Antimicrobial use and antimicrobial resistance: standpoint and prescribing behaviour of Italian cattle and pig veterinarians

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Abstract:	The scientific community considers the improper use of antimicrobials in farm animals among the causes of the insurgent bacterial resistance

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contributing to the wider pool of resistance at the animal/human interface with serious public health implications. The present study aimed to describe the current perceptions regarding antimicrobial use and resistance and the prescribing behaviour of two different target groups: cattle and pig veterinary practitioners working in Italy.

A semi-structured questionnaire was designed and administered using the Computer-Assisted Web Interviewing method to a panel of Italian veterinarians.

Among the 789 participants who completed the questionnaire, 53.5% and 12.2% were cattle and pig veterinarians, respectively. Differences between the two groups emerged in their opinions concerning different topics. For example, 69.4% and 85.8% of cattle veterinarians claimed to "somewhat or strongly agree" with the statements "prescribing broad-spectrum antibiotics in breeding farms increases antimicrobial resistance (AMR)" and "the preventive use of antibiotics fosters the development of AMR", against the observed 59.4% and 69.8% of pig veterinarians. Moreover, 26% of pig veterinarians "somewhat or strongly agree" with the statement "alternative methods currently available could be an efficient alternative to antimicrobial treatment", against 16.1% of cattle veterinarians. At the same time, no differences between the two groups emerged regarding the danger inadequate antimicrobial usage in animals poses on both animal and human health.

The collected data represent the first step in designing communication and training strategies for veterinarians who have the crucial role of prescribing antimicrobials in the livestock sector.

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Antimicrobial use and antimicrobial resistance: standpoint and prescribing behaviour of Italian cattle and pig veterinarians

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The scientific community considers the improper use of antimicrobials in farm animals among the causes of the insurgent bacterial resistance contributing to the wider pool of resistance at the animal/human interface with serious public health implications. The present study aimed to describe the current perceptions regarding antimicrobial use and resistance and the prescribing behaviour of two different target groups: cattle and pig veterinary practitioners working in Italy. A semi-structured questionnaire was designed and administered using the Computer-Assisted Web Interviewing method to a panel of Italian veterinarians. Among the 789 participants who completed the questionnaire, 53.5% and 12.2% were cattle and pig veterinarians, respectively. Differences between the two groups emerged in their opinions concerning different topics. For example, 69.4% and 85.8% of cattle veterinarians claimed to "somewhat or strongly agree" with the statements "prescribing broad-spectrum antibiotics in breeding farms increases antimicrobial resistance (AMR)" and "the preventive use of antibiotics fosters the development of AMR", against the observed 59.4% and 69.8% of pig veterinarians. Moreover, 26% of pig veterinarians "somewhat or strongly agree" with the statement "alternative methods currently available could be an efficient alternative to antimicrobial treatment", against 16.1% of cattle veterinarians. At the same time, no differences between the two groups emerged regarding the danger inadequate antimicrobial usage in animals poses on both animal and human health.

The collected data represent the first step in designing communication and training strategies for veterinarians who have the crucial role of prescribing antimicrobials in the livestock sector.

Highlights

- 85.8% of cattle vs. 69.8% of pig veterinarians agreed with the statement "the preventive use of antibiotics fosters the development of AMR"

- 64.5% of cattle and 69.1% of pig veterinarians declared they suggest/prescribe alternative approaches to the use of antimicrobials

- "Hygiene-biosecurity-management" and "nutritive principles" are the alternative strategies most suggested by cattle and pig veterinarians, respectively

Introduction

Antimicrobial usage and antimicrobial resistance in veterinary medicine

Antimicrobial usage (AMU) in human and veterinary medicine was one of the most important innovations of the 1900s. Starting in the 1930s, many antibacterial substances were discovered and applied, including prophylactics, to intervene effectively in often-lethal pathologies, thus reducing mortality rates (Aarestrup 2015).

Current animal breeding systems often involve AMU for the prevention and treatment of infectious diseases as well as the improvement of productivity and feed efficiency (Oliver et al. 2011; Page and Gautier 2012). In modern breeding, appropriate AMU has undoubted advantages and contributes to the growing demand for animal proteins for human consumption worldwide (Van Boeckel et al. 2015).

Nevertheless, the wide AMU in the treatment and prevention of infectious diseases over the years has caused an evolutionary response by the microbial population to develop various forms of resistance against the applied antimicrobials (Michael et al. 2014).

Inappropriate AMU is partly responsible for the spread of resistant microbial strains in both humans and animals (Berge et al. 2006; Jensen et al. 2006). There are many connections among humans, animals, and the greater environment that allow the transfer not only of resistant bacteria but also of mobile genetic elements that permit horizontal transfer between different bacterial species (Woolhouse et al. 2015).

Excessive and/or improper AMU in farms can favour the growth of resistant bacterial

strains, with the consequent potential spread to humans, representing a serious threat to

public health (Page and Gautier 2012; World Health Organization 2014; Roca et al.

2015). Furthermore, the development of resistant bacteria can compromise the effective

treatment of microbial diseases in animals, thus jeopardising the welfare of both food

and companion animals (Lloyd 2007; Trevisi et al. 2014).

For these reasons, the request for more prudent AMU in farm animals is becoming

increasingly urgent (McEwen 2006; Aarestrup et al. 2008; Prescott 2008).

