm during the last-month and six-month periods according to bin contents and self-report are listed in Table 3.

3.3.1 Bin contents—A total of 204 bottles, 34,665 mLs of antibiotics and 293 intra-mammary infusions ("chisguetes") were deposited in the bins during the six-month study. The mean (SD) number of bottles, mLs and infusions placed in the bins on each farm during the six-month study was 10.2 (6.73), 1733 (1187) and 14.7 (28.4), respectively. The active ingredients encountered (in order of decreasing frequency) were oxytetracycline, penicillin ± streptomycin, trimethoprim-sulfamethoxazole, gentamycin ± tylosin, enrofloxacin and cephalosporin. The intra-mammary infusions (with each infusion tube representing one dose) consisted mostly of cloxacillin and ampicillin; however, one farmer also used ceftiofur infusions. In addition, 16 of 20 farmers (80%) deposited non-antibiotic drugs in the bins, including vitamin complexes, anti-parasitic drugs, nutritional supplements (calcium, magnesium, phosphorus), diuretics, non-steroidal anti-inflammatory drugs, dexamethasone and oxytocin.

3.3.2 Self-reported data—A total of 140 bottles and 23,934 mLs of antibiotics and 780 intra-mammary infusions were reported to have been used by all 20 farmers during the six-month study. The mean number of bottles, mLs and infusions reported to have been used by each farmer during the six month period was 7 (7.55), 1196 (1370) and 39 (65.4), respectively. Fourteen, 15, six, five, five, two and one farmer reported having used penicillin ± streptomycin, oxytetracycline, trimethoprim-sulfamethoxazole, gentamycin ± tylosin, cloxacillin, enrofloxacin and cephalosporin, respectively, during the six-month period.

3.4 Measures of agreement for continuous variables

3.4.1 Intraclass correlation coefficients—The intra-class correlation coefficients (ICCs) evaluating the correlation between the number of bottles, mLs or intra-mammary infusions placed in the bin and the number of bottles, mLs or infusions reported by farmers were generally low (Table 4). The highest values were found for the infusions (0.59 and 0.52 for the last month and six-month period, respectively), followed by the mLs (0.40 and 0.30 for the last month and six-month period, respectively) and bottles (0.30 and 0.01 for the last month and six-month period, respectively). In all cases, the confidence intervals of the ICCs for the last month and six-month period overlapped, suggesting that both correlations were statistically similar for the two time points.

3.4.2 Bland-Altman analyses—The mean differences in number of bottles, mLs and infusions placed in the bin and reported by the farmer, the standard deviations of these differences and the limits of agreement are reported in Table 4. Statistically significantly larger discrepancies were found for the six-month measures than for the last-month measures for bottles and mLs ($p=0.03$ and $p=0.07$, respectively) but not for infusions ($p=0.41$). For both periods, the farmer reported having used more infusions than were placed in the bins ($\bar{d}<0$), whereas more mLs were placed in the bin than were reported by farmers ($\bar{d}>0$). No consistent trend was observed for bottles ($\bar{d}<0$ for the last month and $\bar{d}>0$ for the six-month period).

Bland-Altman plots, which plot the mean measure against the difference in measures, graphically display the biases ($\bar{d}$) and variability of the two methods relative to the 95% limits of agreement and the line of equality (y=0). Figures 1a, 2a and 3a represent the Bland-Altman plots for bottles, mLs and infusions, respectively, for the last month; Figures 1b, 2b and 3b represent the same respective plots for the six-month period.

According to the Bland-Altman plots, for all measures (bottles, mLs, infusions) both the last month and the six-month periods, the absolute value of $\bar{d}$ grew as the mean number of measures increased. For bottles and mLs, the mean difference tended to be positive more often than negative (i.e., the bins contained more measures than were reported by the farmers). Relatively few intra-mammary antibiotic infusions were used during the last month, and in all cases, the farmer reported using more infusions than the bin contained ($\bar{d} \leq 0$). For the six-month period, as the mean number of infusions increased, $\bar{d}$ values became more divergent and exclusively negative, that is, the farmers reported using more infusions than the bins contained.

3.4.3 Regression analyses—Given that the Bland-Altman plots displayed larger discrepancies between methods with higher values of the measures, we conducted regression analyses to examine the extent of any systematic bias between bin and self-reported measures. When self-reported measures are similar to the quantities from the bins, the regression line should be coincident with the line of equality (x=y), i.e., the slope of this regression line should be equal to one. The slopes of the regression lines comparing self-reported measures to bin measures are reported in Table 4. For last-month bottles and last-month mLs, the slopes of the regression lines were not significantly different from unity (p=0.99 and p=0.54, respectively). For all other measures, the slopes were statistically significantly different from one, indicating poor agreement between the methods.

3.5 Consistency of antibiotic use

If antibiotic use is more or less consistent throughout the year, antibiotic use over the six-month period should be approximately six times as high as antibiotic use in the last month. We therefore compared the ratio of six-month antibiotic use to last-month antibiotic use for each method (Table 5). For bottles, the ratios were close to six (6.98 and 4.24 for bins and self-report, respectively) and not significantly different from each other (p=0.120). For mLs, the ratios were more divergent (19.3 and 5.62 for bins and self-report, respectively) and not significantly different from each other (p=0.089). For the intra-mammary infusions, the ratios were more similar (5.23 and 3.83 for bins and self-report, respectively) and not significantly different from each other (p=0.17). These results suggest that, with the possible exception of bin-mLs, antibiotic use on a monthly basis appeared relatively constant.

