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Research article

Factors associated with irrational antimicrobial use on pig and layer farms in Chiang Mai–Lamphun and Chon Buri provinces, Thailand

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Abstract

This research study was conducted to identify the factors associated with irrational antimicrobial use taking place in pig and layer farms in Chiang Mai–Lamphun and Chon Buri Provinces. The approach included twelve focus group discussions (FGDs) occurring among relevant stakeholders. Research questions were described by thematic analysis. Additionally, a cross-sectional survey of 125 pig and 126 layer farm owners/managers using a validated self-administered questionnaire was performed. Multiple logistics regression was used to investigate associations between factors and good-faire practices. Spearman rank correlation was also applied to analyze the direction and degree of the relationship between knowledge, attitudes and practices. It was revealed that the significantly associated factors included farm patterns with prior contracts of farming and these had fair to good practices by as much as 42.95 times (95%CI: 12.87–143.31, $P=0.00001$). The adjusted OR was 19.12 (95%CI: 5.55–65.82, $P=0.00001$) interpreting for the purposes of improved practices in Chon Buri Province. Among the factors that were associated with irrational antimicrobial usage on farms, there were a large number of licensed retail pharmacies, drug stores and other outlets involved in the distribution of antimicrobials throughout the country. Consequently, many antimicrobials can be easily accessed and obtained as over-the-counter substances. It is also common for antimicrobials to be over-prescribed and this is motivated and facilitated by financial incentives, insufficient and poor veterinary services, inadequate monitoring, a poor system of tracking and inspecting drugs along the supply chain, inadequate enforcement regulations pertaining to veterinary pharmaceutical medicines, especially on non-registered and small-scale independent farms.

Keywords: Factor, Irrational, Focus group discussion, Antimicrobial, Farm, Thailand

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INTRODUCTION

Antimicrobial resistance is a serious threat to global health, food security, and national economy (Gandra et al., 2014; WHO, 2001). Overuse of antimicrobial agents in both humans and animals has caused the antimicrobial resistance worldwide (WHO, 2010; Padungtod et al., 2006; Boonyasiri et al., 2014; Nuangmek et al., 2018a). In developing countries, the antimicrobial agents can be purchased easily bought from retail pharmacies without prescriptions, and these can be administered through an accepted standard of self-medication (Morgan et al., 2011; Ocan et al., 2015). In 2009, the value of antimicrobials that are manufactured and imported into Thailand was about 315 million US dollars (Jitraknatee, 2011). In addition, there were 5,371 antimicrobial agents which were registered by the Thai Food and Drug Administration for importation and production in Thailand (Food and Drug Administration, 2017). Additionally, 37% of these antimicrobials were used on livestock, pets and some were administered as medicated premixed substances. All of these could boost the irrational antimicrobial usage both human and farm animals (Sommanustweechai et al., 2018). Proper use of antimicrobials in humans and veterinary is one of the main objectives of the Global Action Plan on Antimicrobial Resistance (WHO, 2015). In Thailand, the goal of reducing antimicrobial consumption by 20% among humans and by 30% in the veterinary field by 2021 was promulgated by the Thai Cabinet in 2016 (FAO, 2017). Hence, relevant stakeholders must cooperate to achieve the goals.

Irrational antimicrobial usage could be found in almost all farming systems worldwide, including in Thailand. This is particularly true in poultry and pig farms where antimicrobials are used extensively (Metlay et al., 2006). Pig and poultry industries in Thailand have developed and grown significantly in recent years and consequently, farming systems have changed from small-scale to large-scale farms with fully integrated systems. Pig production has the highest market share of the total antimicrobial values (66.96%), followed by layer production (3.47%) (AHPA, 2013). Northern and eastern regions of Thailand have a high density of farms that raise animals and these farms house 46.57% of layers and 26.57% of pigs in Thailand (DLD, 2013); therefore, Chiang Mai–Lamphun and Chon Buri Provinces, which are located in the northern and eastern regions respectively, were chosen as the focus of this study. The aim of this research study was conducted to identify the factors related to irrational antimicrobial use on pig and layer farms in Chiang Mai–Lamphun and Chon Buri Provinces. The findings of this research can be used to assist policy makers for designing or updating policies to mitigation of antimicrobial resistance crisis in Thailand.

MATERIALS and METHODS

Study design and data collection

This study was conducted to explore the factors associated with irrational antimicrobial use on pig and layer farms in Chiang Mai–Lamphun and Chon Buri Provinces in Thailand during the period of May 2015 through February 2017. Focus group discussions (with key informants selected from relevant stakeholders involved in the regional and provincial livestock officers

(RPLO), farm veterinary consultants (FVC), cooperative managers (COM), contract farmers (CF), cooperative farmers (COF) and independent farmers (IF)) and a cross-sectional survey of pig and layer farm owners/managers using a validated self-administered questionnaire were used to gather data on the factors associated with the practices of antimicrobial usage on farms.

Focus group discussions

The selection criteria of the participants included seniority, experience with the research topic, and having an active role in the rational use of antimicrobials by relevant stakeholders. The participants were divided into twelve focus group discussions (FGDs). Two FGDs were conducted for regional and provincial livestock officers, two FGDs for farm veterinary consultants and cooperative managers, two FGDs for layer contract farmers, two FGDs for pig contract farmers, two FGDs for layer cooperative and independent farmers and another two FGDs were held for pig cooperative and independent farmers. Fifteen to twenty-five participants took part in each of the FGDs. All FGDs were conducted with the first (AN), third (SC) and fourth (PY) authors serving as facilitators along with a number of professional veterinarians that were there to help facilitate the discussions and to audio-record them for qualitative analysis of the FGDs. Each FGD lasted between 100 and 125 min. A topic guide was developed by the first author (AN), discussed with the co-authors, and revised until a final agreement was reached. A topic guide was implemented that revealed two main challenges associated with the distribution and access of antimicrobials and active pharmaceutical ingredients (APIs) used at the farm level. Both of which are relevant to the control of antimicrobial usage, and the medicated feed and active pharmaceutical ingredients that are administered on farms. In the FGDs, a semi-structured approach was used to guide the discussion toward the research questions, and the facilitators were encouraged as participants to explore the primary discussion in-depth and to reflect upon any of their own issues. After the event, a summary, with the main conclusions, was sent to the participants for comments and clarification. All FGDs were audio-recorded, transcribed and translated where required.