The World Health Organization stated that antimicrobial resistance (AMR)

represents a dire problem due to the potential serious implications for human health and

the global economy (World Health Organization 2014, 2018). The economic impact

consists of increasing costs for effective treatment and hospitalisation, with a

consequent reduction in the workforce (Smith et al. 2011). The AMR crisis is

considered an issue that needs to be addressed with immediacy and effectiveness to

ensure the availability of antimicrobial therapies, particularly in human medicine

(World Health Organization 2014).

Antibiotics are routinely used in breeding farms in three alternative ways.

"Therapeutic use" is the treatment of a sick animal or a group of sick animals following

diagnosis of a disease or an infection. "Prophylactic use" means the preventive use of

antibiotics in healthy animals to prevent the onset of a disease or infection (World

Health Organization 2017). The term "metaphylaxis" is defined as the administration of

a drug to a group of animals after they have been diagnosed with a clinical disease, to

treat sick animals and to prevent further spread of the disease (McEwen and Fedorka-

Cray 2002). In farm animal breeding, it is often more practical to administer

antimicrobials to the whole group through food or water, as implemented, for example,

in poultry farming. Therefore, in metaphylactic treatment, antimicrobials are used for

therapeutic purposes on sick animals and for prophylactic purposes on the remaining

healthy animals of the group (McEwen and Fedorka-Cray 2002).

The current European legislation (Directive 2004/28/EC amending the Directive

2001/82/EC on the Community code relating to veterinary medicinal products)

establishes that AMU on breeding farms is the responsibility of a veterinarian, who is

normally self-employed or employed in the feed industry.

In Italy, veterinarians of the National Service are responsible for pharmacovigilance and

pharmacosurveillance; normally, these veterinarians do not prescribe veterinary drugs,

with particular exceptions (for example, when they are authorised to carry out clinical

activities).

In this scenario, it is essential to increase the veterinarians' awareness of AMR

and prudent AMU in livestock farms, as the prescription of drugs falls within their

responsibilities (World Health Organization 2014; European Centre for Disease

Prevention and Control 2015). The veterinarian therefore has a double task: to prescribe

antimicrobials in a coherent way, and to render farmers aware of the correct use of

antimicrobials.

To define the most appropriate training and refresher paths, it is necessary to identify

knowledge gaps and information needs of veterinarians using appropriate needs

assessment methods (Moore et al. 2002; Dale et al. 2008).

Currently, only a few published studies have aimed to investigate these issues in

an Italian context and to assess veterinarians' awareness of AMR problems (Busani et

al. 2004). To update this knowledge and outline the opinions, habits and prescribing

behaviour of this target population, an Italian national survey was carried out.

In the present study, only some of the results obtained through the survey are described.

In particular, our attention is focused on the different approaches, perceptions and

prescribing habits of two specific target groups: cattle and pig veterinarians. This choice

is justified by the fact that the breeding of cattle and pigs represents an important sector

of the Italian national livestock production (Istituto Nazionale di Statistica 2016).

Aim of the study

Investigating veterinarians' opinions, perceptions and behaviour towards AMU and

AMR in livestock farms is fundamental for: [1] identifying knowledge gaps and causes

of possible misuse of antimicrobial drugs; [2] outlining communication and training

strategies aimed at spreading information; and [3] increasing awareness and eventually

improving prescribing behaviour.

The present study has two aims:

- analyse the potential differences in socio-demographic characteristics, points of

  view and prescribing behaviour of the two different target groups; and

- focus on the attitude of the two target groups towards the application of

  alternative strategies to prevent and control livestock diseases.

Materials and methods

Sampling and data collection

Data were collected between September 27th and November 20th, 2017, using the

Computer-Assisted Web Interviewing method.

The frame population was extracted from veterinarians who were registered to National

Federation of Italian Veterinary Orders (FNOVI) in 2017; therefore, it represents

veterinarians working in 2017.

A list of 13,794 contacts was created by consulting the FNOVI database and including only those who had an email address. An email explaining the project aims and containing the link for completing the questionnaire was sent to all contacts.

To increase the response rate and reduce the non-response bias, a reminder was sent one week after the first email contact. No economic incentives were given to promote the completion of the questionnaire.

The survey was carried out as a census field (Callegaro et al. 2015), leading therefore to a representative sampling frame of the population.

To comply with the privacy policy, there was a privacy agreement request with a checkbox at the beginning of the questionnaire.

The study design meets the requirements established by the Ethics Committee of the Istituto Zooprofilattico Sperimentale delle Venezie.

The questionnaire

A semi-structured questionnaire was designed based on the existing literature (Busani et al. 2004; García et al. 2011; Visschers et al. 2015) and the research team's experience. The questionnaire consisted of the following sections: socio-demographic characteristics; opinions towards AMU and AMR in livestock farms; and prescribing behaviour.

The questionnaire was designed and structured to minimise the error during sampling (Callegaro et al. 2015); in particular two screening questions were introduced to avoid interviewing veterinarians outside the target population (e.g. retired, not dealing with livestock). Moreover, consistency checks (to assess data quality and coherence between questions) were applied to avoid measurement errors.

Before administration, the questionnaire was pre-tested on four veterinarians to identify and eliminate any unclear or dubious questions.

Of the 20 introduced questions, 14 were included in the present study (please see the

Supplemental Material, Table SM1). The other 6 questions were considered irrelevant

to the aim of this study.

Collected data were treated according to the General Data Protection Regulation (EU)

2016/679.