3.6 Measures of agreement for drugs classes

Kappa values for individual drug classes for the bins and self-report ranged from −0.29 to 0.52 (Table 6), indicating that agreement between the methods for individual drug classes was non-existent to fair.

For injectable penicillin and oxytetracycline, last-month kappas were higher than six-month kappas. For the remaining types of antibiotic (intra-mammary infusions, trimethoprim-sulfamethoxadole (TMS) and all other types), six-month kappas were higher than last-month kappas. This suggests that the bins and farmers were more likely to agree on the most commonly-used drugs (penicillin and oxytetracycline) during the short-term (one month) intervals; in contrast, farmers and bins were more likely to agree on the less-commonly used drugs for the longer six-month interval.

An analysis of the marginal homogeneity of the contingency tables displaying the presence/absence of a drug in the bin and the reporting/non-reporting of the drug by the farmer using McNemar's test enabled us to calculate the odds ratios of a bin having a particular drug vs.

the farmer reporting the drug (Table 7). An odds ratio greater than 1 means that the bin was more likely to contain a drug than the farmer was to report it. For the last month, the bins tended to contain fewer products than were reported by the farmer (odds ratios of 0.67, 0.67 and 0.2 for penicillin, oxytetracycline and TMS, respectively). In contrast, during the six-month period, the bins were more likely to contain a drug than a farmer was to report it (odds ratios of 1.5, 3.0 and 4.0 for penicillin, oxytetracycline and TMS, respectively).

4. DISCUSSION

The goal of this study was to compare two methods of collecting data on antibiotic use on small and mid-sized farms in a peri-urban area of Peru. Because neither method has been established as a gold standard, we conducted an exploratory analysis examining the agreement between the methods for both drug amounts and drug categories. If one method tended to consistently report higher amounts of drugs than the other method (and the other method therefore appeared to be consistently under-reporting) or if one method reported the use of a particular drug type while the other did not, than that method could potentially be considered superior to the other and recommended for future studies on similar topics.

We found that the agreement between bins and self-report used to collect data on antibiotic use on farms was relatively poor; we also found that bins appeared to perform better than self-report for longer periods of time and that self-report appeared to perform better for more commonly used drugs on a short-term basis and for intra-mammary infusions. The low intraclass correlations suggest that the continuous data (amounts of antibiotic) generated by each method were poorly correlated, while the low kappa values suggest that the agreement between methods for categorical data (drug types) was relatively low. Regression analyses and Bland-Altman analyses also showed that agreement tended to be worse for the six-month period than for the last month. For both time periods, the bin and self-reported measures tended to diverge (i.e., $|\bar{d}|$ increased) as greater volumes of products were used. In most cases, the limits of agreement were unacceptably large and far beyond what would be considered “clinically acceptable”; consequently, these two methods should not be used interchangeably.

A strength of the bins is that they were unable to “over-report” antibiotic usage; therefore, if a bin contained more products than a farmer reported, then the farmer was under-reporting (and therefore less accurate). However, if a farmer reported having used more products than were contained in the bin, we have no way of knowing if the farmer was over-reporting or if the bins were “under-reporting” (i.e., a farmer forgot to put packaging in the bin or only used part of what was in a bottle). Positive differences between bin and self-report measures ($\bar{d} > 0$) suggest that farmers tended to under-report drug use on their farm. For bottles and mLs, the differences tended to be positive and the odds ratios for all antibiotics except intra-mammary infusions tended to be greater than 1 during the six-month period. As a result, for both bottles and mLs of antibiotics, the bins appeared to represent a more accurate way of measuring consumption than self-report, especially over longer periods of time (e.g., during the six-month period).

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For infusions, the differences in measures were always negative and the odds ratio for one-month and six-month infusion use was always less than one; these results suggest that farmers either over-reported their use of infusions or did not place all of the used infusion tubes in the bins (or both). Given that 16/20 farmers placed no infusions in the bins during the one-month period but only 9/20 farmers reported having used no infusions during this time, it appears more likely that farmers simply did not place their used infusion tubes in the bin. Therefore, it appears that self-report was actually more accurate than bins for intra-mammary infusions.

Several studies have compared the collection of drug packaging to the use of treatment diaries on farms. Carson et al. (2008) compared these two methods of obtaining antibiotic-use data on 24 beef farms in Ontario for a period of 12 months. The authors found that the relative ranking of types of antibiotic used depended on the chosen metric and that the kg of active ingredients/1000 animals differed significantly by method for tetracycline, penicillin, florfenicol, tilmicosin, and spectinomycin. Overall, these authors recommended the use of bins over treatment diaries, as producers had problems recording routine treatments and treatments given during disease outbreaks; furthermore, the bin method was thought to be more accurate, as "producers were enthusiastic about having their "garbage" disposed of for them, protection of confidentiality created little reason for dishonesty, and throwing out empty containers did not take much effort."