A cross-sectional survey

A validated self-administered questionnaire was used to gather information on the potential risk factors related to improper antimicrobial usage on pig and layer farms within the study sites. The sample size for the study was calculated using Epi Info™ 7 software (CDC, 2014). A response distribution of 80% was assumed with a confidence interval of 95% and a margin of error of 5%. By calculation, 125 and 126 of the pig and layer farm owners/managers respectively, were estimated to be the minimum effective sample size. The sample size includes 75 pig farms and 85 layer farms that were located in Chiang Mai and Lamphun Provinces in the northern region of Thailand and 50 pig farms and 41 layer farms in Chonburi Province, which is located in the eastern region of the country. Layer and pig farms in this study were stratified by size into three classes including small, medium or large-scale farms. Layer farms with 1,000 to 10,000 birds were categorized as small-scale; those with 10,001 to 50,000 birds were classified as medium-scale; and those with more than 50,000 birds were stratified as large-scale farms (FAO, 2014). In pig

farms, livestock units were used to categorize the scale of the pig farms. Farms with 6 to 59 livestock units were categorized as small-scale; those with 60 to 600 livestock units were classified as medium-scale; and those with more than 600 livestock units were classified as large-scale farms (ACFS, 2009). Farms included in the study were selected using a convenience sampling method.

Data analysis

All audio-recorded FGDs were transcribed verbatim and processed anonymously. This was followed by thematic analysis, which was conducted using theoretical sampling and theoretical saturation (Marshall and Rossman, 2006; Alhojailan, 2012). Research questions were used to sort and categorize the data in an initial deductive step. After the initial coding, an inductive approach was then applied to formulate a preliminary list of themes. Subsequently, the list of themes was refined in the following coding runs, while subthemes were added. The process was repeated iteratively until a final agreement was reached.

KAP respondents' answers were scored. Regarding the knowledge assessment, one mark was awarded for each correct answer and zero marks were given for each wrong or unsure response. Attitude responses were scored using a five-point Likert scale with potential responses ranging from "Strongly Agree" to "Strongly Disagree". Practices of the respondents were assessed using a four-point Likert scale with potential responses ranging from "Usually" to "Never". The reverse scoring was used for any negative statements in a manner that was similar to the one used in the calculation system. The rating scale is measure as follow Table 1. The total knowledge, attitude and practices scores were categorized into three levels using Bloom's cut off point (60-80%). The categorized level is measure as follow Table 2. All data were analyzed using the Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA) version 17.0 (Mehta and Patel, 1996). Statistical analysis was calculated using Epi Info™ 7 software (CDC, 2014). Multiple logistic regression was used to investigate associations between factors (such as study sites, type of animal, farm owners' experience, farm owners' education, farm pattern, farm registration, farm size, farm owners' knowledge level, farm owners' attitude) and good-fair practices. Variables were included based on $P < 0.05$ significance in univariate analysis. The model was reduced in a backward-elimination procedure. A 10% change in the coefficient was considered evidence of possible confounding. Adjusted Odd Ratio (OR) and 95% confidence interval (CI) were calculated to determine the main effects.

Table 1 Statement of attitude and practices scores were assessed using Likert's scale.

Attitude assessment			Practice assessment		
Choice	Positive Scores	Negative Scores	Choice	Positive Scores	Negative Scores
Strongly agree	4	0	Usually	4	1
Agree	3	1	Sometime	3	2
Neutral	2	2	Rarely	2	3
Disagree	1	3	Never	1	4
Strongly disagree	0	4			

Table 2 Three categorized levels of total knowledge, attitude and practices scores by using Bloom's cut off point (60-80%).

Scores	Categorized levels of Bloom's cut off point		
	Knowledge	Attitude	Practice
Scores (81-100%)	High level	Concerned	Good
Scores (60-80%)	Moderate level	Neutral	Fair
Scores (Less than 60%)	Low level	Not concerned	Poor

Spearman rank correlation was also applied to analyze the direction and degree of the relationship between knowledge and attitudes, knowledge and practices and attitudes and practices wherever applicable using the Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA) version 17.0 (Mehta and Patel, 1996). The absolute value of Spearman's rho was classified into five interval levels as 0.90-1.00 (Very high correlation), 0.70-0.89 (High correlation), 0.50-0.69 (Moderate correlation), 0.30-0.49 (Low correlation) and 0.00-0.29 (Little if any correlation) (Hinkle et al., 2003). The level of statistical significance was set at $P < 0.05$.

RESULTS

Participants were identified from relevant stakeholders that were involved in rational antimicrobial usage on pig and layer farms, namely regional and provincial livestock officers, farm veterinary consultants, cooperative managers, contract farmers, cooperative farmers and independent farmers. These participants were asked to reflect upon their shared owner issues in order to find potential solutions for appropriate use of antimicrobials on farms. Two major themes which included distribution and access to antimicrobials and active pharmaceutical ingredients (APIs) at the farm level and control of antimicrobial use, medicated feed and APIs on farms were considered. Some