For some questions, the results were merged together, modifying the response

options reported in the questionnaire, before the analysis. In particular, the results of the

question "how long have you been working as a veterinarian?" were classified into the

categories: "< 10 years", "10-20 years", and "> 20 years". Referring to the variable

"position", the response options "private practitioners" and "veterinarians employed in

private companies" were aggregated in the "private veterinarians" category, while the

option "veterinarians employed in public institutions" (public veterinarians) remained

the same.

Finally, the response scale of the question "indicate your degree of agreement with the

following statements" was changed to: "not at all or slightly agree", and "somewhat or

strongly agree".

Statistical analysis

Both quantitative and qualitative analyses were performed based on the research

objectives and the nature of the variables.

Regarding quantitative analyses, univariate summary statistics were used to summarise

the two groups of respondents. Bivariate analyses (contingency table and chi-square

test) were then performed to investigate the dependent relationships between categorical

variables. The Mann-Whitney U-test was used to determine differences in the

distributions of ordinal variables expressed on a 1 to 10 Likert scale (Freund and Wilson

2001).

Qualitative analyses were performed to study the responses to the open-ended questions

"do you suggest/prescribe alternative strategies/therapies to antibiotics? If yes, specify

which strategies" and "in your opinion, which strategy could be effective in the AMU

reduction in breeding farms?". Lexicometric analysis was applied to explore the

interviewees' responses. In particular, explorative textual techniques for automatic text

categorisations (Bolasco 2013) were applied to the four textual corpora created, starting

from cattle and pig veterinarians' responses to the two questions, respectively. The

corpora were pre-processed by means of normalisation; the textual segments with

higher occurrences (cut-off equal to 3) were then identified according to Morrone's

statistical relative IS index (Morrone 1993) and included in the analysis as textual units.

Due to the low number of responses to the first question and the presence of technical

terms, the textual units of the two corresponding corpora were manually categorised by

two experts of the research team in two different time points. The results were then

discussed and merged together in the creation of the categories. Finally, two-word

clouds were generated to overview the textual units of the two corpora created from the

responses of the second open-ended question.

The word clouds were created in the Italian language to preserve the correct meanings

of the lexical units.

The level of statistical significance was set at 5% (α=0.05). The quantitative

analysis was performed using Statistical Package for Social Science (SPSS) software

(version 21.0.0.0) for Windows (SPSS Inc., Chicago, Illinois), and the qualitative

analysis was executed using TaLTaC2 software (version 2.10.2) (Bolasco et al. 2000)

and Iramuteq software (version 0.7 alpha 2) (Ratinaud 2009).

Results

Socio-demographic characteristics

Out of 13,794 contacts, 9,390 declined to participate (this number includes those who were eligible for the survey but did not finish the questionnaire compiling process, those who did not click the survey link, and those who stated that they were not interested in participating), 3,615 were not eligible on account of being retired or not dealing with livestock animals, and 789 completed the questionnaire (response rate equal to 7.75%). Among them, 53.5% specified that they mainly specialise in cattle, 12.2% in pigs, 10.3% in small ruminants, 8.2% in poultry species, 8.2% in equines, 2.4% in fish species, 2.2% in rabbits, and 3% in other species.

Data referring to the two larger groups, cattle (g_1, n=422) and pig practitioners (g_2, n=96), were analysed in this study.

In both groups, the majority of respondents were male between 45 and 60 years old. They worked only on livestock animals; they had been working as veterinarians for more than 20 years and mostly worked in the private sector (Table 1). [Table 1 near here]

Opinions towards AMU and AMR in breeding farms

It should be noted that veterinarians, by profession, often deal with more than one animal species. For this reason, respondents were invited to refer to the animal species selected in the question "which supply chain do you mainly deal with?" in the compiled questionnaire.

Referring to the interviewees' opinions towards AMU in the livestock sector or farms on which they work, it emerged that the majority of both cattle and pig veterinarians considered that AMU is not always in line with the National and European guidelines (Figure 1). [Figure 1 near here]

Moreover, the veterinarians' opinions towards AMU and AMR in breeding farms were investigated by requesting their degree of agreement with respect to the set of statements listed in Table 2. [Table 2 near here]

Among cattle veterinarians, the highest degree of agreement emerged with the statement "inadequate AMU in animals is dangerous for human health"; however, among pig veterinarians, the highest degree of agreement emerged with the statement "inadequate AMU in animals is dangerous for their health".

A statistically significant dependence between the respondents' level of agreement and the animal species they specialised in (either cattle or pigs) arose with respect to the following statements: "prescribing broad-spectrum antibiotics in breeding farms increases AMR", "the preventive use of antibiotics fosters the development of AMR", and "alternative methods currently available (homeopathy, phytotherapy, etc.) could be an efficient alternative to antimicrobial treatment".

Prescribing behaviour

The prescribing behaviour of the respondents was investigated on two different levels, including the veterinarians' habit of prescribing antibiotics and their attitude towards suggesting/prescribing alternative strategies/therapies.

Respondents' habits of prescribing antibiotics

Out of 422 cattle veterinarians and 96 pig veterinarians, 72% (n_{g1}=304) and 70.8% (n_{g2}=68), respectively, stated that they prescribe antibiotics. Subsequently, these two subgroups were asked how frequently they prescribe antibiotics with prophylactic purposes and with therapeutic purposes. It emerged that the number of those who prescribe antibiotics for prophylactic purposes was higher among pig veterinarians (Figure 2). Additionally, concerning pig veterinarians, 44.1% stated that they do it often

(every day) or sometimes (1-2 times a week), compared to 31.6% of cattle veterinarians.

