Biosecurity and antimicrobial use in pig production

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1 SUMMARY

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Tiivistelmä - Referat – Abstract

Antimicrobial use (AMU) has led to a development of antimicrobial resistant bacteria that complicate treatment of infectious diseases in animals and humans. Majority of veterinary AMU occurs in pigs, which is known to contribute to the development of antimicrobial resistance (AMR). Especially in large pork producing countries, the majority of antimicrobials are administered as group treatments for pigs that enhances AMR development. Biosecurity means measures that prevent pathogen transmission to a herd (external biosecurity) and within a herd (internal biosecurity). Consequently, when there is a global demand to decrease AMU, biosecurity has been introduced as an alternative to that. In Finland, veterinary AMU is one of the lowest level in the EU and group treatments are not preferred. However, Finnish pig herds have been small-sized in general and disease situation has been relatively good thorough the country thus there has been no need to invest in biosecurity. Herd size is increasing and therefore farmers must adopt alternative methods to decrease the need to use antimicrobials. This study aimed to investigate current biosecurity status of Finnish pig herds and their AMU, and study associations between them. Study population consisted of ten farrow-to-finish herds whose biosecurity status was evaluated by using an international Biocheck.UGent scoring system. AMU of individual herds was collected from national Sikava register covering around 90 % of Finnish pig herds. It is therefore the best available source for AMU data and makes comparison between herds possible. Furthermore, detailed calculation of AMU at different production stages was done.

The biosecurity scores of study herds varied considerably. Mean external biosecurity score was higher than internal biosecurity score (Mean ± SD; 69 ± 1.2 vs. 44 ± 5.3, $P < 0.001$) and better in large herds compared to small herds (LSmeans ± SE; 72 ± 1.3 vs. 66 ± 1.3, $P < 0.05$). AMU tended to increase with decreasing biosecurity according to the study hypothesis. AMU was highest in suckling piglets but there were no significant correlations between the total biosecurity scores and AMU at any age groups studied. Regardless of the small sample size of this study, current findings support other studies indicating the potential to improve biosecurity of Finnish herds in order to avoid increase in AMU.

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3 INTRODUCTION

A concern for excessive use of antimicrobials (AMU) as growth promoters rose up already in the 1960s (Swann et al. 1969). European Commission totally banned the use of antimicrobials as growth promoters in 2006 (IP/05/1687). However, they are still thought to be used to improve productivity at animal facilities, which threatens the efficacy of currently used antimicrobials (Callens et al. 2012). In Finland, antimicrobials used for growth promotion in animals has been forbidden by the national legislation since 1996 (Laki eläinten lääkitsemisestä 387/2014 8§). In the European Union (EU), majority of veterinary antimicrobials are prescribed for the treatment of pigs (EMA 2019). Antimicrobials have often been administered to pigs unnecessarily or misused (Timmerman et al. 2006, Callens et al. 2012) particularly in oral group treatments due to their easier application (Callens et al. 2012, Filippitzi et al. 2014) and in some cases due to their lower cost (Jensen et al. 2011, Filippitzi et al. 2014). Guidelines for prudent use of antimicrobials have been shown to be a tool to reduce prescription of antimicrobials among veterinarians both in companion animals (Jessen et al. 2017) and farm animals (Ungemach et al. 2006). Over the last few years, such guidelines have been developed at the EU (2015/C 299/04) and globally (WHO 2015). In Finland, first national guidelines about prudent AMU were published already in 1996 by the Ministry of Agriculture and since that, last updated version has been published by the Finnish Food Safety Authority (Evira) in 2016 (Evira 2016).

Detailed antimicrobial consumption data can be used to detect inappropriate AMU (Timmerman et al. 2006), to identify underlying risk factors for the emergence of antimicrobial resistance (Catry et al. 2003, Dewulf et al. 2007, JIACRA 2017). AMU in animals in Finland is at fourth lowest level in the EU and covers only 0.1 percent of sold antimicrobials among 31 EU countries measured in tons of active antimicrobial agent (EMA 2019). In 2019, a Finnish health care register for swine farmers (Sikava) restricted the use of fluoroquinolones and 3rd generation cephalosporines on pig farms belonging to a national classification level (Sikava 2019). Since that, those antimicrobials have been allowed to use only according to a separate permission asked from Sikava veterinary advisor (Sikava 2019). Production of Finnish pig farms have increased six-fold within two decades and will increase further whereas the number of farms decreases (MTK 2017). It has raised concerns that the trend towards antimicrobial group treatments has or may become more common also in our country. Number of pigs in different European countries in represented in Figure 1.

In Finland, the health status of pig farms is generally good regarding infectious diseases, as the whole country has been free from many severe infectious diseases including african swine fever (ASF), Aujeszky´s disease (PRV), brucellosis (occurred only in wild boar) and porcine reproductive and respiratory syndrome (PRRS) (WAHIS). Therefore, farmers may not consider disease preventive measures, namely biosecurity, to be important (Sahlström et al. 2014). Similar observations have been made also in other European countries and among other farm animals, such as cattle and sheep (Filippitzi et al. 2014, Dewulf & Van Immerseel 2018). An early definition of a term ´biosecurity´ was introduced in scientific literature by Amass & Clark in 1999. Literally, biosecurity means all the measures applied on farms to prevent infectious agents' transmission between farms (external biosecurity) and between animals within a herd (internal biosecurity) (Amass & Clark 1999). Global animal trade and movement of people promote disease transmission between countries and therefore it is important to investigate biosecurity routines in different regions and populations. Previous studies have been shown that intensity of livestock production, disease occurrence and traditions as well as biosecurity routines differ between countries (Casal et al. 2007, Ribbens et al. 2008, Nöremark et al. 2010, Sahlström et al. 2014). However, comprehensive insights about the biosecurity routines, and how the routines vary among different types of farms, can help identify factors related to high risk for disease transmission (Nöremark et al. 2010, Sahlström et al. 2014).

Many studies have indicated, that improvement of farm biosecurity routines can lead to reduced AMU (Laanen et al. 2013, Postma et al. 2016a, Postma et al. 2016b, Raasch et al. 2018). That information is useful for developing alternatives to maintain a good animal health and welfare instead of unnecessary AMU (Postma et al. 2015, Dewulf & Van Immerseel 2018). Reduction of AMU is well-founded hence all and especially the routine-like use of antimicrobials can lead to the development and selection of antimicrobial resistance (AMR) in bacteria in animals and humans (WHO 2001, Bywater, 2004, JIACRA 2017). Potential threats related to AMR was pointed out already in the late 1990s, when The World Health Assembly (WHA) encouraged to preventive practices for the spread of infections and reduction of AMU in food animal production (WHO 2001). Pig farming has been identified as one of the agricultural sectors in which the use of antimicrobials drives the antimicrobial resistance (Chantziaras et al. 2014, Filippitzi et al. 2014). Diverged resistance rates in bacteria isolated from pigs have been linked to different housing conditions (Langlois et al. 1988) as well as to different production stages (Langlois et al. 1988, Dewulf et al. 2007, Burow et al. 2019) which indicate the multifactorial nature of AMR. In this licentiate thesis, antimicrobial resistance will not be covered in detail but should be kept in mind because of its importance and close connection to the topic of this work.

This licentiate thesis consists of a literature review part including two topics: firstly, biosecurity is described thoroughly and secondly, an overview about AMU in pig production around EU according to the available scientific literature is given. The research part of this licentiate thesis aimed to investigate biosecurity statuses and AMU in 10 Finnish pig herds and to look for possible associations between biosecurity and AMU. Moreover, associations between herd size and biosecurity status, different biosecurity sub-categories and AMU between different age groups were studied. Biosecurity was evaluated by using web-based Biocheck.UGent™ questionnaire and AMU data was collected from the national Sikava register. At the moment of biosecurity evaluations, such a tool had not been in general use among veterinarians and other farm advisors, but it has been recently included as a part of Finnish pig health care system. It was hypothesized that in farms with low biosecurity status AMU is generally higher compared to farms with better implemented biosecurity routines. Another hypothesis was that AMU differs between farms as well as within farms and the highest use occurs at early phases of production cycle. It was also suggested that herd size contributes to biosecurity and AMU. Consequently, I will focus on highlighting the most important changes in biosecurity routines that should be applied on farms in the future and those that have potential in reducing AMU according to current scientific literature.

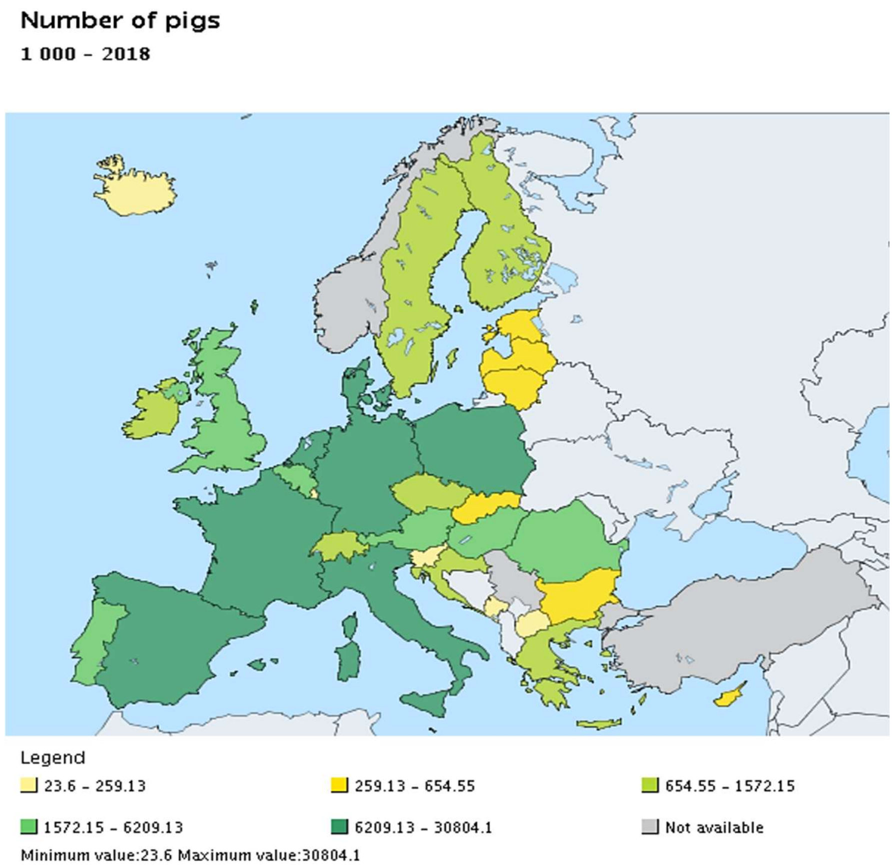

Figure 1. Number of pigs in the EU 2018 (Figure created according to Eurostat database, 2018).