Dunlop et al. (1998) assessed antimicrobial usage on 34 swine farms in Canada using on-farm treatment records and the collection of discarded drug packaging. These authors also found that the bins represented convenient and fairly accurate ways of recording antimicrobial drug use and that the volumes of inventoried antimicrobials were highly correlated with the volume of antimicrobials listed in treatment records (r=0.90, p=0.0001); however, they also found the treatment records underestimated drug use by 35%.

In agreement with these studies, we found that the bins tended to perform better than self-report when data were collected over a longer period of time. However, both methods clearly have their limitations. Self-report can be affected by recall, reporting and social desirability bias. Bins may not contain all of the antibiotics that were used on the farm if farmers forget to place discarded packaging in them, if only a portion of the drug contained in a bottle is used (and the farmer or veterinarian obviously does not want to place a bottle with product remaining in the bin) or if the farmer does not inform all of the workers on the farm of the required protocol. In this study, the differences between bin and self-reported measures were not statistically significantly different for farm owners vs. attendants-in-charge, which suggests that the farm owners informed their workers of the protocol and that the workers were just as adherent to the protocol as the farm owners. However, we noted that 16/20 (80%) of farmers placed other types of drugs in the bin in addition to antibiotics; it is possible that farmers who saw a bin that was already "full" of other drugs may have been less likely to add antibiotic packaging.

This study had a number of limitations that warrant discussion. First, because a convenience sample of farmers was chosen, selection bias may exist; therefore, caution must be exercised before attempting to generalize these results beyond this sample of farms. Recall bias may have also affected our findings. Farmers were told that the study objective was to compare the two methods of collecting data on antibiotic use; they might therefore have thought about and remembered their antibiotic usage more carefully than if they had not been made aware of the study objective.

Second, the chosen metrics (bottles, mLs and infusions of antibiotics) may not be the most informative metrics to use when attempting to collect data on antibiotic usage, especially if there is no clear indication of the units of antibiotic contained in a bottle or in an mL. Other studies examining antimicrobial drug use on farms have used animal defined daily doses (the average daily on-label dosage multiplied by the approximate weight of an adult dairy cow) (Grave et al., 1999; Bondt et al., 2013), antimicrobial drug usage rates (the number of animal defined doses used on a farm per 1,000 cows per day) (Saini et al., 2012), kg of active ingredients/1000-animal days (Carson et al., 2008) and individual-animal treatments (Dunlop et al., 1998). In our study, the drug dosages indicated on the discarded packaging (which could have been used to calculate doses for a standard-sized animal) are rarely followed by farmers; in addition, given the range of sizes of animals on these farms, it would have been impossible to calculate the number of doses used from the information in the bins. The chosen metrics were the most readily available, and because farmers on small farms tend to think more in terms of bottles and mLs of antibiotics than mgs of active ingredients or defined daily doses, these metrics could actually be useful in settings such as those encountered in this study.

Third, it appeared that many farmers did not put “atypical” non-therapeutic antibiotics such as dry cow intra-mammary infusions in the bins despite the fact that they were told to place all antibiotic products in the bin. This may have been because farmers or attendants were not aware that these products contain antibiotics. Similar situations could occur in the case of medicated feeds given to calves (though none of the farms in this study administered such feeds to their animals). Therefore, great care would need to be taken to ensure that farmers understand which products contain antibiotics and to ensure that all such products would be put in the bin and/or mentioned in an interview.

Fourth, most of the farms placed non-antibiotic drugs in the bin despite the fact that bins were labeled “Antibiotics” and that the research team had instructed them to place only antibiotic products in the bin. We were unable to evaluate whether farmers understood the difference between “drugs” and “antibiotics” or whether farm owners may not have properly instructed their workers. Farmers in Cajamarca were often unable to define an antibiotic (Redding et al., 2013); it is possible that this lack of awareness may explain this finding. Finally, the relatively small sample size resulted in a number of non-significant associations in this study.

The strengths of this study included the relatively long follow-up period (six months), the good adherence of the participants to the study protocol, the high participation rate, the ability to compare last-month and six-month results and the use of photos of antibiotics available on the market during the final interviews to enhance recall by providing stimulatory visual cues.

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The results of this study may provide guidance for investigators undertaking similar studies in similar environments. On a short-term basis (one month), the use of self-report can be recommended over the use of bins, which require considerable logistic support. However, for drug use data collected over a more extended period of time, bins, which appear to provide more accurate results than self-report, should be considered. In either case, great care should be taken to thoroughly explain the study protocol to farmers and farm workers and to ensure that study participants are aware of all products (including intra-mammary infusions and medicated feed) that may contain antibiotics or the active ingredient of interest. A system of inventorying drugs (especially bottles) present on the farm at the beginning and end of the study could also be implemented to account for discrepancies in bin and self-report data.