participants thought that many antimicrobials that are used on farms could be easily accessed and obtained over-the-counter, especially on non-registered and independent farms. Additionally, it was believed that veterinarian prescriptions are not needed when antimicrobials are purchased. In Thailand, there are large numbers of licensed retail pharmacies, drugs stores, and other outlets for the distribution of antimicrobials. However, there is also the issue of inadequate or weak enforcement of the regulation of antimicrobial distribution and sales, and this may contribute to the easy availability of antimicrobials. Some participants believed that pharmaceutical companies offer economic incentives to the buyers by financing international travel for many farmers. These issues may contribute to the excessive antimicrobial use that takes place on farms. With regard to the wholesale distribution of antimicrobials to farmers or others who are not licensed retail outlets became prohibited. However, some stakeholders mentioned to the sales of large amounts of antimicrobials to these individuals was not considered. APIs can only be sold by licensed importers and manufacturers. These entities could then distribute the substances to manufacturers who produce the finished products. However, some participants thought that a lack of monitoring and tracking of APIs and inadequate inspections at the drug distributorships and retailers has resulted in abuse of the system. Most contract farmers believed that antimicrobial usage on contract farms had more rational use than on non-contract farms because they were more likely to follow relevant policies and rules pertaining to animal feed and antimicrobial usage on contract farms. Some participants thought that, the cooperative's policies and the rules associated with antimicrobial usage are not strictly followed or enforced by the cooperative's members. Regarding control of antimicrobial use, medicated feed and APIs on farms. Most of the regional and provincial livestock officers thought that the existing legislation and regulations are comprehensive enough to cover all areas of pharmaceutical activities and to protect the public and the health of animals in Thailand; however, weak, improper or ineffective enforcement of the existing legislation and regulation could be promoting the irrational antimicrobial use on farms. Some participants believed that many farms have obtained the standard accreditation by the DLD, however inappropriate antimicrobial use on farms persists. Some participants mentioned that there remains a lack of systematic monitoring and tracking, adequate inspections at the drug distributorship level and weak enforcement of legislation and regulation on farms. Hence, some APIs were being improperly used on farms. Regarding medicated feed on farms, farmers and cooperatives who produced their own medicated feed using a feed mixer do not implement quality control measures. The mention of statements by various stakeholders are shown in Table 3. Thematic analysis resulted in the identification of two major themes. These themes included distribution and access to antimicrobials and active pharmaceutical ingredients (APIs) at the farm level and control of antimicrobial use, medicated feed and APIs on farms. The subthemes that emerged from the analysis are shown in Tables 4 and 5.

In a cross-sectional survey, multivariate logistic regression analysis was used to compare the relevant factors association with this situation and to assess fair to good practices regarding antimicrobial usage on farms. The study examined the factors that are significantly associated with antimicrobial use on

farms. It was found that farm patterns with prior farming contracts have fair to good practices recorded at 42.95 times (95%CI: 12.87–143.31, $P = 0.00001$) compared to the non-contract farms and study sites in Chon Buri and Chiang Mai-Lamphun Provinces. Notably, the adjusted OR was 19.12 (95%CI: 5.55–65.82, $P=0.00001$) for good practices in Chon Buri Province. However, no differences were found in a comparison of the two regions for fair to good practices with regard to the remaining factors such as those related to animal kind, farm owners' experience on farms, farm registration status, farm size, farm owners' knowledge levels and farm owners' attitudes (Table 6).

The correlation among the overall levels of knowledge and attitude toward and practice of using of antimicrobials on pig and layer farms is shown in Table 7. A slight positive correlation between knowledge and attitudes was noted pertaining to these statements ($r=0.1555$, $n=251$, $P=0.014$). However, no correlation was observed between knowledge and practice ($r=0.054$, $n=251$, $P=0.398$) and between attitude and practice ($r=0.083$, $n=126$, $P=0.189$).

Table 3 The major mention of various stakeholders regarding antimicrobial distribution, access and control on farms in Chiang Mai-Lamphun and Chon Buri Provinces.

Stakeholders	The statements are mentioned by various stakeholders
Distribution and access of antimicrobials and APIs at the farm level	
RPLO-1	<i>"Farmers can purchase antimicrobials without a veterinarian's prescription from fully-licensed distributors and great numbers of antimicrobials have been distributed throughout the country".</i>
RPLO-3	<i>"Many licensed retail pharmacies sell antimicrobials directly to livestock farms".</i>
RPLO-8	<i>"These issues were found to exist to a greater extent in Chon Buri Province than in Chiang Mai-Lamphun Province".</i>
RPLO-7	<i>"Some farmers purchase very large amounts of unnecessary antimicrobials because of the economic incentives that are extended to them".</i>
RPLO-1	<i>"Wholesale distribution of antimicrobials to farmers by pharmacies or veterinary professionals or licensed retail outlets could occur"</i>
RPLO-4	<i>"Some farmers were illegally mixing APIs to animal feeds, probably as a cost-saving measure".</i>
RPLO-2	<i>"Leakage of illegal APIs into the market has occurred, some of which are used directly on farms".</i>
RPLO-10	<i>"A lack of monitoring and tracking of pharmaceutical and inadequate inspections at the drug distributorships, retailers and on farms is common".</i>
RPLO-1	<i>"Veterinary pharmaceuticals distributed through the country level is not clearly stated and is not systematically".</i>
IF-2, IF-5, IF-9.	<i>"Farmers can easily purchase antimicrobials from drugstores and pharmacies without a veterinarian's prescription".</i>
IF-2, IF-12, IF-15	<i>"Retail pharmacies directly sell antimicrobials to our farms".</i>
IF-1	<i>"Most independent farms use antimicrobials by self-administration without a prescription".</i>
IF-6	<i>"Some farmers mixed APIs in the feed for animals on farms".</i>
FVC-1, FVC-3, FVC-7, FVC-10	<i>"Some registered farms purchase antimicrobials without a veterinarian's prescription and self-administer the substances on farms without being guided under the supervision of farm veterinarians".</i>
FVC-11	<i>"Farm veterinarians must comply with the Code of Practice for Control of the Use of Veterinary Drugs".</i>