4 LITERATURE REVIEW: BIOSECURITY AND ANTIMICROBIAL USE IN PIG PRODUCTION

4.1 Biosecurity

In animal production, the term biosecurity means protection of a herd from the transmission of infectious agents (Amass & Clark 1999). In practice, biosecurity measures prevent indirect disease transmission between farms (external biosecurity) and both direct and indirect disease transmission between animals within a herd (internal biosecurity) (Amass & Clark 1999, Casal et al. 2007, Dewulf & Van Immerseel 2018). Primarily, both external and internal biosecurity measures aim to maintain a microbial exposure of animals below the infective dose of the pathogenic microbe (Wierup 2000). In practice it is done by identifying the potential sources of infectious agents and based on their relative risk and impact on farm, restricting their potential sources to a minimum (Amass 2005, Cox et al. 2016). General biosecurity measures should be applied farm-specifically because every farm is unique in terms of their risks and prevailing disease pressure as well as susceptibility of a herd (Amass 2005). Moreover, it is in equal importance to monitor and modify applied biosecurity measures in continuously changing situations to maintain a good biosecurity status (Amass 2005, Dewulf & Van Immerseel 2018).

Biosecurity measures have not been implemented properly in many large pork-producing countries (Casal et al. 2007, Raash et al. 2018) nor in Finland (Sahlström et al. 2014). In general, farm size and commercial mode of action influence applied biosecurity practices (Ribbens et al. 2008, Nöremark et al. 2010, Simon-Grifé et al. 2013, Sahlström et al. 2014, Kuster et al. 2015, Postma et al. 2016a). Farmers' lack of knowledge about disease preventive measures and principles of disease transmission can explain observed defects in biosecurity routines (Nöremark et al. 2010). Moreover, differences in production types, disease prevalence and available resources influence applied biosecurity practices (Kuster et al. 2015) as well as farmers´ perceived importance of biosecurity (Casal et al. 2007). Rojo-Gimeno et al. (2016) showed that investments in biosecurity on farms did not jeopardize the farm income and actually resulted in a better profit for the production. However, antimicrobials are often used rather than equipping sufficient biosecurity measures to cover insufficient management (Filippitzi et al. 2014, Postma et al. 2015). Farmers have been shown to be unfamiliar with alternative solutions of reducing their AMU (Postma et al. 2017), which can explain such practices.

Implementation of general biosecurity measures by farmers can be optimized through a combination of nationally legislated and voluntary on-farm measures in European countries (Kuster et al. 2015). Biosecurity evaluation should be based on scientific and preferably measurable results about transmission of infectious diseases (Laanen et al. 2013, Dewulf & Van Immerseel 2018). The University of Gent in Belgium has developed a useful tool for biosecurity evaluation, namely Biocheck.UGent™ scoring system that covers broadly various aspects of measures related to transmission of infectious agents. It is nowadays available for pig, poultry and cattle farms (Biocheck.UGent, official website). The system consists of 109 questions that are divided into six external and six internal biosecurity sub-categories (Laanen et al. 2013). Scores of each question are weighed based on risk-evaluation and transmission patterns of infectious diseases (Laanen et al. 2013). Biosecurity sub-categories and their weights are listed on Table 1. Following chapters in this licentiate thesis will introduce thoroughly specific external and internal biosecurity measures taken into account their importance in disease transmission.

Table 1. Biosecurity sub-categories according to Dewulf & Van Immerseel (2018) ordered by the weight of each sub-category according to Laanen et al. (2013).

EXTERNAL BIOSECURITY	WEIGHT	INTERNAL BIOSECURITY	WEIGHT
Purchase of animals and semen	24	Compartmentalization and equipment use	28
Transport of animals, removal of manure and carcasses	23	Cleaning and disinfection	20
Personnel and visitors	17	Measures related to farrowing and suckling period	14
Feed, water and equipment supply	15	Measures related to weaning period	14
Vermin and bird control	11	Measures related to finishing period	14
Environment and region	10	Disease management	10
Total	100	Total	100

4.2 External biosecurity

Farmers should constantly pay attention to their animals' health status and be aware of possibly occurring national, as well as exotic external threats (Boklund et al. 2004). Biosecurity measures related to preventing pathogens entering farm premises and further to a herd form a basis of external biosecurity (Amass & Clark 1999, Casal et al. 2007). In general, external biosecurity is better implemented on farms than internal biosecurity (Laanen et al. 2013, Backhans et al. 2015, Postma et al. 2016a, Postma et al. 2016b, Filippitzi et al. 2017, Postma et al. 2017). It has been speculated that it is easier for a farmer to adopt external biosecurity practices mostly concerning on restriction of movements of animals and people, compared to alterations of their own routine management (Laanen et al. 2013, Postma et al. 2016a). This was proved in a study by Simon-Grifé et al. (2013), showing that farmers highlighted restricting the entry of people and vehicles as the most important biosecurity measure in preventing disease transmission to a pig farm. Moreover, transport of living animals and removal of carcasses and manure have been identified the most significant risks for disease transmission from external sources (Laanen et al. 2013). Despite a good situation for disease control in Finland (Sahlström et al., 2014), the risk of spread to Finland cannot be precluded.

4.2.1 Purchase of animals and semen

Contacts between livestock holdings are central for the spread of infectious diseases (Nöremark et al. 2010, Dewulf & Van Immerseel 2018). The efficacy of transmission depends on the type and frequency of contacts, as well as implemented on-farm preventive measures (Nöremark et al. 2010, Dewulf & Van Immerseel 2018). The study by Filippitzi et al. (2017) showed that among six large pig producing European countries, purchasing policy was in general the best-implemented biosecurity measure, even though some country-specific differences existed.

Introduction of new animals into a herd implies one of the highest risks for the entry of new pathogens to the whole farm and farmers should pay attention primarily to the source of new animals (Casal et al. 2007). New animals are introduced continuously especially to finishing units (Hybschmann et al. 2011). It is important to buy animals from farms with at least equal, but preferably higher health status than own farm (Casal et al. 2007) to take into account the possibility that purchased animals carry novel infectious agents that are not present on a recipient farm. To minimize the possibility of introduction of a new infection, purchased (breeding) animals should be under a quarantine instead of putting them straight to the herd (Casal et al. 2007). The quarantine period also allows those animals then to cope with a new environment (Dewulf & Van Immerseel 2018). Not only live animals, but also boar semen can be a source of infectious diseases (Amass &

Clark 1999, Filippitzi et al. 2017). Know semen-transmitted disease include brucellosis (*Brucella suis),* leptospirosis, classical swine fever (CSF), foot- and mouth -disease (FMD), porcine circovirus type 2 (PCV-2), parvovirus, PRRS, Aujeszky disease, swine vesicular disease (SVD) and transmissible gastroenteritis (TGE) (Amass & Clark 1999, Filippitzi et al. 2017).

In a recent multi-country investigation (Filippitzi et al. 2017), only 53 % of French farmers had stated that the health status of a farm of origin of purchased animals should be equal or higher and 61 % of the farms purchased breeding animals from several farms. In contrast, Danish farmers had generally a strict protocol for purchased animals due to the specific pathogen-free (SPF) concept, which had been adopted by 87% of the Danish farmers (Filippitzi et al. 2017). In Finland, Sikava, represents quite similar system compared to the Danish SPF-system. Sikava covers about 90 % of the Finnish pig farms (Ina Toppari, personal communication 2019) and five largest slaughterhouse companies are its members (Sikava 2017). The movement of weaner- and finishing pigs is market driven and coordinated largely by slaughterhouse companies. Therefore, owners of the weaner- and finishing units cannot affect the origin of farms of their animals. Otherwise, piglet-producing farms in Finland buy their gilts and breeding boars from separate breeding farms with more stringent biosecurity control. According to a study of Casal et al. (2007), among 167 farmers one fifth of them perceived quarantine as an important biosecurity measure. Nöremark et al. (2010) studied on-farm biosecurity routines in 518 Swedish livestock farms having pigs, cattle or sheep, and nearly half of the farmers introduced their new animals to the herd without a quarantine. However, the use of a quarantine was better implemented among pig farmers (Nöremark et al. 2010), which is also in line with the results from a Finnish study (Sahlström et al. 2014). A quarantine is widely used, especially in sow farms (Casal et al. 2007, Sahlström et al. 2014), whereas finishing farms rely primarily on all in - all out (AI-AO) procedures. Laanen et al. (2013) showed that well-managed purchasing policy is positively associated with a feed conversion rate (FCR) and daily weight gain of finishers, indicating a farm-economic benefit of such a practice.

4.2.2 Animal transport, removal of manure and carcasses and movement of people

An animal transport vehicle can act as a mechanical vector for transmission of pathogens (Amass & Clark 1999) and pathogens can also spread via removal of carcasses and manure (Dewulf & Van Immerseel 2018). Humans are potential mechanical vectors of several different pathogens, and therefore limiting the numbers of farm visitors to the necessary is reasonable (Dewulf & Van Immerseel 2018). It is recommended that transport vehicles are empty and thoroughly cleaned when arriving in the farm and a lorry driver is able to pick up a carcass storage without entering the farm premises (Dewulf & Van Immerseel 2018). Routine cleaning and disinfection of carcass storage should be implemented after carcass removal (Dewulf & Van Immerseel 2018). Moreover, carcasses should be always as a source of infectious material and wearing protective gloves while handling them is advisable (Dewulf & Van Immerseel 2018).

A Swiss study by Kuster et al. (2015) emphasized that measures related to animal movements are the most important and effective factors in preventing important infectious diseases including ASF, FMD, PRRS and enzootic pneumonia (EP) caused by *Mycoplasma hyopneumoniae*. In addition, Cox et al. (2016) investigated relationships between different biosecurity measures and the presence of EP, swine dysentery caused by *Brachyspira hyodysenteriae*, PRRS, and swine influenza in Canadian pig farms. They suggested that the most relevant measures associated with the prevalence of these diseases were procedures for admitting visiting vehicles, insufficient removal of feed residues and a proximity of other commercial pig farms (Cox et al. 2016). Nevertheless, the Swedish study in farrow-to-finish farms showed that a transport vehicle arrived empty on 50-60 % of the studied farms (Backhans et al. 2015). A more recent study of Filippitzi et al. (2017) based on Biocheck.UGent^{TM} data from 574 pig herds from six European countries showed that cleaning and disinfection of transport vehicles has room for improvement especially in Swedish farms. An explanation to it can be a relative good disease situation (Filippitzi et al. 2017) as well as quite low farm density in Sweden (see Figure 1). In the study by Backhans et al. (2015), a separate loading area was present only in 50 % of the studied farms. Similarly, Sahlström et al. (2014) showed that a separate loading area was present in 74 % farrow-to-finish farms, 59 % of sow farms and 25 % of finishing farms in Finland. Among 574 studied farms, 72.5 % did not clean the carcass storage after emptying (Filippitzi et al. 2017). Flippitizi et al. (2017) therefore suggested that regular cleaning and disinfection of carcass storage should be improved in all six EU countries studied, even though a separate carcass storage located in the dirty area of the farm was present in most farms.