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Figure 1a

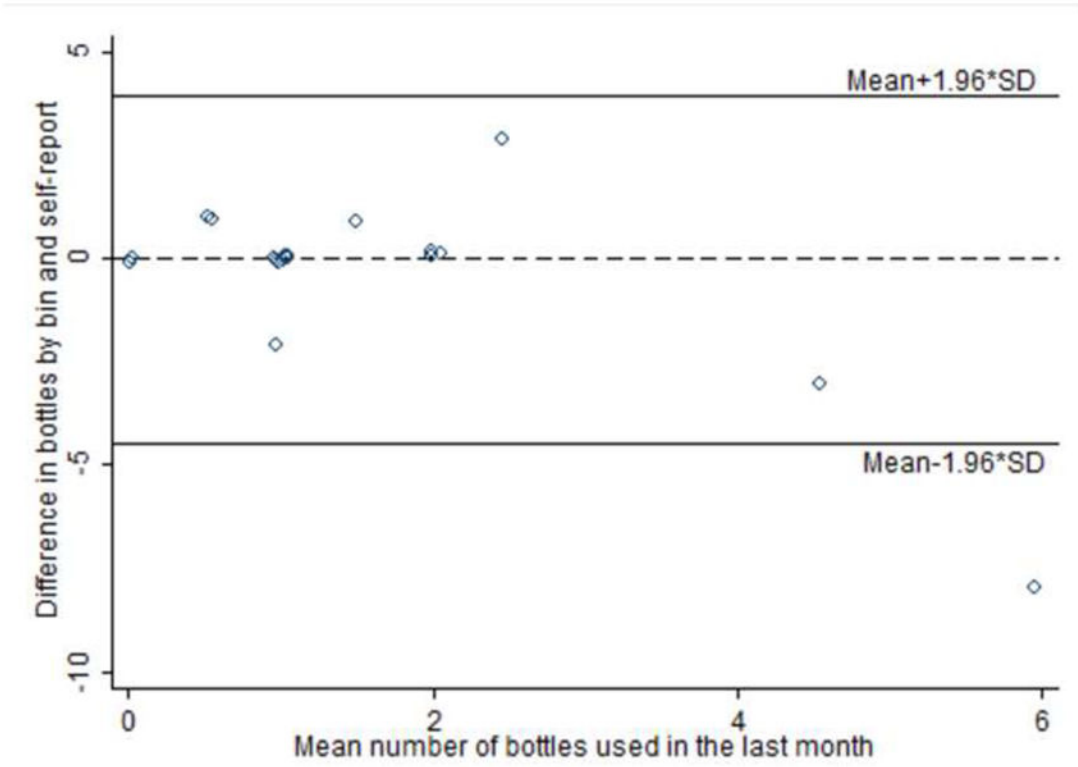
Mean+1.96*SD
Mean-1.96*SD
Difference in bottles by bin and self-report
5
0
-5
-10
0
2
4
6
Mean number of bottles used in the last month

Figure 1b

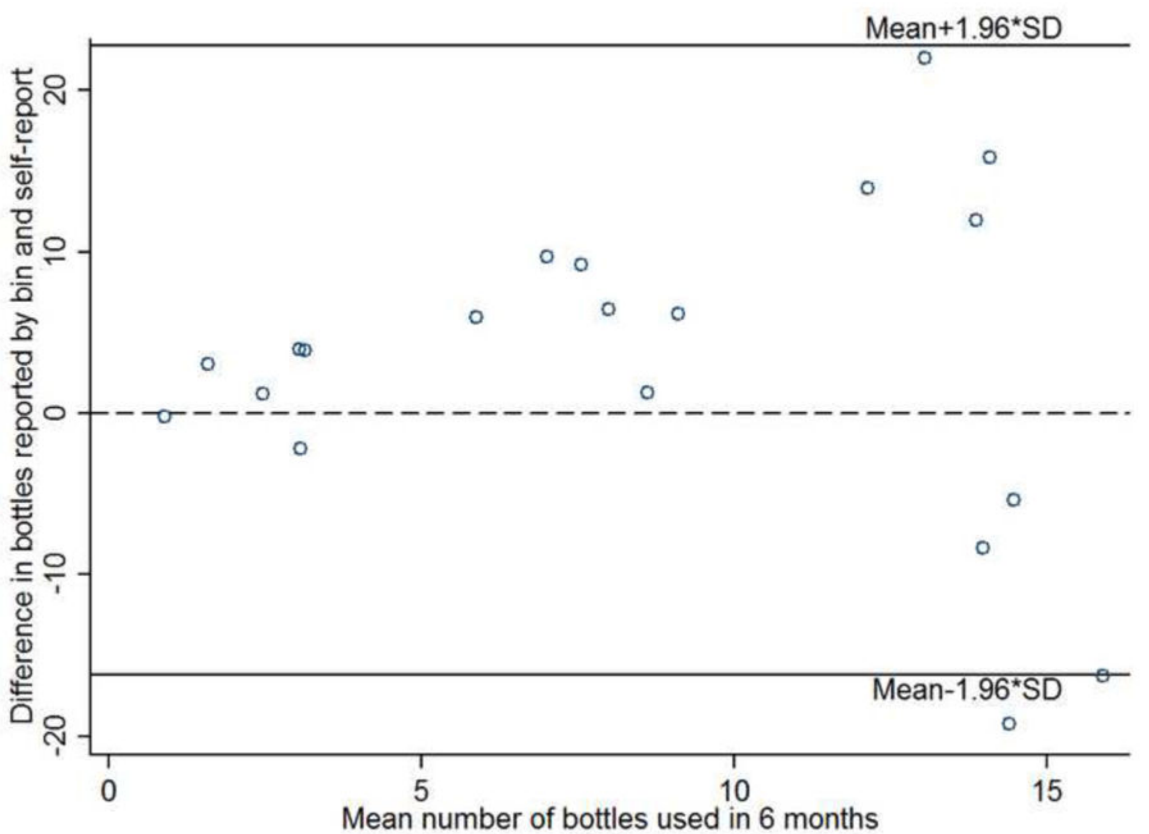

Fig. 1.