All CF	<i>"They can access antimicrobials and feed only from contract companies, and that treatment and prevention procedures of diseases are also under the supervision of DLD-registered farm veterinarians that would be provided by the contract company".</i>
COF-1.	<i>"Some cooperative farmers could purchase antimicrobials without a veterinarian's prescription from other sources, when they do not receive enough support from the cooperative".</i>
COF-4, COF-6, COF-9	<i>"Cooperatives provide all most antimicrobials and feed for member farms".</i>
All COM	<i>"If cooperatives can't supply pharmaceuticals and feed, farm members can obtain them from other sources and the cooperative's policy and rules are resilient for the members".</i>
<hr/>	
Control of antimicrobial use, medicated feed and APIs on farms	
All RPLO	<i>"Antimicrobial usage on farms must follow the regulations set by DLD-registered farm veterinarians; however, insufficient and poor veterinary services are common, especially on non-registered and small-scale farms".</i>
RPLO-3, RPLO-11	<i>"The notification of the livestock farm standard is voluntary. Some farms that obtained registration have not strictly followed the SOP guidelines for farmers".</i>
RPLO-1	<i>"Notification of the livestock farm standard is voluntary, yet some farmers have not adhered to the policies and have administered antimicrobials on farms by self-medication".</i>
RPLO-6	<i>"Good agricultural practice could not be implement on all farms"</i>
RPLO-7.	<i>"Antimicrobial usage on farms does not comply with the TAS 9032-200, because of insufficient and poor veterinary services, especially on non-registered and independent farms".</i>
RPLO-1, RPLO-8	<i>"The farmers who produced their own medicated feed using a feed mixer did not follow quality control measures and were not certified by the relevant authority. This issue has occurred across all cooperatives".</i>
IF-9	<i>"I administrated antimicrobials on my farm by myself".</i>
IF-1	<i>"Some farms have not registered with the relevant authority".</i>
IF-7	<i>"I couldn't pay for veterinary services on my farm".</i>
FVC-5	<i>"Antimicrobial usage without veterinary prescription on farms through self-medication feed practices were known to commonly occur, especially on non-registered and independent farms".</i>
All FVC	<i>"Not only must contract farmers comply with the contract companies' policies or rules, they also must obtain farm registration documentation from the DLD".</i>
FVC-3	<i>"There are not enough farm veterinarian consultants to control antimicrobial use on farms, while most small-scale or independent farm owners could not pay for veterinary services on their farms".</i>
All CM	<i>"Regarding the cooperative policy, farm members may have followed the SOP for farmers, however there was not strict enforcement of the laws for obtaining accreditation for these farms from DLD"..</i>

Note: Key informants selected from relevant stakeholders involved in regional and provincial livestock officers (RPLO); farm veterinary consultants (FVC); cooperative managers (COM); contract farmers (CF); cooperative farmers (COF) and independent farmers (IF)

Table 4 Subthemes of distribution and accessed of antimicrobials and active pharmaceutical ingredients (APIs) on farm level that emerged from the focus group discussions with key informants in Chiang Mai-Lamphun and Chon Buri Provinces.

Stakeholders	Subtheme and important message
Regional and provincial livestock officers	<p>Many antimicrobials use on farms can be easily accessed and obtained over-the-counter.</p> <p>Record of antimicrobials distribution through retail pharmacies, drugstores and farms are not clearly stated and not systematically.</p> <p>Leakage of illegal APIs into the market, some of which are used directly to livestock farms.</p> <p>Inadequate or weak enforcement regulation of drug distribution and sales may result in easy access.</p> <p>The economic incentives of pharmaceutical and wholesale distribution of antimicrobials to farmers could contribute to the excessive antimicrobial use on farms.</p>
Farm veterinary consultants	<p>Veterinarian prescriptions are not needed when antimicrobials are purchased.</p> <p>Self-medication with antimicrobials obtained without a prescription is a common practice on farms, especially independent and non-registration farms.</p> <p>Easy accessed could be boosted the improper antimicrobials use on farms.</p>
Contract farmers	<p>Feed and antimicrobials usage on contract farms are distributed by contract company.</p> <p>Contract farmers can be accessed antimicrobials from only contract company.</p>
Cooperative member farmers	<p>Cooperative was the majority source of antimicrobials and feed for distributing to members.</p> <p>The members are allowed to use of antimicrobials and feed from other sources if it was necessary.</p>
Independent farmers	<p>Feed and antimicrobials usage on farms can be easily accessed form variety sources.</p> <p>Almost farms using antimicrobials by self-medication without prescription.</p> <p>Some of farm used APIs directly on farms.</p>

Table 5 Subthemes of control of antimicrobials use, medicated feed and active pharmaceutical ingredients (APIs) on farms that emerged from the focus group discussions with key informants in Chiang Mai-Lamphun and Chon Buri Provinces.

Stakeholders	Subtheme and important messages
Regional and provincial livestock officers	<p>Antimicrobials usage follow by veterinarian prescription have not occurred in all farms.</p> <p>Insufficient and poor veterinary services are common in non-registered and independent farms.</p> <p>On DLD-registered farms, veterinarian responsible for supervision of their animal health and pharmaceutical prescription, however these farms are voluntary.</p> <p>Improper antimicrobial usage on farms need strictly enforcement by legislation and regulations.</p> <p>The Acts prohibited directly use of APIs in animal feed</p> <p>Inadequate inspection could boost farmers to purchase illegal drugs from drugstores or wholesalers.</p> <p>The farmers who produced their own medicated feed did not have quality control.</p> <p>Feed mills in Thailand must have obtained GMP and HACCP certified in order to sustenance good production quality.</p>
Farm veterinary consultants	<p>Veterinarian prescription could action on some farm</p> <p>Inadequate or lack of antimicrobials monitoring and surveillance on farms was occurred.</p>
Contract farmers	<p>Contract farmers must comply strictly with the company rules.</p> <p>Contract farmers are managed and integrated system by contract companies.</p> <p>Antimicrobials usage on farm will be supported by only contract company.</p> <p>Contract farmers are not allowed to use feeds and pharmaceutical product from other sources.</p>
Cooperative member farmers	<p>Some of antimicrobials usage on farm members are not clearly control by cooperative.</p> <p>Weak enforcement of cooperative policy and rules for antimicrobial usage on farm members.</p> <p>Feed mixer of cooperative which produced medicated feed for members do not obtain standard certify.</p>
Independent farmers	<p>Couldn't supply DLD-registered farm veterinarian to look after animal health and control antimicrobial usage in all farms.</p> <p>Weak enforcement antimicrobial usage on independent farm by legislation and regulations.</p> <p>Feed mixer on farms which produced medicated feed do not obtain standard certify.</p> <p>Some farmers mix APIs directly into their animal feeds.</p>

Table 6 Multivariate logistic regression analysis of factors associated with fair to good practice of antimicrobial usage on pig and layer farms in Chiang Mai-Lamphun and Chon Buri provinces. (n=251).