In general, farmers have applied biosecurity measures related to farm visitors quite well and perceive them as important (Simon-Grifé et al. 2013). In a Danish study by Boklund et al. (2004) conducted on 116 finishing farms, the dressing room was commonly used and the number of farm visitors was generally low, e.g. 44.8 % of the farms had less than 10 visitors yearly. Visitors were taken into account in piglet producing farms in Spain hence all the farms provided boots and clothes for the visitors (Casal et al. 2007). Similar results were obtained in a Swedish study: 85 % of pig farms including all production types provided protective clothing for visitors (Nöremark et al. 2010). Moreover, among six EU countries studied the majority provided farm-specific overalls and boots for the visitors (Filippitzi et al. 2017). Instead, measures related to farmers' personal practices could be improved what comes to the use of a hygiene lock and washing hands when entering the pig house (Filippitzi et al. 2017). Showering before entering the stables seems to be a routine procedure in only the minority of farms with a very high biosecurity status as was shown by Ribbens et al. (2008). Nowadays it is also known that among all biosecurity measures, showering is not a fundamental issue when preventing the pathogen transmission to a farm (Jeroen Dewulf, personal communication 2017). A Finnish study (Sahlström et al. 2014), conducted in pig, cattle and sheep farms showed that hygiene locks were not present in most farms and there were also deficiencies in the use of protective clothing and boots. In Finland, shortcomings in biosecurity can be explained based on a lack of serious infectious diseases (Sahlström et al. 2014), or presumably due to farmers' lack of knowledge concerning different disease preventive measures as highlighted in many other studies (Nöremark et al. 2010, Simon-Grifé et al. 2013, Laanen et al. 2014, Sahlström et al. 2014, Visschers et al. 2015, Postma et al. 2017).

4.2.3 Feed, water and equipment

Contaminated feed and water as well as dirty equipment are potential mechanical vectors of diseases (Dewulf & Van Immerseel 2018). Indirect contamination of feed and water can occur via biological vectors like rodents and birds (Dewulf & Van Immerseel 2018). Feed contamination can occur at any stage during feed manufacturing (Dewulf & Van Immerseel 2018) and many fatal viruses are capable of surviving throughout the feed chain at least in experimental conditions (Dee et al. 2018). Drinking water hygiene is strongly linked to disease transmission between animals as well as transmission of zoonotic agents (Dewulf & Van Immerseel 2018). For example, *M. hyopneumoniae* survives in water up to 31 days (Amass & Clark 1999). Similarly, mineral contaminants originating primarily from industrial water sources can contaminate drinking water (Dewulf & Van Immerseel 2018). For example, fluorine and nitrites as well as heavy metals such as mercury and lead are potentially toxic substances for animals (Dewulf & Van Immerseel 2018). Especially heavy metals are hazardous because they can accumulate in liver, kidney and meat, and therefore pose a risk for human consumers too (Dewulf & Van Immerseel 2018). Moreover, when present in water, they can accumulate to drinkers and contribute bacterial biofilm formation (Dewulf & Van Immerseel 2018). Therefore, a regular water quality control as well as feed hygiene control is perceived important (Dewulf & Van Immerseel 2018).

Backhans et al. (2015) found serious deficiencies regarding to feed transports: 95 % of the Swedish farms allowed lorry drivers to use the clean road while filling up the silos. Similar observations were found also in Belgian, Danish, Dutch, and German pig farms (Filippitzi et al. 2017). Regular microbiological testing of water quality was poorly applied according to Filippitzi et al. (2017) in the six EU countries studied. In Swedish farms, too little attention was paid for equipment hygiene (Nöremark et al. 2010, Backhans et al. 2015, Filippitzi et al. 2017). Less than 10 % of the Swedish farms applied specific measures, i.e. a quarantine period, for newly purchased equipment (Backhans et al. 2015). According to Nöremark et al. (2010), 57 % out of 210 pig farms shared their equipment with other farmers, this practice occurring primarily in commercial farms with intensive production. More specifically, the most common equipment shared between farmers was related to the manure spread (Nöremark et al. 2010). In summary, the introduction of pathogens via daily goods is not well distinguished on farms even though it illustrates a relatively high biosecurity risk.

4.2.4 Control of other animals, insects and farm environment

Companion animals and wild animals can act as a vector for transmission of various diseases (Amass & Clark 1999, Filippitzi et al. 2017). Animal vectors can transmit a disease directly to a herd or indirectly to farm premises for example contaminating the feeding silos (birds, rodents) or water sources (dead wild animals) (Dewulf & Van Immerseel 2018). Measures for rodent control should not be depreciated, because they are risk factors transmitting zoonotic pathogens like *Salmonella* Typhimurium, *Salmonella* Enteritidis (for a review, see Backhans & Fellström 2012). In Finland, it is relevant to consider that *Bordetella bronchiseptica*, *Erysipelothrix rhusiopathiae*, *Haemophilus parasuis* (Glasser's disease), *Streptococcus suis,* PCV-2 and parvovirus and can be transmitted to the farm premises carried by vector animals as was demonstrated by Filippitzi et al. (2017). Additionally, it is known that insects can act as a vector for several bacterial and viral pig pathogens, including *B.bronchiseptica*, *Brachyspira hyodysenteriae, Brucella suis,* CSF, *Clostridium perfringens, Escherichia coli, Lawsonia intracellularis,* PCV-2, PRRSV, Aujeszky disease virus, *Salmonella* spp., *S. suis* and TGE virus (Filippitzi et al. 2017). Moreover, ticks of the genus *Ornithodorus* are known vectors for ASF (Guberti et al. 2019).

Avoiding contacts with wild animals has become an important issue in pig production, because of the risks imposed by the increasing number of domestic pigs and wild boars affected by ASF in many European countries and Asian countries (Guberti et al. 2019). Geographical barriers can indirectly restrict movements of wild boars (Kuster et al. 2015), but ASF virus can survive long periods in secretions and excretions of infected animals (Guberti et al. 2019). According to estimates made by Natural Resources Institute Finland (Luke) in January 2018, the size of Finnish wild boar population was 3155 individuals and the population size has increased by 23.6 percent compared to a previous year (Luke 2018). Therefore, ASF situation in Europe should be taken with a caution also in Finland.

In a Belgian study, dogs and cats had an access to the pig house, even though other strict management practices were implemented in the farm (Ribbens et al. 2008). Moreover, the restriction of companion animals to the pig house was deficient especially in small-sized commercial finishing herds (Ribbens et al. 2008). In a Spanish study by Casal et al. (2007), only 55 % of the farms had rodent control plans, but 71.5 % of them had nets in the windows to avoid the entrance of birds. Furthermore, insect control seems to be more uncommon compared with rodents and birds (Ribbens et al. 2008). For example, only one third of the farms in Spain had insect control plans (Casal et al. 2007).

Farm location and pig density around farm premises determines the risk of pathogen transmission between farms primarily via aerosols and vector animals including insects (Filippitzi et al. 2017). For example, *M. hyopneumoniae*, a causative agent for EP, can spread over three kilometers between farms (Amass & Clark, 1999). In Finland, the situation is different compared to other countries, as livestock population is sparsely distributed throughout the relatively large country (Sahlström et al. 2014). The highest farming densities are even less than 0.5 farms / km^2 including all cattle, pig, sheep and goat farms (Sahlström et al. 2014). Most of the pig farms are located in three primary areas in Western and Southwest Finland (Figure 2.). Only one municipality in that area can be considered dense (> 300 pigs / square kilometer within radius of 10 kilometers) according to a relative location of pig farms.

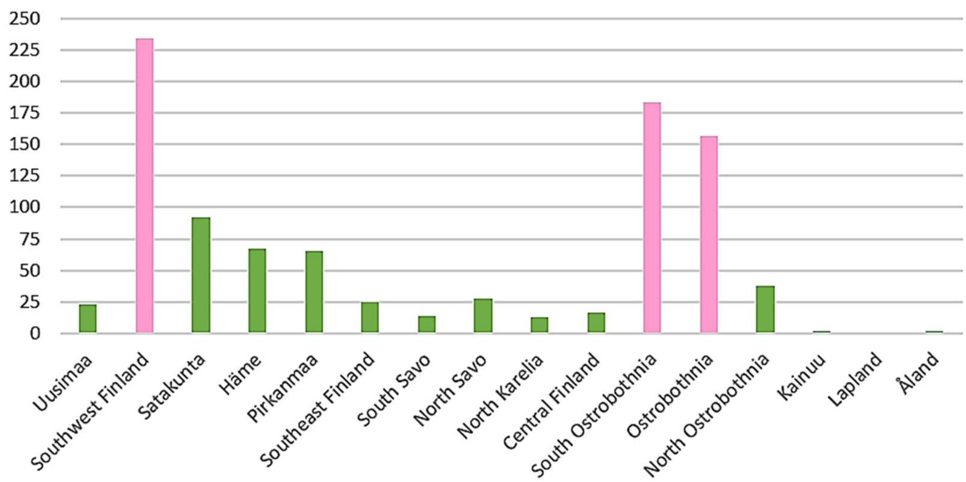

Figure 2. Number of pig farms during 2019 in different ELY-Centres in Finland. Pink columns represent top three regions with the highest number of pig farms (Luke, last update 1.4.2019).

4.3 Internal biosecurity

Internal biosecurity measures focus on restricting the spread of infectious diseases that are already present within a herd (Casal et al. 2007). Several studies have shown that internal biosecurity measures are implemented less strictly than external biosecurity measures (Laanen et al. 2013, Backhans et al. 2015, Postma et al. 2016a) and a similar observation has been recently done in Finland as well (Yun et al., unpublished results). Measures related to equipment use, compartmentalization, and cleaning and disinfection have been given the largest weight in biosecurity evaluation within internal biosecurity sub-categories (Laanen et al. 2013, Table 1). In other words, pathogen transmission within a herd occurs more likely via those routes (Laanen et al. 2013). A positive association was found between the number of sows and finishers and the external biosecurity score, but there were no association between the herd size and internal biosecurity score (Laanen et al. 2013). Animal transports are considered one of the highest risk posing factors in Biocheck.UGent™ scoring system that may explain the found association. Otherwise, Postma et al. (2016a) showed a strong positive association between external and internal biosecurity, which indicates that improvements in any biosecurity measure have a positive effect on farms' overall biosecurity status.

4.3.1 Compartmentalization of working lines and equipment at different production stages

It is generally known that younger animals are more susceptible to diseases (less immunocompetent) than the older ones. Farm management practices at early production stages like cross-fostering and handling of piglets during suckling period has been shown to effect on feed conversion rate (Laanen et al. 2013). Similar observations were made also in a study of Corrégé et al. (2011), who showed that a low rate of cross fostering resulted in less mortality and more pigs with optimum carcass weight at slaughter. Cross-fostering should be limited to one occasion and carry out within 48 h after birth to avoid pathogen transmission between litters (Dewulf & Van Immerseel 2018). In practice, we have observed in Finland that cross-fostering occurs even within a few hours after birth.