[Figure 2 near here]

In both subgroups, more than 80% of the respondents prescribed antibiotics for

therapeutic purposes often (every day), or sometimes (1-2 times a week), and in

particular, the corresponding proportion of pig veterinarians exceeded 85% (Figure 3).

[Figure 3 near here]

Finally, practitioners who prescribed antibiotics were asked to what extent the factors

listed in Table 3 affected the choice of the antibiotic to be prescribed. In general, it

occurred that the main factors were "efficacy", "training/scientific knowledge", "field

experience", and "duration of the withdrawal period". In contrast, the factors that less

affected the choice of the antibiotic were "opinion of the farmer", "pharmaceutical

representatives", "advertisement", and "opinion of the pharmacist". [Table 3 near here]

According to the Mann-Whitney test, differences between the distributions of the two

groups emerged with respect to the factors: "efficacy", "current legislation", "habit",

and "price".

Respondents' attitude to suggesting/prescribing alternative strategies or therapies

The attitude regarding suggesting/prescribing alternative strategies/therapies was

investigated in those who stated that they prescribe antibiotics. In particular, they were

asked how frequently they suggested or prescribed alternative strategies or therapies. As

shown in Figure 4, 64.5% of cattle veterinarians and 69.1% of pig veterinarians

declared that they suggest/prescribe alternative approaches to the use of antimicrobials.

[Figure 4 near here]

Only veterinarians who stated that they suggest/prescribe alternative strategies

(n_{g1}=196, n_{g2}=47) were asked to specify which strategies. The responses grouped in

categories are reported in Table 4. [Table 4 near here]

The alternative strategies most frequently mentioned by cattle veterinarians were

categorised in "hygiene/biosecurity/management", "phytotherapy" and

"homeopathy/homotoxicology", while those most frequently mentioned by pig

veterinarians were categorised in "nutritive principles", "pre-/probiotics" and

"hygiene/biosecurity/management".

The word clouds created, starting from the cattle and pig veterinarians'

responses to the free open-ended question "in your opinion, which strategy could be

effective in the AMU reduction in breeding farms?" are reported in Figures 5 and 6.

[Figures 5 and 6 near here]

A translation of the main words is provided in Supplemental Material (Table SM2).

In the cattle veterinarians' opinion, effective strategies for AMU reduction should be

applied on different fronts, including the management practices of livestock farms,

farmers, animals, veterinarians, biosecurity measures, etc.

From the pig veterinarians' responses, the importance of biosecurity measures emerged,

followed by vaccines and the management of livestock farms.

Discussion

AMR and AMU issues have been largely debated in the recent decades. In the European

context, several studies investigated the opinions, knowledge and perceptions regarding

AMR in different populations, from junior doctors (Pulcini et al. 2010), to dairy cow

farmers (Higham et al. 2018), farmers (Visschers et al. 2015, 2016; Di Martino et al.

2019), and the general public (André et al. 2010). Additionally, the veterinarians' points

of view and prescribing behaviour were investigated in the European context

(Speksnijder et al. 2015; McDougall et al. 2017; Van Cleven et al. 2018). However,

only a few studies have aimed to investigate these issues specifically in the Italian

context. Busani (Busani et al. 2004), for example, performed a telephone survey on

Italian beef and dairy cattle veterinarians. The aim of the investigation was to deepen

the understanding of several aspects of AMR, including veterinarian backgrounds,

training activities, diagnostics, treatments, prophylactic practices for specific diseases,

and the participants' perception of the threat posed by AMR. Starting from the survey

conducted by Busani, we aimed to outline the opinions, habits, and prescribing

behaviour of Italian veterinarians, by means of an online survey.

Socio-demographic characteristics

Most veterinarians who replied to the questionnaire worked with cattle (53.5%) and pigs

(12.2%), and this result reflects the importance of these two animals in the Italian

livestock sector. Most veterinarians specialising in cattle and pigs were male and had

more than 20 years of work experience. In Italy, the overall ratio between male and

female veterinarians is more balanced (57.6% and 42.4%, respectively) compared to the

results of the present survey (Nomisma 2014).

The veterinary profession has changed substantially over the years in terms of the

male/female ratio; the number of female professionals has gradually increased, and

now, in certain countries, they are a majority in the profession (Allen 2016).

Nevertheless, most veterinarians who choose jobs on animal farms are male (Shepherd

and Pikel 2011). The greater propensity of male veterinarians, compared to females, for

specialising in farm animals can explain the relatively high age of respondents and

allows a better interpretation of some opinions and habits, considering the temporal

distance from academic training and the role of age-linked professional experience.

Opinions on AMU and AMR

The protocols and rules to be applied for a prudent AMU are widely described in

various national and international documents and guidelines (Ministero della Salute

2012, 2017; World Health Organization 2014; European Centre for Disease Prevention and Control 2015), which are available to all veterinarians.

Most of cattle (53.3%) and pig (48.9%) veterinarians believe that AMU on the livestock farms in which they operate is not always in line with national and European guidelines. This result is not easy to explain because drug use in Italy is a direct responsibility of veterinarians and therefore of the people who completed the questionnaire. Thus, the interpretation of this outcome has been further explored by investigating the opinions of veterinarians on AMU and AMR.

