# Scoping review of approaches for improving antimicrobial stewardship in livestock farmers and veterinarians

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# Title

Scoping review of approaches for improving antimicrobial stewardship in farmers and veterinarians involved in livestock animal farm management

# Abstract

Background: There has been an increased focus on antimicrobial stewardship (AMS) within the animal health domain (World Health Organization, 2015; O'Neill, 2016). Evidence of the effectiveness of interventions designed to enhance AMS is essential to support the development of this practice. This scoping review summarises for the first time the extent, range, and nature of global research activity on approaches for improving AMS in farmers and veterinarians involved in livestock farm animal management, health & well-being.

Methods: In November 2017 AGRICOLA, CAB Abstracts, EMBASE, MEDLINE, VetsRev and the Web of Science were searched. Studies were selected by two reviewers with 30% of excluded and all included studies being independently reviewed by another reviewer. Inclusion criteria were primary studies or literature reviews focusing on antimicrobial use (AMU) in farming or veterinary practices for food-producing animals. Outcomes were changes in, or factors influencing farmers' or veterinarians' AMS. Exclusion criteria were studies on wild or companion animals or reports of the level of, rather influencing factors for AMS, or knowledge/awareness related to antimicrobial resistance (AMR). Study characteristics and relevant outcomes were extracted, identified facilitators and barriers grouped into categories, and a narrative synthesis was conducted. The PRISMA checklist extension for scoping reviews was used to guide the reporting of the review.

Results: 52 studies were included in the review; seven were intervention studies and 45 were studies of facilitators and barriers of AMU or antimicrobial prescribing (AMP). Studies

were predominantly from high-income countries with only seven studies from low- or middle-income countries. Evidence for effective interventions was limited in terms of number of studies and robustness of evidence. There was some effect for an educational intervention in European cattle farmers and the Yellow Card scheme for Danish pig farmers. Significant facilitators to veterinarians' prudent AMP, in the cattle and pig livestock sector, included education, veterinarians' positive attitudes towards AMU reduction, and diagnostic. For farmers, significant facilitators to reduction of AMU most frequently related to farming management practices.

Conclusion: This review describes a scarcity of robust study designs and recommendations can be confidently made for better designed studies. Furthermore, greater consideration needs to be given to the outcome measures used in such studies. Nevertheless, the review summarises the evidence on the effectiveness of interventions and significant facilitators to farmers' and veterinarians' AMS, which can provide best currently available evidence to guide improvements in different livestock sectors.

Keywords: Antimicrobial Resistance (AMR); Antimicrobial Stewardship (AMS); veterinarians; farmers; livestock; scoping review

Abbreviations: AMP, antimicrobial prescribing; AMR, antimicrobial stewardship; AMS, antimicrobial stewardship; AMU, antimicrobial use

# Introduction

In recent years, there has been an increased focus on antimicrobial resistance (AMR) within the public and animal health domains (World Health Organization, 2015; O'Neill, 2016) with calls for enhanced antimicrobial stewardship (AMS) within both sectors. Evidence of the effectiveness of interventions designed to enhance AMS is therefore essential. Recent systematic reviews have identified the effectiveness of interventions to improve the public's (Pinder et al., 2015; Price et al., 2018) and healthcare professionals' AMS and awareness of AMR (Pinder et al., 2015; Davey et al., 2017), but no similar review exists for farmers and veterinarians.

Action has been taken by governments, veterinarians and farmers as evidenced from a number of regulatory changes that have been made worldwide to address the growing problem of AMR. In Europe, a ban on using antibiotics as growth promoters came into effect in 2006 in order to address the overexploitation or misuse of antimicrobials and tackle AMR (European Commission, 2005). More recently, the European Parliament accepted a new regulation on limiting the prophylactic AMU in food-production, which will become active in 2022 (European Parliament, 2018b, a). One of the European countries that has been particularly prominent in implementing policies on AMU are the Netherlands, where a 63.8% reduction in antimicrobial sales by veterinarians and a corresponding reduction in AMR, in indicator organisms, were observed between 2009 and 2018 (de Greeff et al., 2019). The Dutch action plans included, but were not limited to the close monitoring and centralised reporting of AMU and AMP, AMU reduction targets set by the Government, sanctioning high antimicrobial users and prescribers and restricting the use of critically important antimicrobials (Speksnijder et al., 2015).