A correct working order starts routinely from the youngest age groups followed by pregnant sows and then adult pigs in order to prevent pathogen transmission between more and less susceptible age groups (Dewulf &Van Immerseel 2018). An important principle is to handle sick and quarantined animals after healthy ones and bring dead animals to the carcass storage in the end (Dewulf &Van Immerseel 2018). According to a Swedish study (Backhans et al. 2015), the best applied procedures in this subcategory are related to the working order and the use of age-group specific needles. On the other hand, cleaning of equipment, use of disinfection baths and washing hands between compartments were not well-managed and only 8 % of the Swedish farms required their staff to change clothing and footwear always while working in a pig house (Backhans et al. 2015). Moreover, Biocheck-results from Belgium, Denmark, France, Germany, the Netherlands and Sweden showed that separation of different age groups, maintenance of correct working order, and changing of overalls and boots were poorly implemented (Filippitzi et al. 2017).

The microbial load in a new department can be minimized by applying an AI-AO system that allows a thorough cleaning and disinfection between batches thus minimizing the risk of newly moved pigs getting sick at a new production stage (Wierup 2000). Corrégé et al. (2011) reported that dry period between bathes resulted in lower medication costs from weaning to slaughter. According to a Spanish study (Casal et al. 2007) conducted at 172 farms, AI-AO procedures were in use at 96 % of farrowing units and more infrequently at weaning units of which 53 % of the farms followed the procedure. A Swedish study by Backhans et al. (2015) reported that among 60 farrow-to-finish farms, 90 % followed AI-AO in the finishing unit at department level and 90 % in the weaning unit at the pen level. Conversely, Filippitzi et al. (2017) pointed out that AI-AO procedures have room for improvement in both in nursery and finishing units in Denmark.

4.3.2 Cleaning and disinfection

Cleaning and disinfection (C & D) protocols are essential to follow, because clinically heathy pigs can also transmit pathogens in their secretions and excretions, and thus contaminate their environment (Amass & Clark 1999). Effective C & D prevents both pathogen spread and persistence (Dewulf & Van Immerseel 2018) by decreasing the load of pathogens that have built up over time to the structures (Amass & Clark 1999). For example, *Salmonella* spp., *S. aureus* and *Enterococcus* spp. can survive for a long time in the environment (Luyckx et al. 2016). However, C & D -procedures are often poorly implemented in contrast to other biosecurity measures as have been shown in Finnish, Belgian, Danish, French, German Dutch and Swedish herds (Sahlström et al. 2014, Filippitzi et al. 2017).

Thorough C & D -procedure consists of seven steps: At first, all organic matter needs to be removed mechanically to ensure the effectiveness of further steps towards residual microbes (Dewulf & Van Immerseel 2018). In principle, disinfectants cannot act properly through the remnants of organic matter (Amass & Clark 1999). Secondly, the remaining organic material should be soaked and all visible dirt washed out with a high-pressure cleaning with water (Dewulf & Van Immerseel 2018). Structures are worth disinfecting only after a thorough drying period because of the dilution of disinfectants if added to wet pens (Dewulf & Van Immerseel 2018). One must keep in mind, that effectiveness of disinfectants against different types of micro-organisms is variable (Dewulf & Van Immerseel 2018) and at least bacteria are known to carry genes promoting resistance to disinfectants (Schwatz et al. 2001). Furthermore, to avoid the animal exposure to disinfectant residuals, another drying period is necessary (Dewulf & Van Immerseel 2018). Finally, surface samples should be taken to ensure the efficiency of C & D. (Dewulf & Van Immerseel 2018).

Despite the use of C & D programs, large amounts of faecal residuals have been detected in pen structures (Mannion et al. 2007) with the highest post-cleaning contamination rates in drinking nipples and pen floors (Mannion et al. 2007, Luyckx et al. 2016). Luyckx et al. (2016) studied bacterial residuals in nursery units during a 10-day-long vacancy period after C & D and the procedurehad no beneficial effect on the total bacterial load. The authors speculated that bacteria could have survived in the environment due to the presence of a resistance mechanism, via the protection of residual organic material or because of recontamination during a long vacancy period (Luyckx et al, 2016). The study underlined the importance of all biosecurity measures as a whole to minimize the risk of recontamination and thus secure the profitability of C & D (Luyckx et al, 2016). From a productivity parameter point of view, a study of Laanen et al. (2013) showed that C & D is positively associated with average daily gain (ADG) of pigs.

4.3.3 Disease management

Disease preventive methods should focus on minimizing the target animal populations' exposure to infectious doses of the pathogens (Wierup 2000). It is recommended to move sick animals to the sick pen (Wierup 2000) and sick animals should be always handled after the healthy ones (Dewulf &Van Immerseel 2018). A Swedish study by Backhans et al. (2015) showed that only a half of the 60 farrow-to-finish herds studied moved runts and sick animals to the sick pen and consistently handled sick animals after the healthy ones. Filippitzi et al. (2017) made also similar observations in Swedish and French herds according to the results acquired from Biocheck.UGent™-database. As already discussed in the section 4.2.2, handling of carcasses forms a part of disease management because they are a major source of infectious material for both pigs and humans (Dewulf &Van Immerseel 2018).

Regular diagnostics of infectious diseases supports proper disease management procedures (Dewulf &Van Immerseel 2018). For example, the prevalence of *M. hyopneumoniae*, *B. hyodysenteriae* and Sarcoptic mange are controlled regularly in Finland and freedom of those diseases is a prerequisite of farms belonging to the Sikava. Another effective way to prevent a transmission of an infectious disease is an eradication of the disease causative microbe (Wierup 2000). The aim of an eradication procedure is intended to completely exclude microbial exposure and such procedure should be based on the known epidemiology of the disease (Wierup 2000). Eradication programs can be conducted at the country level but also on a herd level (Wierup 2000).

4.3.3.1 Vaccinations

Vaccinations can be taken for additional health supporting actions and thus applying a vaccination program is advantageous for preventing infections in all production stages (Wierup 2000). A wide study in four European countries showed an association between higher internal biosecurity and a number of various pathogens vaccinated against (Postma et al. 2016a), reflecting the importance of vaccinations as a part of disease preventive measures. A Swedish study (Backhans et al. 2015) showed that scheduled vaccination scheme and treatment protocols were followed by 97 % of the farmers. In Finland, it is highly recommended to vaccinate gilts, sows and boars against infections caused by *E. rhusiopathiae* and parvovirus (Sikava). Most farms use circovirus vaccinations for piglets and *E. coli* –vaccinations for sows. Pigs can be further vaccinated against respiratory infections caused by *A. pleuropneumoniae* and enteric diseases caused by *L. intracellularis* and *Clostridium* spp., if needed.

Vaccinations can be effective only when used correctly and especially the hygiene of injection equipment is remarkable. On pig farms, injection needles are replaced generally whenever they become blunt even though it is recommended to replace the needle between every animal (Dewulf & Van Immerseel 2018). In reality, changing that frequently is often unfeasible and therefore it is considered important to replace needles at least between every batch (Dewulf & Van Immerseel 2018). A recent innovation in pig medication sector is the use of intradermal injection device that can lower the infection risk compared with intramuscular injections with dirty needles. Currently, a few intradermal vaccines are available for pigs including PCV-2, PRV, PRRSV and *M. hyopneumoniae.*

4.4 Antimicrobial use (AMU)

Plentiful bacteria is present continuously at production animal facilities and in different body systems including both pathogenic and beneficial bacteria (Rushton et al. 2014). The term antibiotic refers to a low molecular weight substance produced by a micro-organism that at low concentrations inhibits or kills bacteria, whereas antimicrobial is any natural, semi-synthetic or synthetic substance that kills or inhibits the growth of a micro-organisms with a minor damage to the host (Giguére et al. 2013). Antimicrobials have an impact on micro-organisms including bacteria, viruses, fungi and protozoa (Rushton et al. 2014), but are more potent drugs against bacteria in comparison to other micro-organisms (Giguére et al. 2013) Most antimicrobials have been developed during 1950s and at the end of 20^{th} century (WHO 2001) primarily for the treatment of human infectious diseases (Giguére et al. 2013). Since that, antimicrobials have been used to control pathogenic bacteria in animals in order to decrease the morbidity and mortality of livestock (Rushton et al. 2014), for growth promotion purposes (Giguére et al. 2013) and to prevent transfer of zoonotic pathogens from animals to humans directly or indirectly via food chain (Ungemach et al. 2006).

Antimicrobials can be used therapeutically (tAMU) to treat existing and/or diagnosed bacterial infections meaning that antimicrobials are given preferentially to individual animals with clinical symptoms and with appropriate doses according to the status of disease (Schwarz et al. 2001, Aarestrup 2005). Antimicrobials given for preventive purposes and administered to animals of the same production stage are considered group treatments (Callens et al. 2012). Group treatments can be administered either metaphylactically (mAMU) or prophylactically (pAMU) (Timmerman et al. 2006, Callens et al. 2012) typically via feed or water (EMA 2019). Metaphylaxis means the administration of antimicrobials to the entire animal group even though only some animals of the group show clinical symptoms (Aarestrup 2005, Callens et al. 2012). However, in mAMU it is expected that most of the group will become affected (Aarestrup 2005, Callens et al. 2012). Prophylaxis refers to the treatment of healthy animals known to be at risk of developing a disease (Filippitzi et al. 2014). In pig farming, pAMU is used to prevent stress-induced clinical diseases during e.g. animal transportation as well as enteric and respiratory outbreaks in "critical time points" like around weaning (Rushton et al. 2014) along with the purpose to control respiratory and enteric diseases especially among finishers (Callens et al. 2012, Sjölund et al. 2016). Therapeutic use is preferred in Finland and in other Nordic countries where pAMU is not routinely performed compared to many other European countries (EMA 2019). Group treatments are problematic, especially because dosing of an antimicrobial is often inaccurate (Timmerman et al. 2006, Callens et al. 2012). Moreover, many animals do not suffer from clinical disease at the point of the treatment, which causes unnecessary medications (Rushton et al. 2014, Evira 2016). However, farmers regard group treatments as an easier, cheaper and less labour intensive way to prevent diseases (Callens et al. 2012).