As shown in Table 2, some responses given by cattle veterinarians compared to pig veterinarians (prescription of broad-spectrum antibiotics, preventive use of antibiotics and use of alternative strategies to antimicrobials) probably reflect the different approaches of practitioners operating on two different types of livestock production. In the case of cattle, the veterinarian has a clinical approach to both individual animals and group clinics, while in pig farming the veterinarian's activity is almost exclusively aimed at the health management of the animal groups. This different approach necessarily involves a different AMU and can generate a different perception of the problems related to AMR. In general, both cattle and pig veterinarians agreed with the fact that inadequate AMU in livestock has clear animal (86% and 83.3%, respectively) and human (86.7% and 80.2%, respectively) health implications. The percentage of professionals who disagreed with the above statements is still high and probably reveals a gap in knowledge and awareness on the AMR issue.

Taking into account the good level of awareness (> 80%) of veterinarians about the clear implications for both humans and animals regarding antimicrobial misuse in the livestock sector, it is even more perplexing that only in a limited number of farms (cattle 40.3% and pigs 46.9%) are antimicrobials used according to national and

European guidelines (Figure 1). As suggested by De Briyne et al., it is probable that external factors (owner influence, ease of drug administration, price or other economic elements) affecting AMU in the farm are involved (De Briyne et al. 2013).

Approximately one-quarter of cattle and pig veterinarians do not completely believe that antimicrobials are over-used and that AMR is a major problem. On the one hand, more than 80% of veterinarians recognise that inadequate AMU can generate problems for human and animal health; on the other hand, more than a quarter of veterinarians do not consider AMR a relevant problem in Italy. Nevertheless, official documents state that "In Italy, AMR remains among the highest in Europe, almost always above the average" (Ministero della Salute 2017). This outcome also indicates a major gap in knowledge on the topic.

Finally, there is a lack of awareness regarding the impact of the use of broad-spectrum antibiotics on AMR; 30.6% of cattle veterinarians and 40.6% of pig veterinarians are little or not at all in agreement with the fact that the use of broad-spectrum antibiotics in livestock production may facilitate an increase in AMR (Karam et al. 2016).

Antimicrobial prescribing habits

An interesting aspect concerns the prophylactic use of antibiotics, with many veterinarians declaring to prescribe antibiotics for preventive use. This may be explained by the fact that it is sometimes difficult to distinguish between the metaphylactic and prophylactic use of antibiotics. In daily practice, respondents may consider as prophylaxis the metaphylactic drug use in a group of animals after the clinical diagnosis of a disease in a few individuals.

Antibiotics can be used in livestock for therapeutic or preventive purposes, and the veterinarian must prescribe their application after having identified the aetiological

agents involved and their antimicrobial sensitivity (European Centre for Disease Prevention and Control 2015).

The answers provided by both cattle and pig veterinarians on the prophylactic use of drugs show a certain discrepancy between what is recommended in all guidelines (strict limitation of prophylactic use of antibiotics) and what happens in daily practice. It is necessary to underline, however, some peculiarities that concern the different types of breeding. In some types of breeding, for example, in pigs, the use of "*per os*" antimicrobials is commonly carried out (Burow et al. 2014) through medicated feeds in particularly stressful phases of the production cycle (Li 2017). Therefore, medicated feed can be applied for both therapeutic and prophylactic purposes.

Another important factor to be taken into account for the interpretation of the data concerns the type of cattle breeding; the study did not discriminate between dairy cow, fed lot cattle and veal calf production. Each type of breeding has specific characteristics regarding the administration of drugs for prophylactic use; as an example, we should consider the possible extensive use of antibiotics in dairy cattle during the dry period (Wittek et al. 2018).

Regarding the frequency of drug prescription for therapeutic use, we observed a difference between veterinarians of cattle and pigs (Figure 3) that reflects, again, the different approach to health problems in these two types of breeding systems. A greater frequency (daily) of drug prescription for therapeutic use can be connected to a greater demand for clinical interventions on single animals, as probably happens in cattle operations; however, in pigs daily drug prescription for prophylactic use is more relevant, assisting to the overall health management (and treatment) of animal groups (Figure 2).

Finally, potential factors influencing the choice of the antibiotic by the veterinarian were evaluated (Table 3). The "efficacy" of the antibiotic and veterinary "field experience" were the two common factors between cattle and pig breeding and were considered the most important for identifying the antibiotic to be used. For cattle veterinarians, it was essential to evaluate, among other factors, the "duration of the withdrawal period", i.e. the waiting period since the last treatment, before using the animal products for human consumption (e.g. milk). In dairy cows, the length of the withdrawal period was an important parameter to estimate the economic losses due to antimicrobial treatment, which mainly resulted from failure to collect and sell the milk produced from treated lactating cows (Shim et al. 2004). Training and scientific knowledge as well as regulatory aspects were important for pig veterinarians. External elements, such as advertising, the opinion of pharmacists, representatives from pharmaceutical companies or the opinion of farmers, did not seem to influence veterinarians' choice of antibiotics. The indication to avoid using critically important antimicrobials (CIAs) arose in the middle of the ranking, suggesting that this element was not particularly known or understood by professionals.