Efforts in targeting AMR in livestock farming have also been observed in other parts of the world. For example China, one of the world's largest food producers, implemented in 2016 the National Action Plan that involved setting the maximum antimicrobial residue levels, restricting the use of certain antimicrobials, sales of antimicrobials by prescription only, and establishment of a surveillance system, which has resulted in a decrease in AMU on Chinese farms in recent years (Wu, 2019).

As a first step towards synthesising the current evidence on factors influencing farmers' and veterinarians' AMS in the context of livestock farmed animals, a scoping review was performed. In this review livestock farmed animals are defined as any animal reared for food and a scoping review as an evidence synthesis of the broad area of interest in order to map the existing evidence, identify research approaches used in the field, and to identify knowledge gaps (Peters et al., 2015). AMS is defined as a coherent set of actions (Dyar et al., 2017) associated with benefit to the animal, while minimising the risk of the emergence of AMR. This includes prudent AMP, prudent AMU and infection prevention through management of animal health and the system of farming. "Prudent AMP" refers to veterinary AMP for the treatment of infection according to veterinary good practice guidelines and "prudent use" relates to farmers' compliance with prescribers' advice when administering antimicrobials.

# Review objective

This scoping review investigated the extent, range, and nature of research activity on approaches for improving AMS in farmers and veterinarians involved in livestock farm animal management, health and well-being.

# Methods

The PRISMA checklist extension for scoping reviews (PRISMA-ScR) was used to guide the conduct and reporting of the review (Tricco et al., 2018). AGRICOLA, CAB Abstracts, EMBASE, MEDLINE and VetsRev databases along with relevant ones on the Web of Science gateway were searched in November 2017 for empirical studies. In order to ensure a comprehensive systematic search, no limits were set on language, study design or date of publication (Lefebvre et al., 2011). A combination of key words and index terms were searched related to AMU in livestock farming or veterinary practices with outcomes related to knowledge or awareness of AMR and AMS, including prudent AMP, prudent AMU, and infection prevention practices. An example of the search strategy applied to MEDLINE database is available in Supplementary file 1.

Eligibility criteria included primary studies or evidence syntheses focusing on AMU or AMP in farmed animals reared for food in the context of animal farming or veterinary practices with outcomes related to the change in or factors influencing farmers' or veterinarians' knowledge or awareness of AMR, infection prevention practices, veterinarians' AMP or farmers' prudent AMU. Studies focusing on wild or companion animals and studies reporting the level of knowledge or awareness of AMR, or AMS without a mention of change in behaviour or influencing factors were excluded from the review.

Study selection was performed between November 2017 and March 2018. Titles and abstracts of identified records were screened against the eligibility criteria by one of two reviewers (LG, CK) along with a 30% subset of excluded studies, and all potentially relevant records being independently checked by a second reviewer (LG or CK). Disagreements were resolved through discussion. All records meeting the inclusion criteria were further reviewed for eligibility by a third reviewer (LP). For the foreign-language papers, an online

translation tool was used to translate the text of the papers, while numerical data did not require translation.

Study characteristics, including the country of origin, study aims, design, type of stakeholder (e.g. farmers or veterinarians), type of farm, study sample, intervention (for intervention studies only), methods and relevant outcomes were extracted, using a tool designed for the study (Supplementary file 2), by a single reviewer, and a narrative synthesis was conducted for intervention and non-intervention studies. The number of intervention and non-intervention studies was identified per livestock sector (cattle, pigs, poultry, lamb, aquatics and generic food-producing animals) along with the number of facilitators and barriers for farmers and veterinarians. A total of 338 facilitators and barriers were identified. These were grouped into eight categories for analysis as defined by Coyne et al. (2016). These included: (1) *Veterinarian-client relationship*, such as client pressure or mutual relationship*;* (2) *External pressures* (e.g. regulatory pressures or social norms)*;* (3) *Drug-related factors* (e.g. Prophylaxis AMU or availability of antimicrobials*;* (4) *Disease epidemiology & outcomes* (e.g. diagnostic testing or vaccination)*;* (5) *Agricultural factors* (e.g. farm management practices, housing conditions)*;* (6) *Responsibility* (e.g. for animal health and well-being or for public health)*;* (7) *Knowledge* (e.g. knowledge, beliefs or perceptions on AMU or AMR, or the level of education)*;* (8) *Economic factors* (e.g. treatment costs or veterinarian's awareness of farmers' economic pressures)*.* More details on the type of factors included in each of the eight categories can be found in Supplementary file 3 (Table 2 & 3; p. 4-27). A thematic map, presented in Coyne et al. (2016*)* was used to guide decisions on allocating identified facilitators and barriers to the categories. Each barrier and facilitator was assigned to only one category by a single reviewer (LG), and checked by a second reviewer (LP) with uncertainties discussed until an agreement was reached. The allocation of the identified facilitators and barriers to categories was made after data extraction. As the review was of a

scoping design, and due to the variety of study designs included in the review, no formal quality assessment was performed (Peters et al., 2015).