All AMU can contribute to the development of AMR (Chanziaras et al. 2014, JIACRA 2017, Burow et al. 2019). Antimicrobials that are currently used in pigs belong to the same antimicrobial classes that are used in human medicine (Schwarz et al. 2001, Rushton et al. 2014), and many pathogenic bacteria including *Escherichia coli*, *Salmonella* spp. and *Campylobacter* spp. are zoonotic hence possessing threat for human health as well (JIACRA 2017). According to OIE (2016), the majority of 110 OIE member countries do not yet have complete and relevant legislation to ensure appropriate conditions for the import, manufacturing, distribution and use of veterinary medicinal products. In the EU, veterinary antimicrobials are prescription-only drugs and thus they are not available in free markets (Rushton et al. 2014). Moreover, there can be additional restrictions and requirements prior to the prescription of antimicrobials, for example the need for a veterinary visit (Rushton et al. 2014). Many countries require farmers to keep records on which animals have received which substance and dosage on a given date (Rushton et al. 2014), and this is also the case in Finland (Laki eläinten lääkitsemisestä 387/2014 20§). Treatments must be included in written documents for animals being sent to the slaughterhouse, if the treatment is given within a withdrawal period (Rushton et al. 2014, 387/2014 25§). Because antimicrobials that are administered to farm animals are usually given by the farmers (Rushton et al. 2014), they play an important role in controlling the AMU in their animals (Callens et al. 2012). Among farmers, a cost of treatment and given withdrawal times play an important role in making treatment decisions (Page & Gautier, 2012).

It is important to investigate antimicrobial consumption data to evaluate herds' disease status and inappropriate AMU, as well as to identify risk factors for the AMR (Timmerman et al. 2006, Callens et al. 2012, OIE 2016, Collineau et al. 2017). According to annual veterinary antimicrobial sales reports published by European Medicines Agency (EMA), pig production is one of the highest antimicrobial using sectors among livestock species in many European countries (EMA 2019) and pig farming has been identified as one of the sectors in which the AMU drives the development of AMR (Chantziaras et al. 2014, Filippitzi et al. 2014). However, information about antimicrobial sales and real use do not correlate enough, and therefore investigation of AMU cannot be done precisely (Rushton et al. 2014, OIE 2016).

Overall, the most sold antimicrobials in 2017 measured as proportion of milligrams per population correction unit (mg/PCU) were tetracyclines (30.4 %) penicillins (26.9 %) and sulfonamides (9.2 %) which accounted for 67 % of the total sales (EMA 2019). Population correction unit (PCU) is a mathematical tool to set sales of antimicrobials in proportion to the animal population´s estimated weight in the course of treatment (EMA 2019). PCU is usually calculated for separate animal categories and/or for different production stages within animal categories by using theoretical weights determined for each group in question (EMA 2019). It should be kept in mind that report covers all veterinary antimicrobials including both food-producing and companion animals (EMA 2019). Separated by animal species, pigs accounted for 32.1 % of the PCU which was followed by cattle (31.3 %), poultry (14.4 %) and sheep/goats (14.1 %) (EMA 2019). According to the report, the total sales of antimicrobials decreased by 32.5 % during the investigation period 2011-2017 in 25 countries from which sales data was available for the whole period (EMA 2019). Sales of different antimicrobial classes according to EMA (2019) for the year 2017 are summarized in Figure 3.

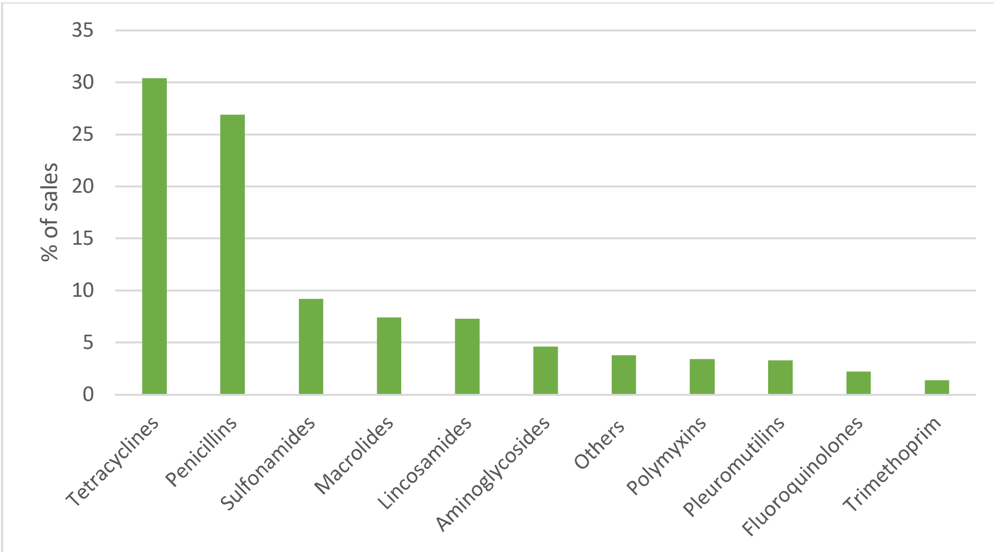

Figure 3. Sales of antimicrobial agents by antimicrobial class as percentage of the total sales for food-producing species, in mg/PCU, aggregated by 31 European countries, for 2017. Others* include amphenicols, cephalosporins, other quinolones and other antibacterials (classified according to ATCvet system). (Figure reproduced according to EMA 2019).

Reduction of the AMU should be achieved without worsening the animal welfare (Postma et al. 2015) and it can be achieved by improving management system together with disease preventive measures (Postma et al. 2017). European Commissions "Guidelines for the prudent use of antimicrobials in veterinary medicine" (2015/C 299/04) state that antimicrobials should only be used when other methods, such as good hygiene, strict AI-AO -system and vaccination protocols have failed. In the following sections, I will concentrate on antimicrobial compounds used in pig production, reasons for antimicrobial treatments and differences in AMU related to different production stages. Moreover, I will consider shortly the relationships between AMU and biosecurity practices.

4.4.1 AMU in suckling piglets, weaned piglets and finishers

Scientific literature about AMU is scattered and somehow scarce in terms of a detailed investigation of administration of antimicrobials to pigs and in many publications, AMU encompasses group treatments. In a study of Callens et al. (2012) rates, appropriateness and indications of group treatments administered to pigs during their lifespan in 50 Belgian farrow-to-finish farms were evaluated. Group treatments were applied on 98 percent of farms, of which 93 % were prophylactic. Overall, the most frequently used antimicrobial class was beta-lactams (27.6 %) which consisted mainly of both oral and injectable administration of amoxicillin (Callens et al. 2012). Orally administered amoxicillin was mainly used to treat streptococcal infections of piglets at the end of post weaning period whereas injectable broad-spectrum penicillins and cephalosporins were primarily administered for preventing diarrhea in piglets during the suckling period (Callens et al. 2012). Polymyxins were administered almost equal amounts (27 %) to beta-lactams followed by macrolides and lincosamides (17.7 %), trimethoprim-sulfadiazine (11.5 %) and tetracyclines (10.0 %) (Callens et al. 2012). Orally administered colistin that is a polymyxin antimicrobial, was used primarily used to prevent post-weaning diarrhea and injectable tulathromycin, a macrolide antimicrobial, to prevent respiratory symptoms in newborn piglets (Callens et al. 2012). Only 20 % of all treatments were administered during the finishing period and primarily for the treatment of respiratory diseases with either tetracyclines or trimethoprim-sulfadiazine. It is worth mentioning, that according to the study almost half of the herds studied used antimicrobials belonging to the WHO critically important list even though in much lesser amounts compared to other antimicrobials (Callens et al. 2012)

In a similar study made by Timmerman et al. (2006), group treatments were administered in 88 % of investigated 50 Belgian finisher herds. Timmerman et al. (2006) reported that 6.5 % of participated farms used fluoroquinolones that is markedly more than in the study of Callens et al. (2012) of which only one farm (2.0 %) had been used fluoroquinolones for newborn piglets. According to register-based data from Finland, fluoroquinolones had been administered at least to one animal in 7 % of pig farms in 2017 and 77 % were administered for suckling piglets (Sikava register information, Ina Toppari 2019).

Moreover, a recent study investigated in four EU countries showed that in addition to Belgian farms, group treatments are also preferred in French and German farms whereas Swedish farms used most commonly parenteral treatments (Sjölund et al. 2016). In Finland, similar information about antimicrobial administration has not been put together but it is a general practice to prefer parenteral treatments as a first treatment option. In a multi-country study by Sjölund et al. (2016) 26 % of all treatments were given to suckling piglets, 69 % to weaned piglets and only 5 % at finisher stage. Exceptionally in Sweden, the majority of antimicrobials were given to suckling piglets that can be partially explained by relatively higher weaning age of 35 days in Sweden compared with other countries (Sjölund et al. 2016). In overall AMU, top three antimicrobial classes used were aminopenicillins (30.0 %), polymyxins (17.7 %) and macrolides (15.0 %) (Sjölund et al. 2016). Those antimicrobials were mainly used for the treatment of weaning diarrhea (Sjölund et al. 2016). The most used antimicrobial class administered to weaners was polymyxins followed by aminoglycosides and tetracyclines (Sjölund et al. 2016). Hence, results seem to be in line with previous studies showing that the highest level of AMU takes place at early production stages (Timmerman et al. 2006, Jensen et al. 2011, Callens et al. 2012). Moreover, it was found that especially in German herds, treatment of suckling piglets was associated with further treatment at weaner and finishing stages (Sjölund et al. 2016). However, finisher stage is on average shorter in German farms compared with Belgian, French and Swedish farms (Sjölund et al. 2016) indicating more intensive production in Germany. This finding supports the hypothesis of larger AMU in intensive production facilities where a disease pressure is potentially higher (Sjölund et al. 2016). Gastrointestinal disorders at weaner stage seemed to be one of the biggest challenges in pig production (Jensen et al. 2011, Sjölund et al. 2016) followed by respiratory infections (Jensen et al, 2011). Overall, large differences in AMU exist both between herds (Timmerman et al. 2006, Callens et al. 2012, Callens et al. 2015, Sjölund et al. 2016) and between countries (Sjölund et al. 2016). In a recent pilot study conducted in Finland, large between-herds variations were also observed in AMU (Yun et al., unpublished results).

4.4.2 AMU in sows

Jensen et al. (2011) investigated all antimicrobials prescribed for pigs in Danish pig production between 2002 and 2008 based on VetStat system developed for the recording of prescribed antimicrobials in veterinary use. According to their analysis, 26 % of prescribed antimicrobials were administered in sow units including sows and piglets (Jensen et al. 2011). During the study period of seven years it was noted that AMU in sow units increased by 65 % over time and penicillins were the most used antimicrobial class (Jensen et al. 2011). Pleuromutilins were the second most common antimicrobial class prescribed (16 %) followed by trimethoprim-sulfadiazine (14 %) and tetracyclines (14 %) (Jensen et al. 2011). VetStat classification has six main disease categories: gastrointestinal (GI), respiratory, urogenital, mammary and systemic disorder, and the sixth group including central nervous system (CNS), locomotor system or skin related disorders (Jensen et al. 2011). The most common indication of antimicrobial treatment in sow units was CNS, locomotor system or skin disorders followed by urogenital and GI disorders (Jensen et al. 2011). Injectable compounds were preferred except for the treatment of GI and respiratory infections (Jensen et al. 2011). Because sow units include also antimicrobial treatments administered to piglets, it could be suggested that pigs are actually receiving the majority of reported treatments, because AMU has been reported to be high among piglets in general (Callens et al. 2012, Sjölund et al. 2016). Furthermore, Jensen et al. (2011) reported that only 10 % of antimicrobials were prescribed for diseases in the urogenital system or the udder – diseases more typical for sows.