Alternative strategies to antimicrobials

As shown in Table 2, only a minor percentage of veterinarians believed that alternative methods could be effectively used instead of antimicrobials. However, in everyday practice, alternative measures were recommended with interestingly high frequency (Figure 4). This discrepancy can be explained by evaluating the answers provided by veterinarians for the open-ended question regarding this topic, as grouped in Table 4 and represented graphically in a word cloud (Figures 5 and 6).

In addition to "alternative therapies", such as prebiotics, probiotics, essential oils, and homeopathy, which are currently much debated (Keller and Sundrum 2018),

there are "alternative strategies" of recognised effectiveness (hygiene, biosecurity,

health management schemes, vaccines) that are recommended to the farmer as an

alternative to AMU.

The answers to the relevant open-ended question allowed for a better understanding of

the differences in sensitivity and perspectives of veterinarians, and highlighted the need

to apply other measures or tools to limit AMU in livestock.

Conclusion

This survey highlighted veterinarians' knowledge gaps and information needs about

AMR and prudent AMU. Several discrepancies emerged between the veterinarians'

opinions, perceptions and self-reported behaviour. As previously mentioned, the choice

of antibiotic administration must be supported by scientific motivations and knowledge

of the relevant legislation; however, the behaviour declared (for example, the use of

broad-spectrum antibiotics, prophylactic use of antibiotics, and CIAs) does not seem in

line with prudent AMU in the considered types of livestock production systems in Italy.

Hence, the need to provide appropriate training strategies with the aim of

adopting a behaviour more consistent with the guidelines for prudent AMU in cattle and

pig production systems has emerged.

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No potential conflict of interest was reported by the authors.

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Table 1. Socio-demographic characteristics of the two target groups (n_{g1}=422, n_{g2}=96)

Characteristics	Cattle veterinarians (%)	Pig veterinarians (%)
Gender		
Male	85.8	79.2
Female	14.2	20.8
Age		
< 45	36.3	34.4
45-60	52.1	46.9
> 60	11.6	18.7
You deal with …		
Livestock animals	64.2	79.2
Both pets and livestock animals	35.8	20.8
How long have you been working as veterinarian?		
< 10 years	23.7	16.7
10-20 years	20.1	29.2
> 20 years	56.2	54.1
Position		
Private veterinarian	68.5	72.9
Public veterinarian	31.5	27.1

Table 2. Respondents' agreement with some statements on AMU and AMR (n_{g1}=422, n_{g2}=96)

Statements	Cattle veterinarians (%)	Pig veterinarians (%)	Chi-square	p-value
Inadequate AMU in animals is dangerous for their health				
Not at all or slightly agree	14.0	16.7		
Somewhat or strongly agree	86.0	83.3	0.456	.500
Inadequate AMU in animals is dangerous for human health				
Not at all or slightly agree	13.3	19.8		
Somewhat or strongly agree	86.7	80.2	2.686	.101
Antimicrobials are over-used in Italian breeding farms				
Not at all or slightly agree	23.5	25.0		
Somewhat or strongly agree	76.5	75.0	0.102	.749
AMR is a relevant problem in Italy				
Not at all or slightly agree	23.2	28.1		
Somewhat or strongly agree	76.8	71.9	1.027	.311
Prescribing broad-spectrum antibiotics in breeding farms increases the antimicrobial resistance				
Not at all or slightly agree	30.6	40.6		
Somewhat or strongly agree	69.4	59.4	3.609	.050

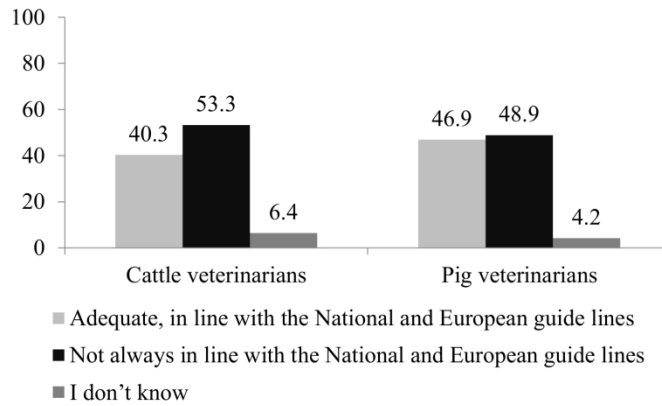|				
The preventive use of antibiotics fosters the development of AMR				
Not at all or slightly agree	14.2	30.2		
Somewhat or strongly agree	85.8	69.8	14.05	.000
Alternative methods currently available (homeopathy, phytotherapy, etc.) could be an efficient alternative to antimicrobial treatment				
Not at all or slightly agree	83.9	74.0		
Somewhat or strongly agree	16.1	26.0	5.233	.022

Table 3. (If yes) Factors influencing the choice of antibiotics to be prescribed. Median values (Likert scale from 1 minimum to 10 maximum, $n_{total\ sample}$=372, n_{g1}=304, n_{g2}=68)