Variables	Adjusted OR (95%CI)#	P-value
Study site		
Chon Buri vs Chiang Mai-Lamphun province	19.12 (5.55–65.82)	0.00001*
Animal kind		
Pig vs layer	1.33 (0.57–2.24)	0.719
Farm owners' experience		
Five year and over vs less than 5 year	0.62 (0.29–1.78)	0.376
Farm owners' education		
Over primary vs primary education	0.57 (0.28–1.13)	0.105
Farm pattern		
Contract vs non contract farming	42.95 (12.87–143.31)	0.00001*
Farm registration status		
Registered vs non registered farm	1.26 (0.36–4.14)	0.755
Farm size		
Small scale- vs medium to large scale-farm	1.97 (0.97–3.98)	0.059
Farm owners' knowledge level		
High vs moderate to low level	1.03 (0.49–2.18)	0.941
Farm owners' attitude		
Concern vs neutral to not concern	0.73 (0.38–1.41)	0.347

* Variable is significant at the < 0.01 level.

Assessed by multivariate logistic regression, including risk factors for study site, animal kind, farm owners' experience, farm pattern, farm registration status, farm size, farm owners' knowledge level and farm owners' attitude.

Table 7 Correlation among knowledge, attitudes and practices of antimicrobial use on pig and layer farms in Chiang Mai-Lamphun and Chon Buri Provinces. (n=251).

Variables	Spearman's rho	P-value
Knowledge & Attitude	0.155	0.014*
Knowledge & Practice	0.054	0.398
Attitude & Practice	0.083	0.189

* Correlation is significant at the 0.05 level.

DISCUSSION

This study highlights the factors associated with irrational antimicrobial usage on pig and layer farms in Chiang Mai-Lamphun and Chon Buri Provinces in order to support further insights for the planning and developing of strategies to promote the appropriate antimicrobial use on these farms. Key informants who had promoted appropriate antimicrobial usage on farms were chosen to participate in FGDs including farm owners who are the key decision-makers with regard to the use of antimicrobials on their farms (Willock et al., 1999), farm veterinary consultants who have a good reputation among farmers and who supervise farmers in appropriate antimicrobial usage on farms (Friedman et al., 2007; Garforth et al., 2013), regional and provincial livestock office authorities who are involved in activities for the post-marketing of veterinary drugs/biologics such as through law enforcement, the monitoring and surveillance of veterinary medicinal products on farms, as well as the cooperatives' managers.

As identified by the study participants, one of the main factors is the circumstance associated with the distribution and access of antimicrobials and APIs at the farm level. The participants agreed that many antimicrobials used on farms could be easily accessed and obtained over-the-counter. This finding is similar to what has been previously reported and has stated that many antimicrobials have been easily purchased without veterinarian prescription and that antimicrobial usage is common by self-administration in low- and middle-income countries (Kumaranayake et al., 2000; Teerawattananon et al., 2003; Suleman et al., 2016). Additionally, in Thailand, there are a large number of licensed retail pharmacies, drugs stores, and other outlets involved in the distribution of antimicrobials throughout the country (Sommanustweechai et al., 2018). The inadequate and/or weak enforcement of the regulations of antimicrobial distribution and sales and weak pharmaco-vigilance also contribute to the easy availability of antimicrobials throughout the country. Besides, some pharmaceutical companies boost their market share by offering certain economic incentives to farmers such as by financing international travel for leisure purposes to farmers. The over-prescribed antimicrobials by financial incentives contribute to the excessive antimicrobial use on farms (Iversen and Luras, 2000). Regarding the sale of large amounts of antimicrobials to individuals, the sale and distribution of drug products is only allowed to hospitals, clinical institutes, pharmacies or veterinary professionals by wholesalers who have obtained a wholesale license (Alan et al., 2015). Consequently, wholesale distribution of antimicrobials to farmers is prohibited. However, the sales of large amounts of antimicrobials to farms still exists. These issues contribute to the excessive provision of antimicrobials to farms. According to the Drug Act B.E. 2510 (1967), APIs must only be sold by licensed importers and manufacturers who can then distribute the substances to manufacturers for the purposes of producing finished products (The drug Act, 1967). According to the 2015 Animal Feed Quality Control Act, such direct use of APIs in animal feed is prohibited (Animal Feed Quality Control Act, 2015). However, there exists a lack of monitoring and tracking of APIs and inadequate inspections at the drug distributorships and among retailers. Consequently, some APIs are being directly administered to animals in feed on farms. In line with previous reports, many farmers illegally mixed APIs into animal feed, probably

as a cost-saving measure (Sommanustweechai et al., 2018). These issues have likely boosted the irrational antimicrobial use on farms.