Callens et al. (2015) measured AMU in total of 60 sows from three farrow-to-finish herds during one production cycle in order to evaluate AMR rates of sows and potential transfer of resistant bacteria to their offspring. During prepartum period, antimicrobials were not administered to sows in any of the herds studied (Callens et al. 2015). In one herd, marbofloxacin was used within gestation and lactation periods whereas in another herd, lincomycin-spectinomycin was used at corresponding stages (Callens et al. 2015). One of the studied herds did not administer any antimicrobials for sows during the investigated production cycle (Callens et al. 2015). According to Sjölund et al. (2016), the most used antimicrobial classes for breeding animals (sows, gilts and boars) were amphenicols (13.5 %) pleuromutilins (13.1 %) and trimethoprim-sulfonamides (11.9 %). However, those antimicrobials represented only a minor part in overall AMU: 0.1 %, 0.9 % and 5.4 % respectively (Sjölund et al. 2016). Sjölund et al. (2016) found also that treatment incidences (TIs) for breeding animals, suckling piglets and finishers were associated indicating that higher AMU for breeding animals resulted in a higher AMU for other age groups as well. Such finding implies that when antimicrobials are used in AMU during early production stages may lead to further consumption on latter production stages (Sjölund et al. 2016). On the other hand, AMU at different production stages within one farm may reflect the general accustomed habits of farmers.

4.4.3 AMU and biosecurity

Improvements in overall biosecurity has potential to reduce the prophylactic use of antimicrobials (Laanen et al. 2013). Proper management of diseased animals likely decreases a risk of pathogen transmission within a herd leading to a reduced infection pressure (Laanen et al. 2013). Moreover, reduced infection pressure within a herd results in lower need for AMU (Laanen et al. 2013). In recent years, an increased need has appeared to investigate associations between implemented biosecurity and its benefits compared with reduced AMU (Postma et al. 2016b, Postma et al. 2017). Postma et al. (2016b) studied associations between AMU, biosecurity status, herd characteristics and technical parameters. In conclusion, they revealed that reduced AMU was associated with a better external biosecurity status, a longer farrowing rhythm and a higher weaning age (Postma et al. 2016b). A longer farrowing rhythm can allow more time for C & D, which results in a lower disease pressure against pigs in following litters (Postma et al. 2016b). Better external biosecurity status also lowers the disease pressure coming outside of the herd and therefore it is relevant to assume that the need for antimicrobials is lower (Postma et al. 2016b). Laanen et al. (2013) have shown a strong positive correlation between external and internal biosecurity indicating that also implemented internal biosecurity may contribute with a lower AMU from birth until slaughter.

Postma et al. (2017) have shown in their study that improvement of biosecurity level together with optimization of herd management and advice about prudent AMU by veterinarians can result in significant reduction of AMU. They made biosecurity evaluation in 61 Belgian farrow-to-finish farms and according to the results, herd-specific action plans were developed (Postma et al. 2017). After an 8-month improvement period an increase in external biosecurity was observed – mainly in subcategories "purchasing policy", "removing animals, manure and carcasses", and "vermin and bird control" (Postma et al. 2017). Overall, a reduction of 52% in AMU from birth to slaughter and 32 % reduction for sows was achieved (Postma et al. 2017). Notably, there was a significant reduction also in the use of critically important antimicrobials such as 3^{rd} and 4^{th} generation cephalosporines and fluoroquinolones (Postma et al. 2017). The results indicate that there are possibilities for improvements on farm-level especially related to those measures with generally identified deprivations. The main finding in the study of Collineau et al. (2017) was, that especially in dense pig areas, low AMU was achieved by strict control of personnel and visitor, working order from youngest to oldest pigs together with good compartmentalization practices (Collineau et al. 2017). Moreover, in dense pig areas the higher number of vaccinations used was associated with lower AMU (Collineau et al. 2017). Reduction of overall AMU could be achieved by improving management especially in nursery units, because consumption rates seemed to be highest there (Callens et al. 2012, Sjölund et al. 2016).

In their intervention study, Postma et al. (2017) achieved statistically significant improvements in weaned piglets per sow per year (WSY), FCR, ADG and mortality rates in the finisher period and weaning age together with generally improved biosecurity levels. During an 8-month intervention period, improvements were remarkable especially in internal biosecurity, which increased 7.0 points in total and improvement was noted in all subcategories (Postma et al. 2017). In conclusion, farmers can achieve significantly better production results with lower AMU by improving their biosecurity level even in individual subcategories, because improvements in one subcategory result in changes in other subcategories as well (Laanen et al. 2013, Collineau et al. 2017, Postma et al. 2017).

5 MATERIAL AND METHODS

5.1 Related projects and ethical approval

This licentiate thesis was conducted as a part of the Makera-funded project Management and prevention of antimicrobial resistance (LÄKÄ). The study procedure was approved by the Ethical committee of the Viikki Campus Research, University of Helsinki (7/2016).

5.2 Farm characteristics and animals

A total of thirteen herds in Western and South-Western part of Finland participated in the present study. Finnish slaughterhouse company Snellman Lihanjalostus Oy recruited participating herds. The study herds were given the abbreviations from A to J. Seven of them were farrow-to-finish type (C, D, E, F, G, H, J) and three of them were piglet producing herds (A, B, I). Piglets from those three sow herds were sold to three separate finishing units (AA, BB, II) after they reached the weight of 25 kg. Sow herds A, B and I, and the corresponding finishing herds were considered as three farrow-to-finish herds thus resulting in 10 farrow-to-finish herds participating in the study. Herds were divided to small- and large-sized herds based on higher or lower median number of total animals. Herds characteristics are summarized in Table 2.

Table 2. Herd characteristics of ten study herds. PP=Piglet producer, F=Finishing herd, FF=Farrow-to-finish herd.

Herd	**Herd type**	**Herd size**	**N of sows**	**N of suckling piglets**	**N of weaners**	**N of finishers**	**N, total**
A/AA	PP / F	Small	107	3227	2857	1367	7558
B/BB	PP / F	Large	380	9714	10384	773	21251
C	FF	Small	122	3902	2180	2058	8262
D	FF	Small	240	5525	5963	311	12039
E	FF	Small	65	1959	1809	169	4002
F	FF	Large	347	9994	11263	2635	24239
G	FF	Large	248	6677	5123	3832	15880
H	FF	Large	236	4986	4841	2001	12064
I/II	PP / F	Large	286	8064	8715	1910	18975
J	FF	Small	56	1702	2379	744	4881
Total	-	-	**2087**	**55750**	**55514**	**15800**	**129151**
median (min-max)			238 (56-380)	5256 (1702-9994)	4982 (1809-11263)	1639 (169-3832)	12052 (4002-24239)

5.3 Data collection

Two researchers visited the herds three times during the life cycle of one pig batch between December 2016 and June 2017. A period between first and third herd visit was approximately five months. The researchers evaluated the herds' biosecurity status during the second farm visit on piglet producing herds and during the third farm visit on farrow-to-finish and finishing herds. AMU data was collected from internet-based Sikava register and sent to the researchers in Excel form by the advisor veterinarian of Sikava. Information about antimicrobial use was of each herd was collected for one-and-a-half-year period – one year before and a half year after the first herd visit. The register categorizes herds according to their health status into three different levels, namely basic, national and special level. All participating herds belonged at least to the national level and were thus obliged to keep the medication records in the Sikava system.

5.3.1 Biosecurity evaluation

The biosecurity status was evaluated by using Biocheck scoring system (Biocheck.UGent™). The biosecurity question form is available in the internet (https://biocheck.ugent.be/en/questionnaires/pigs) and sub-categories are covered in detail in the literature review. Because the scoring system is available in English, the questions were translated to Finnish in order to ensure an understanding of the farmers and thus minimize the interview bias.

5.3.2 Quantification of antimicrobial use

Sikava medical data included the following information: product name and antimicrobial class, indication, duration of therapy (in days) and dosage. According to Sikava data, a separate Excel was done in which all antimicrobial classes used on farms were identified. Penicillin was separated from other beta-lactam antimicrobials, and macrolides, lincosamides and streptogramin B were classified altogether as MLSB. All other treatments e.g. vaccinations, anthelmintic, pain killers and hormones were excluded. Calculation of treatment incidences (TI) was done according to the following formula described by Timmerman et al. (2006):

$$\mathrm{TI} = \frac{\text{Total amout of active substanaces administered (mg)}}{\mathrm{DDD}\left(\frac{\mathrm{mg}}{\mathrm{kg}}\right) \times \text{number of days at risk} \times \text{number of animals at risk} \times \text{standard weight (kg)}} \times 1000\ pigs\ at\ risk$$

The TI is a technical unit of measurement of AMU, which quantifies the number of animals out of a theoretical group of 1000 animals administered daily with antimicrobials. A list of defined daily doses (DDD) was obtained from the publication by Postma et al. (2015). The days at risk for the different age categories were set as suckling piglets = 28 days, weaners = 42 days, finishers = 130 days, breeders = 365 days and corresponding standard weights of pigs in each age category were 2 kg, 7 kg, 35 kg and 220 kg. The TI for pigs from birth to slaughter (TI 200) was calculated with a standardized life span of 200 days at risk. Moreover, proportions of all antimicrobial classes administered to different age groups were calculated.

5.5 Statistical analysis

SAS v.9.4. (SAS Institute, 2012) was used for statistical processing of the data. The mean biosecurity scores, TIs and animal numbers were tested for normality in order to select for appropriate statistical test. One-tailed t-test was used to find associations between the mean values of biosecurity scores (10 values/sub-category) and Finnish average scores (one value/sub-category) including all twelve sub-categories. Furthermore, paired t-test (2-tailed) was used to study association between the means of total external and total internal biosecurity scores.

Generalized linear model (GLM) was used to test the effect of herd size (as the categorical independent variable) to the biosecurity scores. All biosecurity sub-categories, total external, total internal and total biosecurity were fit into the model in which herds were divided by the higher or lower median number of total animals (see Table 3.).

Generalized linear mixed model (GLIMMIX) was used to analyze differences between the mean TIs in different age groups. Due to skewness of the TI-values, Poisson distribution with a logarithmic link function was fitted into the model. Age was set as a fixed variable and a herd as a random variable in the model. Moreover, Type III test was applied for testing the fixed effect of age to the TI-values and post-hoc analysis (Tukey-Kramer test) was used for further comparison between two age groups to study significant differences in the least square means (LS means) separately. Non-parametric analysis using Spearman correlation coefficients was used to study correlations between TIs in different age groups and number of animals in herds.