Fig 1a: Bland-Altman plot of bottles of antibiotics collected in bins and reported by farmers on a sample of 20 farms in Cajamarca, Peru during the last month of the six-month study period

Fig 1b: Bland-Altman plot comparing bottles of antibiotics collected in bins and reported by farmers on a sample of 20 farms in Cajamarca, Peru during the entire six-month study period

Figure 2a

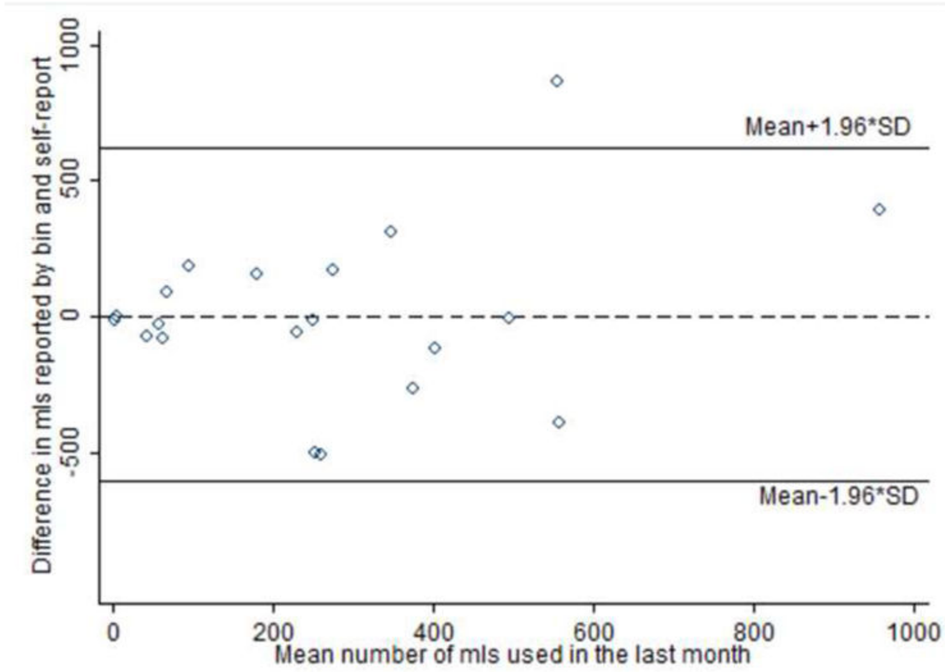

Figure 2b

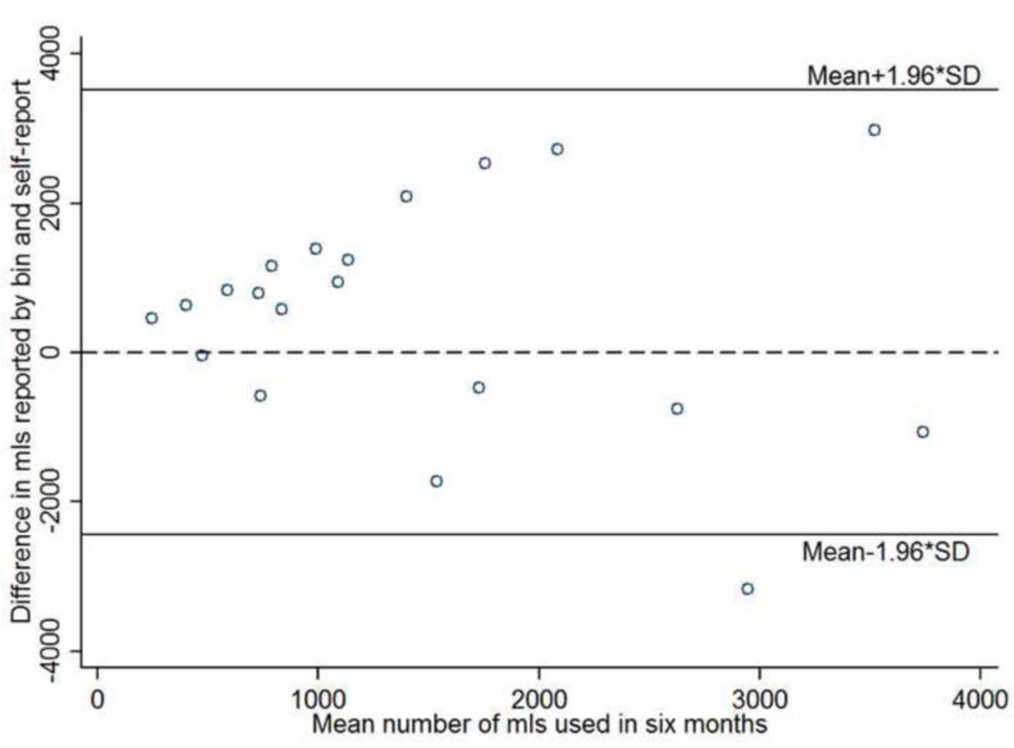

Fig. 2.