Another of the main factors revealed in this study was the lack of control of antimicrobial use and the use of feed that had been medicated with APIs on farms. The relevant legislation and regulation exist to control pharmaceutical activities and to protect the public and the health of animals in Thailand. These policies include the Act B.E. 2510 (1967) and its five amendments, in which the control of the pre- and post-marketing of veterinary drugs/biologics is stipulated (The drug Act, 1967). Additionally, the treatment and control of diseases on farms by farm veterinary consultants must comply with the Code of Practice for Control of the Use of Veterinary Drugs (TAS 9032-2009) (ACFS, 2009). Besides, medicated feed is regulated under the 2015 Animal Feed Quality Control Act (Animal Feed Quality Control Act, 2015). However, irrational antimicrobial use that occurs on farms has continued due to weak, improper or ineffective enforcement of the existing legislation and regulation. This conclusion is similar to those of previous reports that have been published in Ethiopia (Suleman et al., 2016). Most of the participants believe that the TAS 9032-2009 stipulates the supervisory veterinary drug use on farms; however, all farms did comply with this code. The notification of the livestock farm standard was issued to enforce measures related to farm management in order to produce safe and hygienic animal products for consumers under the responsibility of the DLD. To gain livestock farm standard accreditation, each farm must implement good agricultural practices following the standard operating procedure (SOP) for farmers and have a DLD-registered farm veterinarian on site that is responsible for the supervision of the animals' health and to oversee pharmaceutical prescriptions (ACFS, 2003; 2008). Although, farms are required to obtain standard farm accreditation from the DLD, the inappropriate use of antimicrobials on farms persists. Because the notification of the livestock farm standard is voluntary, some farms that have obtained registration have not strictly followed the SOP for farmers. Antimicrobial usage on registered farms must follow guidelines set by DLD-registered farm veterinarians; however, insufficient and poor veterinary services are common, especially on non-registered and small-scale farms. However, contract farmers must comply with contract companies' policies or rules and they must obtain farm registration approval from the DLD. Accordingly, contract farming continues to implement more appropriate antimicrobial use on contract farms than on other farms. With regard to APIs, they must be distributed to manufacturers for the production of finished products and their direct use in animal feed is prohibited (Sommanustweechai et al., 2018; The drug Act, 1967). However, a lack of monitoring and tracking, inadequate inspections at the drug distributorships and weak enforcement of legislation and regulation on farms still remain. Hence, some APIs were being used directly on farms in line with previous studies (Sommanustweechai et al., 2018; Vincent ter, 2017), especially on non-registered farms and small-scale independent farms, which were known to have insufficient and poor veterinary services. The existing laws and regulations prohibit illegal antimicrobials being mixed into medicated feed on farms (Animal Feed Quality Control Act, 2015.). In Thailand, medicated feed on farms should be supplied by feed mills or are prepared by feed mixers on farms. Feed mills must have obtained GMP and HACCP certification in order to sustain good production

quality; however, the farmers who produced their own medicated feed using a feed mixer did not implement measures of quality control (Sommanustweechai et al., 2018). This outcome would include the feed mixers belonging to the cooperatives that produce medicated feed and dispense it to farm members. Therefore, feed mixers on both farms and cooperatives must be strictly controlled in order to contribute to the rational antimicrobial use on farms. Consequently, the 2018 notification of the Ministry of Agriculture and Cooperatives was announced in the Royal Gazette. This will come into force on February 26, 2020. These notifications prohibit illegal antimicrobials and APIs being mixed into medicated feed on farms, and state that feed mixers must have obtained certification for proper production quality including the control of medicated feed for sale and distribution (Notification of the Ministry of Agriculture and Cooperatives, 2018).

The Thai Cabinet has announced its plan to achieve the goal of reducing antimicrobial consumption by 30% in veterinary medicines by 2021 (FAO, 2017). This study was conducted to find solutions for appropriate use of antimicrobials on pig and layer farms. In a multivariate logistic regression analysis, it was revealed that contract farms have fair to good practices at about 43 times (95%CI: 12.87–143.31, $P = 0.00001$) compared to those on non-contract farms. This result indicated that antimicrobial usage on contract farms had more rational use than on other farms. Contract farms can access antimicrobials and feed only from contract companies, while the treatment and prevention of diseases are also under the supervision of veterinarian consultants who have been registered by the DLD authority and who must follow the company's policies and rules. Contract farms must be registered by the DLD authority and antimicrobial usage on farms must comply with the Code of Practice for Control of the Use of Veterinary Drugs (TAS 9032-2009) (ACFS, 2009). In addition, self-medicated feed and direct use of APIs on farms and access to antimicrobials by wholesale distribution is not allowed on contract farms. In turn, antimicrobial use on non-contract farms, such as independent farms and non-registered farms, occur because antimicrobials are easily accessed and obtained over-the-counter. Most small-scale independent farmers cannot afford veterinarian consultants for their farms. They illegally administer antimicrobials on the farms by self-medication. Additionally, improper or ineffective enforcement of the existing legislation and regulations on non-contract farms remains a problem. Similarly, the cooperative's policies and rules involving antimicrobial usage is not strictly enforced by its members. Therefore the cooperative member farmers were allowed to use antimicrobials and feed from other sources when it was necessary. These issues have boosted irrational antimicrobial use on these farms. Regarding specific farm sites, pig and layer farms situated in Chon Buri Province have better practices than those in Chiang Mai-Lamphun Province by about 19 times (95%CI: 5.55–65.82, $P = 0.00001$). This is because most farms in Chon Buri Province were medium to large-scale farms with fully-integrated systems and the farms have obtained appropriate farm registration from the DLD. However, in previous studies, farmers at both sites had low levels of knowledge, poor attitudes, and employed poor practices in the use of antimicrobials on farms (Nuangmek et al., 2018b). These issues have contributed to the irrational antimicrobial use on farms.

A correlation among overall knowledge, attitudes and practices (KAP) toward antimicrobial usage on pig and layer farms was observed (Table 7). A weak positive correlation between knowledge and attitudes was noted pertain-

ing to these statements ($r = 0.1555$, $n = 251$, $P = 0.014$). However, there was no correlation between knowledge and practices ($r = 0.054$, $n = 251$, $P = 0.398$) and between attitudes and practices ($r = 0.083$, $n = 126$, $P = 0.189$). Our study indicated that there was no direct correlation of pig and layer farmers when considering knowledge, attitude or perception and the farmers' behaviour toward antimicrobial use. Likewise, this finding is in accordance with those of previous studies in many countries like Britain and Holland (Davey et al., 2002; Stille et al., 2008). The education of target groups alone may not necessarily improve the misuse and abuse of antimicrobials in the country (McNulty et al., 2007). In order to avoid irrational antimicrobial usage, clear guidelines should be provided for antimicrobial use on farms and the implementation of restrictive policies on antimicrobial prescriptions should be developed. Additionally, in order to maintain rational antimicrobial use on farms, strict enforcement of laws and regulations must be considered.