Table 3. Statistical procedure for the comparison of least squares means of different age groups, s = suckling piglets, w = weaners, f = finishers, b = breeders.

Differences of age Least Squares Means

age	_age	Estimate	Standard Error	DF	t Value	Pr > |t|
b	f	-0.2394	0.8580	36	-0.28	0.7818
b	s	-1.8514	0.6904	36	-2.68	0.0110
b	w	-0.9586	0.7549	36	-1.27	0.2123
f	s	-1.6120	0.6236	36	-2.58	0.0139
f	w	-0.7192	0.6944	36	-1.04	0.3073
s	w	0.8929	0.4719	36	1.89	0.0665

6 RESULTS

6.1 Biosecurity of study herds

Biocheck scores of the study herds are represented in Table 4 and variation in biocheck scores between herds is illustrated in Figure 5. The biosecurity scores of study herds varied considerably and especially the internal biosecurity scores tended to be lower than Finnish average (Table 4). Overall, the mean external biosecurity score was higher than the internal biosecurity score (Mean ± SD; 69 ± 1.2 vs. 44 ± 5.3, $P < 0.001$; Table 4). The mean scores for 'cleaning and disinfection' and 'compartmentalization and use of equipment' showed numerically lowest among sub-categories of the internal biosecurity in the study herds (22 vs. 48, $P < 0.05$; 40 vs. 49, $P = 0.09$, respectively, Table 4). The external biosecurity score was better in large herds compared to small herds (LSmeans ± SE; 72 ± 1.3 vs. 66 ± 1.3, $P < 0.05$).

Table 4. Biosecurity scores of study farms.

Subcategory	Median	Range	Mean ± SD	Finnish average*
Total biosecurity	54	45-71	57 ± 9	64
External biosecurity	69	65-76	69[a] ± 4	72
Purchase of animals and semen	88	68-100	87 ± 9	84
Transport of animals, removal of manure and carcasses	69	26-83	67 ± 16	68
Feed, water and equipment supply	48	23-62	45 ± 15	52
Personnel and visitors	77	24-100	71 ± 23	75
Vermin and bird control	70	50-100	71 ± 13	71
Environment and region	68	10-90	61 ± 29	82
Internal biosecurity	41	24-72	44a ± 17	56
Disease management	60	40-100	60 ± 21	71
Farrowing and suckling period	57	29-64	51 ± 15	53
Nursery unit	57	21-86	57 ± 20	61
Finishing unit	68	21-93	59 ± 29	71
Compartmentalization and equipment use	37	21-61	40[a)] ± 14	49
Cleaning and disinfection	6	0-75	22[a)] ± 30	48

* The Finnish average values were obtained from Biocheck.UGent web page 8.10.2018

[a)] Result differed significantly from the Finnish average values

6.2 Antimicrobial classes used in study herds

In total, six different antimicrobials were used including penicillin, beta-lactams other than penicillin (solely amoxicillin), sulpha-trimethoprim, tetracyclines, fluoroquinolones and antimicrobials belonging to macrolide-lincosamin-streptogramin B (MLSB) –group (Figure 4). Among all age groups except for weaners, penicillin was the most commonly used antimicrobial. Moreover, beta-lactams, sulpha-trimethoprim and tetracyclines were used in all age groups. Fluoroquinolones were the most common antimicrobial administered for weaners (36.7 %) followed by penicillin (30.5 %) and sulfa-trimethoprim (20.3 %).

6.3 Treatment incidences

The mean TI for suckling piglets was significantly higher than the TI for finishers or breeders ($P <$ 0.05, for both, Table 5). The mean TI for weaners did not significantly differ from the other age groups. The TI for suckling piglets tended to be positively correlated with the TI for weaners (n = 10, $r_s = 0.60$, $P = 0.07$, Table 5). Descriptive information on the treatment incidences is shown in Table 4. The TI for breeders tended to correlate negatively with the number of sows in the herds (n = 10, $r = - 0.56$, $P = 0.09$) but any other correlations between AMU and the number of animals were not found.

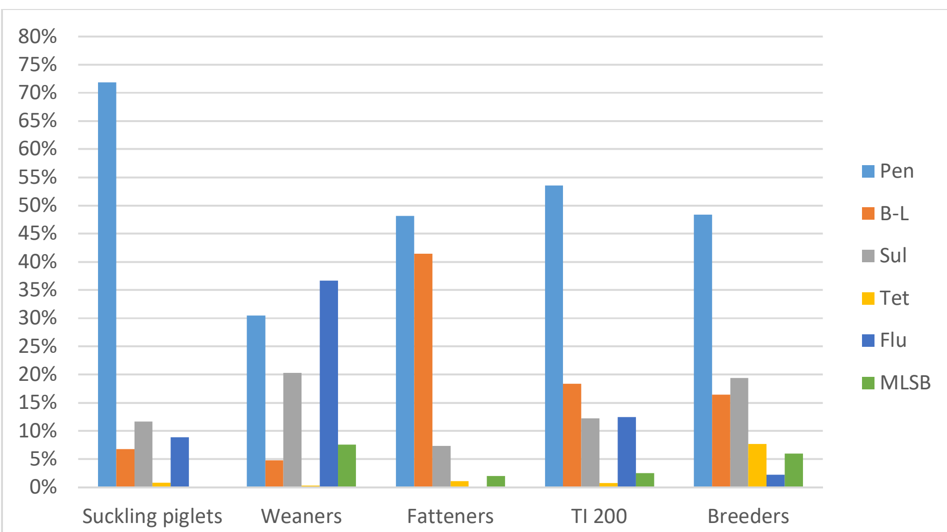

Figure 4. Antimicrobial classes used in ten Finnish farrow-to-finish study herds and proportions of the total use of antimicrobials contributing to the total TI in different age groups. B-L =beta-lactams excluding penicillin, Flu = fluoroquinolones, MLSB = macrolides, lincosamides and streptogramin B, Pen = penicillin, Sul = sulfa-trimethoprim, Tet = tetracyclines.

Table 5. Treatment incidences (TIs) of different age groups of pigs for one year in ten Finnish farrow-to-finish study herds. TI 200 indicates treatment incidence for pigs from birth until slaughter with a standardized life span of 200 days.

[a)] p = 0.07

	TI suckling piglets	TI weaners	TI finishers	TI 200	TI breeders (gilts, sows, boars)
Mean (± SD)	46.6[a)] (± 61.2)	19.1[a)] (± 23.7)	9.3 (± 6.6)	16.5 (± 10.5)	7.3 (± 6.8)
Min.	0.6	0	2.3	2.2	0.2
Median	36.8	13	7.4	16.1	5.1
Max.	207	75.8	20.7	33.3	18

6.4 Correlation between biosecurity and AMU/TIs

There were no significant correlations between the total biosecurity scores and the TIs in different age groups in the herds. However, it seemed that herds with higher biosecurity scores had lower AMU versus herds with lower biosecurity scores did not have notably higher AMU.

Farm	B	H	D	F	I	C	J	E	A	G
Purchase of animals and semen	79	100	68	88	90	100	84	82	87	88
Transport of animals, removal of manure and carcasses	82	26	63	65	74	74	83	67	70	65
Feed, water and equipment supply	59	33	57	40	62	23	23	53	44	57
Personnel and visitors	62	88	88	88	62	65	24	100	48	88
Vermin and bird control	70	60	70	50	65	70	100	80	70	70
Environment and region	50	80	60	70	90	10	80	10	65	90
Disease management	60	40	80	40	70	60	40	100	70	40
Farrowing and suckling period	64	29	43	43	64	29	64	50	64	64
Nursery unit	86	50	57	57	50	.	57	86	21	50
Finishing unit	82	21	36	93	93	21	71	79	64	29
Compartmentalization and equipment use	54	21	46	29	56	32	36	61	38	25
Cleaning and disinfection	70	0	0	20	45	0	0	75	13	0
External biosecurity, total	70	65	68	70	75	65	66	70	66	76
Internal biosecurity, total	68	24	40	43	59	26	41	72	41	31
Total biosecurity	69	45	54	57	67	46	54	71	54	54

Figure 5. Distribution of biosecurity scores between ten study herds (A-J) arranged according to the increasing AMU from left to right. Red cells represent low biosecurity, yellow moderate and green high biosecurity scores. Blank white cell indicates missing value.

7 DISCUSSION

Previous studies and findings of this licentiate thesis support the belief, that the importance of relatively easily practicable biosecurity measures have not been recognized by farmers. Interesting and fairly worrying issue is that inadequately applied biosecurity measures relate to sub-categories that are considered the most important based on the risk of transmission of infectious agents. Those include C & D, compartmentalization of working lines and equipment, transport of animals, manure and carcasses as well as feed, water and equipment supply.

In general, external biosecurity is better implemented on farms than internal biosecurity (Laanen et al. 2010, Laanen et al. 2013, Backhans et al. 2015, Postma et al. 2016a, Postma et al. 2016b, Filippitzi et al. 2017, Postma et al. 2017), which is in line with the findings of this study. Farmers seem to adopt more easily habits that are related to the restriction of external threats like access of visitors to the animal facilities. Also in this study, a consistent finding of this study was the high scores of external biosecurity category “Purchase of animals and semen”. Piglet-producing farms in Finland buy their gilts and breeding boars from separate breeding farms with more stringent biosecurity control that may explain the good results. What comes to animal transportation, the movement of weaner- and finishing pigs is market driven and coordinated largely by slaughterhouse companies that might favor a better biosecurity level of transports. On the other hand, Sikava which is coordinated by Animal Health ETT regulates the rules related to the health status of farms.

The introduction of pathogens via feed, water and equipment was poorly considered on the study farms even though it illustrates a relatively high biosecurity risk. Similar findings were done also in previous studies (Nöremark et al. 2010, Backhans et al. 2015, Filippitzi et al. 2017). However, many fatal viruses, including ASF, are capable of surviving throughout the feed chain at least in experimental conditions (Dee et al. 2018). The situation of severe infectious pig diseases in Finland is very good and therefore farmers may not consider disease preventive measures to be important (Sahlström et al. 2014). Furthermore, the situation is different compared to other countries, as livestock population is sparsely distributed throughout the relatively large country (Sahlström et al. 2014).

Cleaning and disinfection is consistently a sub-category that gets the lowest score in biosecurity evaluation (Sahlström et al. 2014, Filippitzi et al. 2017), and got numerically lowest score also in this study. In terms of herd health management, effective C & D is known to prevent both pathogen spread and persistence (Dewulf & Van Immerseel 2018), reflecting the whole ideology about the concept of biosecurity. Despite the use of C & D programs, large amounts of faecal residuals have been detected in pen structures (Mannion et al. 2007) with the highest post-cleaning contamination rates in drinking nipples and pen floors (Mannion et al. 2007, Luyckx et al. 2016). Hence it is noteworthy, that considering only one part of biosecurity is not enough in protecting the herd from the transfer of pathogens.