Fig 2a: Bland-Altman plot comparing milliliters of antibiotics collected in bins and reported by farmers on a sample of 20 farms in Cajamarca, Peru during the last month of the six-month study period

Fig 2b: Bland-Altman plot comparing milliliters of antibiotics collected in bins and reported by farmers on a sample of 20 farms in Cajamarca, Peru during the entire six-month study period

Figure 3a

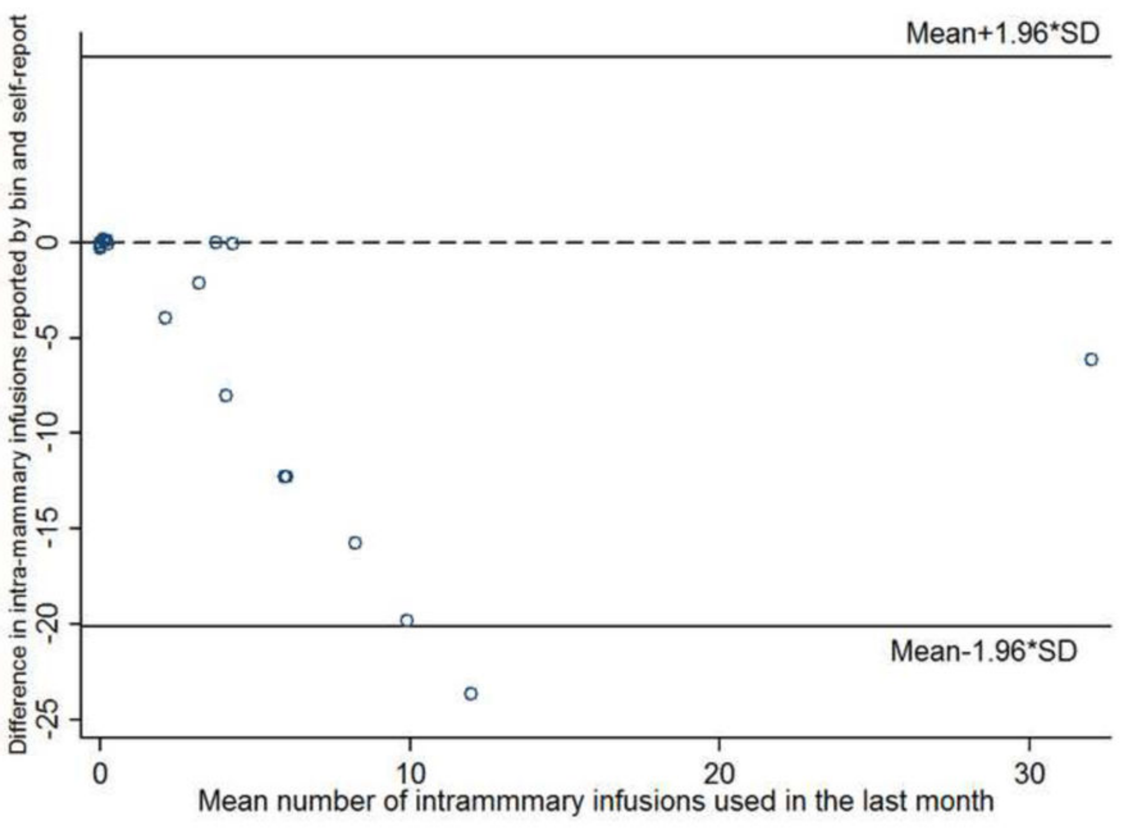
Mean+1.96*SD
Mean-1.96*SD
Difference in intra-mammary infusions reported by bin and self-report
0
-5
-10
-15
-20
-25
0
10
20
30
Mean number of intrammmary infusions used in the last month