CONCLUSION

This study revealed that the irrational antimicrobial usage on farms is influenced by the large number of licensed retail pharmacies which can sell antimicrobials over-the-counter. Additionally, antimicrobials are over-prescribed as a consequence of financial incentives that are offered by pharmaceutical companies, insufficient and poor veterinary services, inadequate monitoring, weak systems employed for tracking and inspecting drugs along the supply chain, inadequate or weak enforcement of the regulations on veterinary pharmaceutical medicines, and overall weak pharmaco-vigilance. These issues contribute to excessive antimicrobial use and have boosted the irrational antimicrobial use on farms, especially on non-registered and small-scale independent farms. In order to curtail irrational antimicrobial usage, clear guidelines must be provided for antimicrobial use on farms and the implementation of restrictive policies on antimicrobial prescriptions should be developed. Importantly, stringent enforcement of laws and regulations and effective monitoring, tracking and inspection of using antimicrobial agents along the supply chains must be implemented strictly.

LIST of ABBREVIATIONS

FGDs: Focus group discussions; OR: Odd ratio; RPLO: Regional and provincial livestock officers; FVC: farm veterinary consultant; COM: Cooperative manager; CF: Contract farmers; COF: Cooperative farmer; IF: Independent farmer; APIs: Active pharmaceutical ingredients; KAP: Knowledge, attitude and practice; FDA: Thai Food and Drug Administration; DLD: Department Livestock Development; GMP: Good manufacturing practice; HACCP: Hazard analysis critical control point; SOP: Standard operating procedure.

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REFERENCES

- ACFS; National bureau of agricultural commodity and food standards. 2003. Ministry of agriculture and cooperatives. Thai agricultural standard: Good agricultural practice for layer farm, May B.E. 2546 (May 2003).
- ACFS; National bureau of agricultural commodity and food standards. 2008. Ministry of agriculture and cooperatives. Thai agricultural standard (TAS 6403-2009) B.E.2551 (2008): Good agricultural practice for pig farm; 28 December B.E. 2551 (2008).
- ACFS; National bureau of agricultural commodity and food standards. 2009. Thai Agricultural Standard TAS 9032-2009. Code of Practice for Control of the use of Veterinary Drugs: National Bureau of Agricultural Commodity and Food Standards, Ministry of Agriculture and Cooperatives. The Royal Gazette Vol.126 Special Section 187D.
- Alan, A., Siraprapha, R., Areeya, P. 2015. Distribution and marketing of drugs in Thailand. Thomson (pp. 383–98).UK: Reuters (Professional) UK Limited.
- Alhojailan, M.I., 2012. Thematic analysis: a critical review of its process and evaluation. WEI International European Academic Conference Proceedings.<https://www.westeastinstitute.com/wp-content/uploads/2012/10/ZG12-191-Mohammed-Ibrahim-Alhojailan-Full-Paper.pdf>. Accessed March 15, 2015.
- AHPA; Animal Health Products Association. 2013. AHPA Market information. A T Printing Co., Samut Sakhon, Thailand. 361 p.
- Animal Feed Quality Control Act, B.E. 2558. 2015. Published in the Government Gazette Thailand. (5 march 2015) volume 132, section 15 kor.(in Thai)
- Boonyasiri, A., Tangkoskul, T., Seenama, C., Saiyarin, J., Tiengrim, S., Thamlikitkul, V. 2014. Prevalence of antibiotic resistant bacteria in healthy adults, foods, food animals, and the environment in selected areas in Thailand. *Pathog.Glob.Health.* 108, 235–245.
- CDC; Centers for Disease Control and Prevention. 2014. Epi Info™ 7. CDC. Available at: <http://wwwn.cdc.gov/epiinfo/7/index.htm>. Accessed September 22, 2015.
- Davey, P., Pagliari, C., Hayes, A. 2002. The patient's role in the spread and control of bacterial resistance to antibiotics. *Clin. Microbiol. Infect.* 8, 43–68.
- DLD; Department of livestock development. 2013. Thai livestock farmer database system. Information Technology Center; <http://ict.dld.go.th/th2/index.php/th/report/276-report-thailand-livestock/reportsurvey56/480-report-survey56-2>. Accessed September 22, 2015.
- FAO. 2014. Rationale for Size Category. FAO. Available at: <http://www.fao.org/3/a-x6170e/x6170e0t.htm>. Accessed September 22, 2015.
- FAO. 2017. Thailand's National Strategic Plan on Antimicrobial Resistance 2017-2021. Available at: <http://www.fao.org/faolex/results/details/en/c/LEX-FAOC169834/>. Accessed December 22, 2017.
- Food and Drug Administration. 2017. Medicine registration. Nonthaburi. Available at: <http://www.fda.moph.go.th/sites/drug/Shared%20Documents/Statistic/registration55-59.pdf>. Accessed March 15, 2018.