Disease management and procedures related to the different age groups seem to be somehow contradictory. According to Laanen et al. (2013), proper management of diseased animals likely decreases a risk of pathogen transmission within a herd leading to a reduced infection pressure further resulting in a lower need for AMU. In our dataset, all those sub-categories seem to have large variations between the farms. Our data is supported by a Swedish study by Backhans et al. (2015) showing that only a half of the 60 farrow-to-finish study herds moved runts and sick animals to the sick pen and consistently handled sick animals after the healthy ones. Moreover, cleaning of equipment, use of disinfection baths and washing hands between compartments were not well-managed and only 8 % of the Swedish farms required their staff to change clothing and footwear always while working in a pig house (Backhans et al. 2015). Filippitzi et al. (2017) also showed that separation of different age groups, maintenance of correct working order, and changing of overalls and boots were poorly implemented according to the results acquired from Biocheck.UGent™-database. At any time when animals are injected, the hygiene of injection equipment is important even though a general manner on pig farms is to replace the injection needles whenever they become blunt. Vaccination protocols are integrated to the disease management procedures and at least in Finland, most breeding farms have some kind of vaccination scheme at least for sows and piglets. Therefore, scores of disease management sub-category might appear at moderate level even though severe shortcomings occur within that or related categories. A wide study of Postma et al. (2016a) conducted in four European countries showed an association between higher internal biosecurity and a number of various pathogens vaccinated against reflecting a strong link of vaccinations as a part of disease preventive measures. The biosecurity scores of the study farms varied considerably and especially the internal biosecurity scores tended to be lower than Finnish average.

A previous study by Laanen et al. (2013) showed a positive association between the number of sows and finishers and the external biosecurity score, but there were no association between the herd size and internal biosecurity score. This is consistent with the finding of this study, where the external biosecurity score was higher in large herds compared to small herds. Many studies have shown that farm size and commercial mode of action influence applied biosecurity practices

(Ribbens et al. 2008, Nöremark et al. 2010, Simon-Grifé et al. 2013, Sahlström et al. 2014, Kuster et al. 2015, Postma et al. 2016a). It is likely that larger farms suffer from greater economic losses during the disease outbreak than smaller farms, and this may be one of the reasons why larger farms generally have better biosecurity status as Kuster et al. (2015) have speculated it. On the other hand, larger farms are in general newer, owners are younger and more educated compared with small "family farms" owned by older farmers.

According to Finnish national estimates, production of Finnish pig farms have increased six-fold within two decades and will increase further whereas the number of farms decreases (MTK 2017). Some publications have highlighted that antimicrobials are often used with the cost of sufficient biosecurity measures (Filippitzi et al. 2014, Postma et al. 2015). More intensive conditions may increase the risk of transmission of certain diseases (Jones et al. 2013) and raise new kind of animal health problems (Rushton et al. 2014). For instance, there has been a growing need to treat enteric and respiratory infections (Rushton et al. 2014), especially in weaning pigs (Hybschmann et al. 2011, Callens et al. 2012, Sjölund et al. 2016). Therefore, a concern of more excessive AMU in pig farming in Finland has raised. The limited data of this study showed only that the TI for breeders tended to correlate negatively with the number of sows in the herds. In the case of breeding stock, their health status may be evaluated more accurately compared to piglets and growing pigs thus resulting in more medications.

Overall, large variations in AMU exist both between farms (Timmerman et al. 2006, Callens et al. 2012, Sjölund et al. 2016) and between countries (Sjölund et al. 2016), even though certain antimicrobial head the statistics continuously. In the EU, tetracyclines (30.4 %) penicillins (26.9 %) and sulfonamides (9.2 %) accounted for 67 % of the total sales of antimicrobials for food-producing animals (EMA 2019). However, information about antimicrobial sales and real use do not correlate enough yet and national databases about AMU have been developed. Still, scientific literature about AMU is scattered and somehow scarce in terms of a detailed investigation of administration of antimicrobials to pigs and in many publications, AMU encompasses group treatments making comparison of publications unreliable. In Finland it is typical that farmers have a separate handwritten bookkeeping at the pig house, which is then saved into electronic form in Sikava. A natural source of bias in such circumstances are defects in saving the data. Anyway, penicillin and other beta-lactams, sulpha-trimethoprim and tetracyclines were used through the production chain in this study – similar compounds than at the EU level.

Yet, Finland is one of the Nordic countries using less antimicrobials for animals than other countries in Europe (EMA 2019). All in all, national policies and veterinary mode of action have a potential to impact on farm-level AMU. In the EU, veterinary antimicrobials are prescription-only drugs and thus they are not available in free markets (Rushton et al. 2014) and additionally Finnish veterinary practitioners are not allowed to give antimicrobials to farmers without a health care agreement, proper clinical procedures and advice. Furthermore, the amount of given antimicrobials is indicatively restricted and some extra limitations about the use of critically important antimicrobials exist. Notably, fluoroquinolones were the most common antimicrobial administered for weaners based on TIs with a value of 36.7 %. Previous studies have been reported lower fluoroquinolone use at herd level, for example. Timmerman et al. (2006) 6.5 %, Callens et al. (2012) 2% and wider national data of Finland showed 7 % use in 2017 (Ina Toppari, personal communication 2019). Furthermore, at the EU level, fluoroquinolones accounted for 2.2 of the total sales of veterinary antimicrobials (EMA 2019). However, in this dataset, fluoroquinolones were used on six herds out of ten of which one herd had been used a remarkably large amount compared to others. The only indication for the use of fluoroquinolones was diarrhea that implies perhaps the different script of herd veterinarians in prescribing and advising the use of antimicrobials.

Results of Sjölund et al. (2016) seem to be in line with a current study as well as previous studies showing that the highest level of AMU takes place at early production stages (Timmerman et al. 2006, Jensen et al. 2011, Callens et al. 2012). In contrast to previous publications, therapeutic use is preferred in Finland and in other Nordic countries instead of prevailing group treatment practices in many other European countries. According to Sjölund et al. (2016), treatment of suckling piglets was associated with further treatment at weaner and finishing stages, implying that AMU during early production stages may lead to further consumption on latter production stages. On the other hand, AMU at different production stages within one farm may reflect the general accustomed habits of farmers. Similarly, in our dataset, the AMU for suckling piglets tended to be positively correlated with the AMU for weaners, but not with latter production stages or with overall AMU. Such finding may be related to the relatively low sample size of our study. We hypothesized that in farms with low biosecurity status AMU is generally higher compared to farms with better biosecurity routines. As an observation, herds with better biosecurity status seemed to be using less antimicrobials compared to herds with lower biosecurity status (see Figure 5).

Two publications speculated that reduction of overall AMU could be achieved by improving management especially in nursery units, where consumption rates seemed to be the highest (Callens et al. 2012, Sjölund et al. 2016). Prophylactic AMU have been strongly linked to the prevention of disease outbreaks accompanied with stressful situations such as weaning and animal transportation. Early production stages are over-represented in terms of therapeutic AMU as can be seen from the results of this study. In pig farming, antimicrobials are used prophylactically to prevent stress-induced clinical diseases during e.g. animal transportation as well as enteric and respiratory outbreaks in "critical time points" like around weaning (Rushton et al. 2014) along with the purpose to control respiratory and enteric diseases especially among finishing pigs (Callens et al. 2012, Sjölund et al. 2016).

Postma et al. (2016a) showed a strong positive association between external and internal biosecurity, which indicates that improvements in any biosecurity measure have a positive effect on farms' overall biosecurity status. Inspired by that, Postma et al. (2017) achieved remarkable reduction of AMU by improving management system together with disease preventive measures. An overall reduction of 52% in AMU from birth to slaughter and 32 % reduction for sows was achieved as a result of improvements especially on sub-categories "purchasing policy", "removing animals, manure and carcasses", and "vermin and bird control" (Postma et al. 2017). The total, external, and internal biosecurity scores were not correlated with the TIs in different age groups in the investigated herds which may also have been influenced by the small sample size of our study. Nevertheless, farmers play an important role in controlling the AMU in their animals because in the end, they are the ones making the treatment decisions. It has been reported that a cost of treatment and given withdrawal times play important roles in decision-making (Page & Gautier, 2012). Moreover, farmers regard group treatments as an easier, cheaper and less labour intensive way to prevent diseases (Callens et al. 2012). According to Laanen et al. (2014) farmers are highly motivated by improving profits with better productivity in disease prevention. Moreover, Danish piglet producers gain higher price if they keep high biosecurity level (Filippitzi et al., 2017), and therefore supporting farmers financially could be one way to encourage them to invest in biosecurity measures and indirectly lower AMU.

Because pig farming has been identified as one of the agricultural sectors in which the use of antimicrobials drives the antimicrobial resistance (Chantziaras et al. 2014, Filippitzi et al. 2014), it is considerably important to apply alternative solutions for preserving a good health status of a herd. Diverged resistance rates in bacteria isolated from pigs have been linked to different housing conditions (Langlois et al. 1988) as well as to different production stages (Langlois et al. 1988, Dewulf et al. 2007, Burow et al. 2019) which indicate the multifactorial nature of AMR. From a human point of view this is noticeable because antimicrobial compounds used in pigs highly overlap with human medicine.

Shortcomigs of this study were the quality of AMU data and low sample size. Double-saving of medical records to a note and further saving in electronical form to Sikava may lead to some disappearance of data. Moreover, it is known that some farmers consider the work quite laborious and may not be motivated to settle down on saving the records besides other farm work. The register is also built in a way that some medications can be saved under a wrong age group. More participating herds would be needed to assess more deeply the associations between biosecurity and AMU. Nevertheless, this small sample size showed at least similar trends in biosecurity and AMU compared to wider studies.

As a conclusion, the key factor influencing the herd health status is a farmer. Largely, farmer´s attitudes and common understanding about biosecurity determine the practices. Whether the farmer ignores biosecurity, transmission of pathogens to a herd and within a herd occurs more likely thus lowering the herd´s health status and leading to increasing AMU. In the future, improvements in the biosecurity status of a single farm should be based on targeted measures of a health status of the herd allowing focusing on the most relevant farm specific measures needed in order to better the health status of a herd. Veterinarians are the key persons to advise farmers towards prudent AMU and to motivate farmers in improving the health status of their herd. More studies are needed to strengthen the belief about the importance of biosecurity in lowering the need to use antimicrobials. There is a need to develop more accurate data collection systems to further evaluate the trends in AMU and also harmonize data collection between countries. Linked to the concept of OneHealth, animals, humans and the environment are strongly overlapping sectors of life thus sharing the responsibility to slow down the development of antimicrobial resistant bacteria between every contributors. As long as pig farming is one of the paramount sectors using antimicrobials, work has to be done to better the situation. To date, improving biosecurity is on high in a list of potential factors to focus on more deeply. Regardless of small sample size of this study, current findings are parallel with other studies thus indicating the potential to improve biosecurity of Finnish farms in order to avoid growth in AMU.

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