Figure 3b

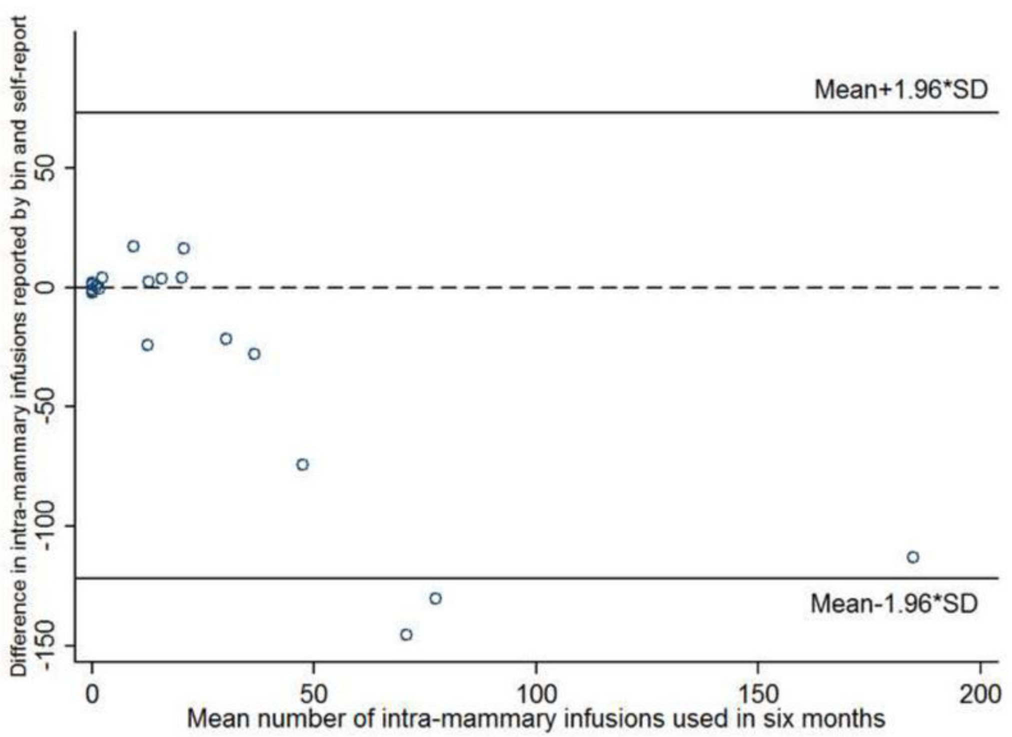

Fig. 3.

Fig 3a: Bland-Altman plot comparing intra-mammary infusions of antibiotics collected in bins and reported by farmers on a sample of 20 farms in Cajamarca, Peru during that last month of the entire six-month study period

Fig 3b: Bland-Altman plot comparing intra-mammary infusions of antibiotics collected in bins and reported by farmers on a sample of 20 farms in Cajamarca, Peru during the entire six-month study period

Table 1

Examples of methods used to acquire pharmacoepidemiological data in human and veterinary medicine and selected references of studies using the relevant methods.

Human Medicine		Veterinary Medicine	
Method	**Reference**	**Method**	**Reference**
In-person interviews of patients	Glintborg et al., 2007; West et al., 2013	Mailed/online questionnaires	McEwen et al., 1991; Dewey et al., 1999; Zwald et al., 2004; Sawant et al., 2005; Jordan et al., 2009
State or national-level health care databases	Hennessy, 2006; Hennessy et al., 2007	State or national-level surveillance systems	Dewey et al., 1999; Ruegg and Tabone, 2000; Merle et al., 2012; Stege et al., 2003; Bos et al., 2013
Drug sales records	Wirtz et al., 2010	Drug sales records	Grave et al., 1999; Chauvin et al., 2005; Kools et al., 2008; Mitema, 2009; Bondt et al., 2013
Medical records	Strom et al., 2011	In-person interviews of farmers	Luna-Tortos et al., 2006; Timmerman et al., 2006; Hill et al., 2009; Callens et al., 2012; Persoons et al., 2012
Pharmacy records	Stewart and Lynch, 2011	On-farm treatment records	Meek et al., 1986; Carson et al., 2008; Pardon et al., 2012; van der Fels-Klerx et al., 2012
Patient diaries	Parker et al., 2007	Tissue drug levels	Jones and Seymour, 1988
MEMS cap measurements	Parker et al., 2007	Collection of drug packaging	Dunlop et al., 1998; Carson et al., 2008; Saini et al., 2012
Drug levels in the body	Bisson et al., 2008		

Table 2

Characteristics of farms and farmers (n=20) enrolled in a study comparing methods of acquiring antibiotic usage data in Cajamarca, Peru

Farm or farmer characteristic	Mean (SD; min; max)	No. of respondents (%)
Lactating cows	33.0 (20.4; 6; 90)	-
Total cows	40.6 (25.1; 11; 120)	-
Calves	21.8 (13.6; 5; 50)	-
Daily milk production (L)	392 (231; 75; 1000)	-
Age of farm owner (n=20)	50.2 (11.7; 28; 67)	-
Age of attendant-in-charge (n=14)	40.6 (13.6; 16; 69)	-
Men working on farm	3.2 (2.0; 1; 8)	-
Women working on farm	3 (1.7; 1; 7)	-
Education level of farm owner		
Primary school completed	-	4/20 (20)
Secondary school completed	-	4/20 (20)
University completed	-	12/20 (60)
Education level of attendant-in-charge		
Some primary school	-	6/14 (42.9)
Some secondary school	-	5/14 (35.7)
Some university	-	3/14 (21.4)
Destination of milk		
Nestle	-	8/20 (40)
Gloria	-	5/20 (25)
Cheesemakers	-	7/20 (35)

Table 3

Bottles, mLs and intra-mammary infusions of antibiotics used in the last month and during the entire six-month study period on 20 farms in Cajamarca, Peru, according to bin data and self-reported data