- Friedman, D.B., Kanwat, C.P., Headrick, M.L., Patterson, N.J., Neely, J.C., Smith, L.U. 2007. Importance of prudent antibiotic use on dairy farms in South Carolina: a pilot project on farmers' knowledge, attitudes and practices. *Zoonoses Public Health*. 54, 366–375.
- Gandra, S., Barter, D.M., Laxminarayan, R. 2014. Economic burden of antibiotic resistance: how much do we really know? *Clin. Microbiol. Infect.* 20, 973–980.
- Garforth, C.J., Bailey, A.P., Tranter, R.B. 2013. Farmers' attitudes to disease risk management in England: a comparative analysis of sheep and pig farmers. *Prev. Vet. Med.* 1.10, 456–466.
- Hinkle, D.E., Weirsham W., Jurs, S.G. 2003. *Applied statistics for the behavioral sciences: Fifth edition.* Houghton Mifflin.
- Iversen, T., Luras, H. 2000. Economic motives and professional norms: the case of general medical practice. *J. Econ. Behav. Organ.* 43, 447–470.
- Jitraknatee, A. 2011. Antibiotic values. In: Kiatying-Angsulee, N., Kessomboon, N., Maleewong, U., eds. *Situation report on drug system 2010: antimicrobial resistance and antibiotic use.* 21–25.
- Kumaranayake, L., Mujinja, P., Hongoro, C., Mpembeni, R. 2000. How do countries regulate the health sector? Evidence from Tanzania and Zimbabwe. *Health Policy Plan.* 15, 357–367.
- Marshall, C., Rossman, G.B. 2006. *Designing qualitative research.* 2nd ed. Thousand Oaks, Calif.: Sage Publications; p. 154–63.
- McNulty, C.A., Boyle, P., Nichols, T., Clappison, P., Davey, P. 2007. Don't wear me out—the public's knowledge of and attitudes to antibiotic use. *J. Antimicrob. Chemother.* 59, 727–738.
- Mehta, C.R., Patel, N.R. 1996. Exact test. In: *SPSS exact test 7.0 for windows.* Chicago, IL: SPSS Inc.
- Metlay, J.P., Powers, J.H., Dudley, M.N., Christiansen, K., Finch, R.G. 2006. On behalf of the second colloquium of the international forum on antibiotic resistance, antimicrobial drug resistance, regulation and research. *Emerg. Infect. Dis.* 12, 183–190.
- Morgan, D.J., Okeke, I.N., Laxminarayan, R., Perencevich, E.N., Weisenberg, S. 2011. Non-prescription antimicrobial use worldwide: a systematic review. *Lancet. Infect. Dis.* 11, 692–701.
- Notification of the Ministry of Agriculture and Cooperatives. 2018. On prohibited medicated feed for producing, importing, sale, and administration, Published in the Government Gazette Thailand (26 February B.E. 2561); No. 135, extra Part 73.
- Nuangmek, A., Rojanasthien, S., Chotinun, S., Yansakul, P., Tadee, P., Thamlikitkul, V., Tansakul, N., Patchanee, P. 2018a. Antimicrobial resistance in ESBL-producing *Escherichia coli* isolated from layer and pig farms in Thailand. *Acta. Sci. Vet.* 46, 1538.
- Nuangmek, A., Rojanasthien, S., Patchanee, P., Yano, T., Yansakul, P., Chotinun, S., Tadee, P. 2018b. Knowledge, attitudes and practices toward antimicrobial usage: a cross-sectional study of layer and pig farm owners/managers in Chiang Mai, Lamphun, and Chonburi provinces, Thailand, May 2014 to February 2016. *Korean J. Vet. Res.* 58, 17–25.
- Ocan, M., Obuku, E.A., Bwanga, F., Akena, D., Richard, S., Ogwal-Okeng, J., Obua, C. 2015. Household antimicrobial self-medication: a systematic review and metaanalysis of the burden, risk factors and outcomes in developing countries. *BMC Public Health.* 15, 742.
- Padungtod, P., Kaneene, J.B., Hanson, R., Morita, Y., Boonmar, S. 2006. Antimicrobial resistance in *Campylobacter* isolated from food animals and humans in northern Thailand. *FEMS Immunol. Med. Microbiol.* 47, 217–225.

- Sommanustweechai, A., Chanvatik, S., Sermsinsiri, V., Sivilaikul, S., Patcharanarumol, W., Yeung, S., Tangcharoensathien, V. 2018. Antibiotic distribution channels in Thailand: results of key-informant interviews, reviews of drug regulations and database searches. *Bull World Health Organ.* 96, 101–109.
- Stille, C.J., Rifas-Shiman, S.L., Kleinman, K., Kotch, J.B., Finkelstein, J.A. 2008. Physician responses to a community-level trial promoting judicious antibiotic use. *Ann. Fam. Med.* 6, 206–212.
- Suleman, S., Woliyi, A., Woldemichael, K., Tushune, K., Duchateau, L., Degroote, A., Vancauwenberghe, R., Bracke, N., De Spiegeleer, B. 2016. Pharmaceutical regulatory framework in Ethiopia: a critical evaluation of its legal basis and implementation. *Ethiop. J. Health Sci.* 26, 259–276.
- Teerawattananon, Y., Tangcharoensathien, V., Tantivess, S., Mills, A. 2003. Health sector regulation in Thailand: recent progress and the future agenda. *Health Policy.* 63, 323–338.
- The drug Act, B.E. 2510. 1967. [Internet]. Thailand: Thailaws.com. Available at: http://www.thailaws.com/law/t_laws/tlaw0071_1.pdf. Accessed March 19, 2018. (in Thai)
- Vincent, B. 2017. Antimicrobial reduction in the spotlight at VIV Asia. *Pig Progress*; Available at: <http://www.pigprogress.net/Health/Articles/2017/4/Antimicrobial-reduction-in-the-spotlight-at-VIV-Asia-115220E/>. Accessed March 19, 2018.
- WHO. 2001. Global Strategy for Containment of Antimicrobial Resistance. Geneva, Switzerland: World Health Organisation. Available at: http://www.who.int/drugresistance/WHO_Global_Strategy_English.pdf. Accessed September 22, 2015.
- WHO. 2010. Medicines: rational use of medicines. Geneva, Switzerland: World Health Organisation. Available at: <http://www.who.int/mediacentre/factsheets/fs338/en/index.html>. Accessed March 15, 2018.
- WHO. 2015. Global Action Plan on Antimicrobial Resistance. World Health Organization, Geneva. Available at: http://apps.who.int/iris/bitstream/10665/193736/1/9789241509763_eng.pdf?ua=1. Accessed March 15, 2018.
- Willock, J., Deary, I.J., McGregor, M.M., Sutherland, A., Edwards-Jones, G., Morgan, O., Dent, B., Grieve, R., Gibson, G., Austin, E. 1999. Farmers' attitudes, objectives, behaviors, and personality traits: The Edinburgh study of decision making on farms. *J. Vocat. Behav.* 54, 5–36.

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