Factors	Total sample	Cattle veterinarians	Pig veterinarians	Standardized test	*p*-value
Efficacy	10	9	10	2.964	.003
Field experience	9	9	9	1.687	.092
Training/scientific knowledge	9	8	9	0.754	.451
Current legislation	8	8	9	2.723	.006
Duration of the withdrawal period	9	9	8	-1.264	.206
AMR risk	8	8	8	-0.871	.384
Laboratory diagnosis including drug susceptibility testing	8	8	8	1.600	.110
Ease of administration	8	8	7.5	0.457	.647
Guidelines or national/international protocols on the rational use of drugs	7	7	7	0.394	.693
Price	7	7	6	-2.894	.004
Avoiding CIAs (critically important antimicrobials)	6	6	5	-0.967	.333
Easy access in the market	6	6	6	-1.092	.275
Opinion of a colleague	6	6	6	1.341	.180
Habit	5	6	4	-3.550	.000
Fear of penalties	5	5	6	0.702	.482
Opinion of the farmer	3	3	3	1.006	.314
Pharmaceutical representatives	3	3	3	-1.692	.091
Advertisement	2	2	2	-1.608	.108
Opinion of the pharmacist	1	1	1	-0.253	.801

Table 4. Main alternative strategies suggested by the cattle veterinarians and the pig veterinarians (total occurrences and percentages, n_{g1}=196, n_{g2}=47).

Main alternative strategies to antimicrobials	Cattle veterinarians			Pig veterinarians		
	Occurrences	%	Rank	Occurrences	%	Rank
Hygiene/Biosecurity/Management	48	15.7	1	11	13.1	3
Phytotherapy	46	15.1	2	9	10.7	4
Homeopathy/Homotoxicology	42	13.8	3	1	1.2	8
Anti-inflammatory	41	13.4	4	5	5.9	6
Vaccines	34	11.1	5	7	8.3	5
Nutritive principles	23	7.5	6	14	16.7	1
Immunostimulants	16	5.3	7	3	3.6	7
Pre-/Probiotics	10	3.3	8	12	14.3	2
Disinfectants/Antiseptics	8	2.6	9	1	1.2	8
Essential oil	3	1.0	10	5	5.9	6
Acidifying substances	1	0.3	11	9	10.7	4
Other	33	10.8	-	7	8.3	-

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Figure 1. Do you think that AMU in the breeding farms in which you work is … (%; n_{g1}=422, n_{g2}=96)

Figure 1. Do you think that AMU in the breeding farms in which you work is … (%; ng1=422, ng2=96)

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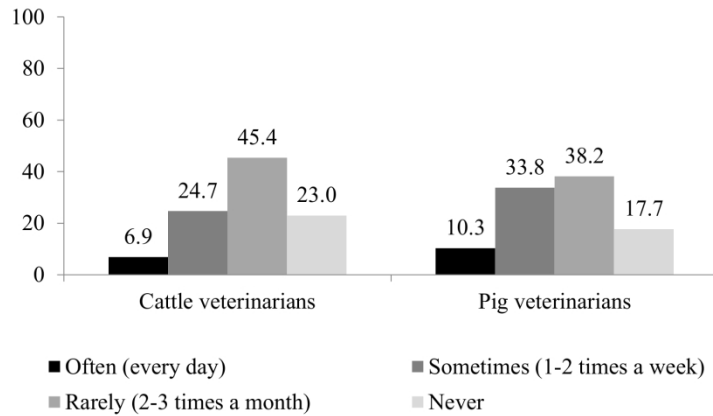Figure 2. (If Yes) How frequently do you prescribe antibiotics for prophylactic purposes? (%; n_{g1}=304, n_{g2}=68)

Figure 2. (If Yes) How frequently do you prescribe antibiotics for prophylactic purposes? (%; ng1=304, ng2=68)

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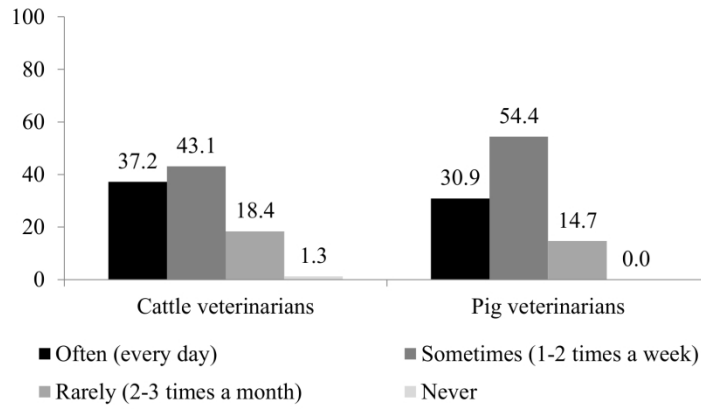Figure 3. (If yes) How frequently do you prescribe antibiotics for therapeutic purposes? (%; n_{g1}=304, n_{g2}=68)

Figure 3. (If yes) How frequently do you prescribe antibiotics for therapeutic purposes? (%; ng1=304, ng2=68)

185x114mm (300 x 300 DPI)

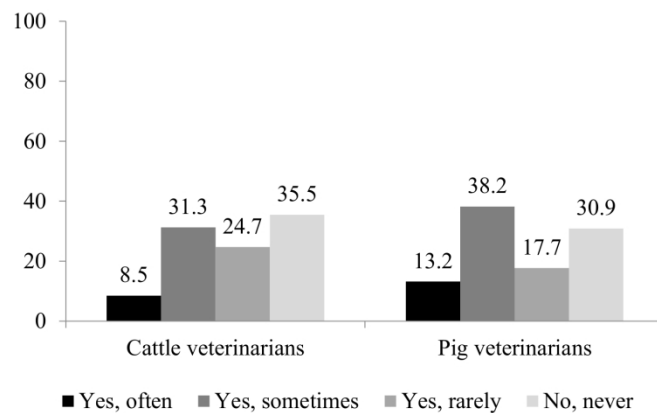Figure 4. Do you suggest or prescribe alternative strategies/therapies to antimicrobials? (%; n_{g1}=304, n_{g2}=68)

Figure 4. Do you suggest or prescribe alternative strategies/therapies to antimicrobials? (%; ng1=304, ng2=68)

185x106mm (300 x 300 DPI)

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Figure 5. Word cloud of the strategies proposed by the cattle veterinarians[a]

[a] Words with a greater number of occurrences included "Breeding farm", "Animal", "Farmer", "Biosecurity", "Veterinarian", "Antibiotic", "Animal welfare", and "Welfare".