# Findings

The search identified 4,405 potential articles for inclusion. After screening titles and abstracts for eligibility criteria, 75 potentially relevant papers were selected. Three of the 75 potentially relevant papers identified during titles and abstracts screening could not be retrieved through the databases that the research team had an access to. An attempt was made to request full-texts of unavailable papers from the authors, however this was not successful and the papers were excluded. Apart from one Swiss paper published in the German language (Malik et al., 2015), full-texts of all included papers were available in English. Following the full-text screening process and application of the inclusion criteria, 52 studies were included in the review (Figure 1). Of the 52 included studies, seven were intervention studies and 45 were studies of facilitators and barriers of AMU or AMP.

The majority (n= 29) of the included studies were of a survey design. The remaining studies were qualitative studies (n=10), mixed-methods studies (n=4), secondary analysis of data (n=3), case control studies (n=2), a randomized controlled trial, a quasi-experimental design study, a non-controlled before-after study, and a rapid assessment literature review. Full details on study characteristics of all 52 included studies can be found in Supplementary file 3.

Most studies (n=45) were conducted in high income countries, predominantly in Europe, including the Netherlands (n=7), UK (n=7), Denmark (n=6), Switzerland (n=5), Belgium

(n=2), France (n=2), Republic of Ireland (n=1), Italy (n=1), Sweden (n=1) and Spain (n=1). Seven studies were European multisite studies conducted in more than one high-income country, with the number of countries ranging from two to 25. Five studies from high-income non-European countries included USA (n=4) and New Zealand (n=1). Seven studies were conducted in low- to middle-income countries, including Peru (n= 2), Cambodia (n=1), Nigeria (n=1), Sri Lanka (n=1), Sudan (n=1) and Vietnam (n=1).

With regards to the livestock types, the majority of studies focused on cattle (n=20) and pig (n=16) livestock sectors. Four studies looked at poultry farming and there was one study related to sheep farming and another related to aquatic farming, namely shrimp farms. Furthermore, in 10 studies the context was farming of food-producing animals in general with the type of animals farmed not being specified, or with a number of animal types included.

## Intervention studies

Intervention studies (n=7) focused on AMU in pigs (n=4) and cattle (n=3). Apart from Arnold et al. (2004) study concerning both, farmers' AMU and veterinarians' AMP, all intervention studies focused solely on farmers' AMU. The intervention studies included one randomised controlled trial (Speksnijder et al., 2017) one quasi-experimental study (Rojo-Gimeno et al., 2016), one case control study (Kuipers et al., 2016), one non-controlled before-after study (Raymond et al., 2006) and three retrospective secondary analyses of AMP data (Arnold et al., 2004; Jensen et al., 2014; Dupont et al., 2017), with Dupont et al. (2017) study involving also a cross-sectional survey in addition to secondary data analysis. Full details of study characteristics and findings of the interventions studies can be found in Supplementary file 3 (Table 1, p. 2).

*Pig sector*

An intervention that demonstrated some effect on AMU in the pig livestock sector was the Danish Yellow Card Scheme. The scheme involved national surveillance of veterinary antibiotic use and the requirement for the farmers to reduce their AMU if a pre-set threshold was exceeded. This study demonstrated a decrease of 25% in the total AMU per pig following the intervention (Jensen et al., 2014). A later investigation conducted by Dupont et al. (2017) evaluated the effects of wider measures implemented to reduce AMU following the introduction of the Yellow Card Scheme in Denmark. They found that farmers and veterinarians most frequently indicated measures such as the increased use of vaccines (52% of farmers and 35% of veterinarians), reduction in group AMU in herds (44% of farmers and 58% of veterinarians) and staff education (22% of farmers and 26% of veterinarians, the type of education was not specified) had contributed to the reduction in AMU in their pig herds.