Farm ID	Bin measure/self-report measure					
	Last month			Six-month period		
	Bottles	mLs	Intra-mammary infusions	Bottles	mLs	Intra-mammary infusions
1	10/2	350/470	4/4	20/8	1530/2000	24/20
2	6/3	1150/750	2/4	22/6	5000/2000	13/10
3	0/0	0/0	0/0	3/0	450/0	0/0
4	1/1	250/250	0/0	10/18	1400/4500	0/0
5	1/4	1000/120	0/0	8/24	3500/720	0/0
6	1/1	200/250	29/35	2/4	450/1000	128/240
7	2/2	350/200	0/24	11/5	2400/400	11/144
8	1/1	50/80	0/0	9/3	750/114	2/0
9	1/1	500/500	0/0	1/1	500/500	0/0
10	2/2	350/750	0/16	9/8	2200/3000	8/84
11	1/1	100/20	0/0	12/6	1520/600	16/0
12	0/1	0/500	0/8	5/1	1750/500	0/24
13	0/1	0/500	0/0	5/1	1100/500	0/0
14	0/1	0/75	0/4	24/2	1350/200	28/12
15	0/0	0/0	0/12	12/2	1150/300	20/40
16	1/2	250/500	0/12	12/17	3250/4250	24/50
17	1/1	250/100	0/0	12/3	1650/300	3/0
18	2/2	500/200	0/20	3/2	1000/200	0/0
19	2/0	200/0	0/0	5/24	720/2400	0/144
20	1/1	15/90	4/4	19/5	2995/450	16/12

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Table 4

Intraclass correlation coefficients, slope of the regression line comparing self-reported measures and bin measures, and bias, variability of the bias and limits of agreement for bin measures and self-reported measures in a sample of 20 farmers asked to collect discarded drug packaging and recall antibiotic usage in Cajamarca, Peru

		ICC	95% CI of the ICC	Slope of regression line (bin measure vs. SR measure)	P-value indicating a significant difference from 1 for the slope	Mean bias[a]	SD	LL and UL[b] of agreement
Last month	Bottles	0.30	0.00–0.63	0.99	0.99	−0.3	2.15	−4.51; 3.91
	Volume (mLs)	0.40	0.11–0.69	0.54	0.11	8	313	−605; 621
	IMM infusions	0.59	0.370–0.80	0.42	<0.001	−5.2	7.61	−20.1; 9.72
Six months	Bottles	0.01	0.00–0.46	0.01	<0.001	3.2	10.0	−16.4; 22.8
	Volume (mLs)	0.30	0.00–0.63	0.26	0.001	536	1520	−2443; 3515
	IMM infusions	0.51	0.27–0.76	0.30	0.001	−24.4	49.8	−122; 73.2

[a] The mean bias represents the difference between bin measures and self-report measures

[b] The LL and UL represent the mean bias-1.96*SD and the mean bias+1.96*SD, respectively.

IMM=Intra-mammary, CI=confidence interval, ICC=Intraclass correlation coefficient, SD=standard deviation, LL=lower limit, UL=upper limit

Table 5

Ratio of six-month to last-month measures of antibiotic usage data collected on a sample of 20 farms in Cajamarca, Peru

	Ratio[a]	SD	P-value for Wilcoxon rank sum test comparing bin and self-reported measures
Bin bottles	6.98	5.27	0.12
Self-reported bottles	4.24	4.12	
Bin volume (mLs)	19.3	50.1	0.09
Self-reported volume (mLs)	5.62	7.51	
Bin intra-mammary infusions	5.23	1.21	0.17
Self-reported intra-mammary infusions	3.83	1.90	

[a]If antibiotic use is consistent over the six-month period, the expected ratio is 6

Table 6

Agreement between antibiotic-use data collected in bins and self-reported by farmers (n=20) in Cajamarca, Peru, for individual drugs classes

		Prevalence in bin	Prevalence by self-report	Percent Agreement	Kappa	Kappa P-value
Last month	Penicillin IM	0.40	0.45	0.75	0.49	0.01
	IMM Penicillin	0.20	0.25	0.55	−0.29	0.90
	Oxytetracycline	0.40	0.45	0.75	0.49	0.01
	TMS	0.15	0.35	0.70	0.24	0.11
	Other types of antibiotic	0.20	0.20	0.70	0.063	0.39
Six months	Penicillin	0.75	0.70	0.75	0.38	0.05
	IMM Penicillin	0.55	0.30	0.75	0.52	0.004
	Oxytetracycline	0.85	0.65	0.60	−0.013	0.53
	TMS	0.50	0.35	0.75	0.50	0.009
	Other types of antibiotic	0.75	0.43	0.70	0.43	0.009

IM=intramuscular, IMM=intramammary, TMS=trimethoprim-sulfamethoxazole

Table 7

Marginal agreement between antibiotic-use data from bins and self-reported by farmers (n=20) for individual drug types in Cajamarca, Peru

		Odds ratio [a]	**P-value**
Last month	Penicillin	0.67	0.65
	Intra-mammary penicillin	0.8	0.73
	Oxytetracycline	0.67	0.65
	TMS	0.2	0.10
	Other types of antibiotic	1	1
Six months	Penicillin	1.5	0.74
	Intra-mammary penicillin	0.92	0.03
	Oxytetracycline	3.0	0.16
	TMS	4.0	0.18
	Other types of antibiotic	Undefined	-

[a]The odds ratio compares the probability of a bin containing the drug to the probability that the farmer reported using the drug and was obtained using McNemar's test.