Figure 5. Word cloud of the strategies proposed by the cattle veterinarians

193x180mm (300 x 300 DPI)

Figure 6. Word cloud of the strategies proposed by the pig veterinarians[a]
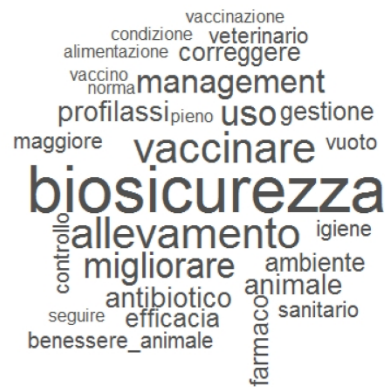
[a] Words with a greater number of occurrences included "Biosecurity", "Breeding farm", "Vaccinate", and "Improve".

Figure 6. Word cloud of the strategies proposed by the pig veterinarians

193x141mm (300 x 300 DPI)

Supplemental material

SM Tables:

Table SM1. Questions of the questionnaire included in the study

Section	Questions	Response options
Screening questions	Are you currently working as veterinarian?	Yes; no
	You deal with…	Livestock animals; pets; both livestock animals and pets; neither
Socio-demographic characteristics	Gender	Male; female
	Age	< 45; 45-60; >60
	How long have you been working as veterinarian?	< 5 years; 5-10 years; 10-20 years; > 20 years
	Which supply chain do you mainly deal with?	Fish; poultry; cattle; rabbits; equines; small ruminants; pigs; other
	Position	Freelance veterinarians; veterinarians employed in private companies; veterinarians employed in public institutions
Opinions towards AMU and AMR in breeding farms	Do you think that AMU in the breeding farms you work is…	Adequate, in line with the National and European guidelines; not always in line with the National and European guidelines; I don't know
	Indicate your degree of agreement with the following statements:	
	- "inadequate AMU in animals is dangerous for their health"	Not at all agree; slightly agree; somewhat agree; strongly agree
	- "inadequate AMU in animals is dangerous for human health"	Not at all agree; slightly agree; somewhat agree; strongly agree
	- "antimicrobials are over-used in Italian breeding farms"	Not at all agree; slightly agree; somewhat agree; strongly agree
	- "AMR is a relevant problem in Italy"	Not at all agree; slightly agree; somewhat agree; strongly agree

	- "prescribing broad-spectrum antibiotics in breeding farms increases AMR"	Not at all agree; slightly agree; somewhat agree; strongly agree
	- "the preventive use of antibiotics fosters the development of AMR"	Not at all agree; slightly agree; somewhat agree; strongly agree
	- "alternative methods currently available (homeopathy, phytotherapy, etc.) could be an efficient alternative to antimicrobial treatment"	Not at all agree; slightly agree; somewhat agree; strongly agree
Prescribing behaviours	In the exercise of your profession, do you prescribe antibiotics?	Yes; no
	(If yes) how frequently do you prescribe antibiotics for prophylactic purposes?	Often (every day); sometimes (1-2 times a week); rarely (2-3 times a month); never
	(If yes) How frequently do you prescribe antibiotics for therapeutic purposes?	Often (every day); sometimes (1-2 times a week); rarely (2-3 times a month); never
	(If yes) Factors influencing the choice of antibiotics to be prescribed	Likert scale 1-10 (1 where 1 means "it does not affect it at all" and 10 "it affects it a lot")
	Do you suggest or prescribe alternative strategies or therapies to antimicrobials?	Yes, often; yes, sometimes; yes, rarely; no, never
	(If yes) Which alternative therapies/strategies do you prescribe/suggest?	Open-ended question
	(If yes) In your opinion, which strategies could be efficacy in the AMU reduction in breeding farms?	Open-ended question

Table SM2. Translation of the main lexical units of the word clouds

Figure 5		Figure 6	
Allevamento	Breeding farm	*Biosicurezza*	Biosecurity
Animale	Animal	*Allevamento*	Breeding farm
Allevatore	Farmer	*Vaccinare*	Vaccinate
Biosicurezza	Biosecurity	*Migliorare*	Improve
Veterinario	Veterinarian	*Uso*	Use
Antibiotico	Antibiotic	*Profilassi*	Prophylaxis
Benessere animale	Animal welfare	*Antibiotico*	Antibiotic
Benessere	Welfare	*Animale*	Animal
Migliorare	Improve	*Ambiente*	Environment
Prevenzione	Prevention	*Efficacia*	Efficacy
Vaccinazione	Vaccination	*Farmaco*	Drug
Farmaco	Drug	*Correggere*	Correct
Igiene	Hygiene		
Terapia	Therapy/Treatment		
Utilizzo	Use		