Outcomes, other than AMU, have also been investigated in pig farming. Arnold et al. (2004) evaluated the possible negative effects of the Swiss ban on nutritive antimicrobial growth promotion on AMU in pig farming. Low doses of antimicrobials added to feed promotes animals' growth but contributes to the development of AMR (Milanov et al., 2016). Arnold et al. (2004) hypothesised that banning the use of nutritive growth promoters could lead to increased use of antibiotics for therapeutic reasons but found no such increase in this study (3.4mg/kg prescribed daily doses (PDD)/population) in comparison to AMU prior to the intervention (3.6mg/kg PDD/population).

The costs of educational interventions for pig farmers were explored by Rojo-Gimeno et al. (2016). They assessed the economic impact of a tailored management plan consisting of measures to improve biosecurity, general management, vaccination and AMU reduction in

pig farms in Flanders. It demonstrated that costs incurred by new biosecurity measures (3.96 euros /sow/year), and new vaccinations (0.00 euros/sow/year) did not exceed the cost reduction achieved by lowering the use of antimicrobials (7.68 euros /sow/year). Furthermore, reducing AMU did not have negative impact on animals' health as the mortality of the finisher pigs was significantly reduced by -1.1% (p=0.03) following the intervention in comparison to pre-intervention (Rojo-Gimeno et al., 2016).

*Cattle sector*

An education intervention for USA cattle farmers, which also included active guidance, monitoring and feedback of AMU, demonstrated some effect on AMS (Raymond et al., 2006). There was a tendency towards a decrease in use of antibiotic medicated milk replacer for calves following the intervention with 51% of farmers reporting cessation of this practice; however, 12% of respondents who initially reported not using medicated milk replacer, initiated this undesired behaviour following the intervention (Raymond et al., 2006). Nevertheless, following the intervention other desirable changes in farmers' self-reported AMS were found, with 37% of respondents reporting decreased AMU, 27% changing their vaccination programme, 19% implementing additional biosecurity practices, 22% reporting additional colostrum management including testing of colostrum quality and calf immunity, and 28% reporting working with their veterinarian to develop herd disease treatment protocols (Raymond et al., 2006).

There were inconclusive findings in two intervention studies that had the aim of providing guidance to dairy farmers on AMU in the Netherlands. These interventions were the active guidance that involved meetings with a project team and provision of feedback to farmers on their AMU (Kuipers et al., 2016), and implementation of an animal health planning programme (Speksnijder et al., 2017). Both studies showed a significant AMU reduction in the intervention and the control groups.

In summary evidence for effective interventions was limited in terms of number of studies and robustness of evidence. There was some effect for an educational intervention in European cattle farmers and the Yellow Card scheme for Danish pig farmers.

## Non-intervention studies

The review identified 45 non-interventions studies that focused on factors influencing farmers' AMU (n=31), veterinarians' AMP (n=6) or both, AMU and AMP (n=8). A total of 144 facilitators and 194 barriers were identified. These were detailed along with study characteristics and all facilitators and barriers to both, veterinarians' prudent AMP and farmers' AMU in Supplementary file 3 (Table 2, p. 4 & Table 3, p. 11 respectively). However, when categorising facilitators and barriers, 14 could not assigned to any of the eight categories. These related to veterinarian's or farmer's characteristics, such as country of origin, age or gender. Therefore, this left the total of n=136 categorised facilitators and n=188 categories barriers that are discussed in this paper. A graphical representation of these is presented in Figure 2. The figure illustrates the number of facilitators and barriers to prudent AMP and farmers' prudent AMU identified for each category per livestock sector. We present a narrative summary of the facilitators and barriers for veterinarians' prudent AMP followed by those for farmers' prudent AMU categorised by livestock sector. A brief summary of all facilitators and barriers is given followed by a focus on statistically significant facilitators and barriers.

### All facilitators and barriers to veterinarians' prudent antimicrobial prescribing

Fourteen non-intervention studies investigated factors influencing veterinarians' prudent AMP. Facilitators (n=41) and barriers (n=59) to prudent AMP were identified for cattle, pig

and generic livestock sectors only. As shown in Figure 2, the most common facilitators to prudent AMP were related to the categories of *Disease epidemiology & outcomes* (n=8) in the cattle sector, *Agricultural factors* (n=6) and *Knowledge* (n=4) in the pig sector, and *Responsibility* (n=5) in food-producing animals.

With regards to barriers, in the cattle sector these were most frequently related to *Knowledge* (n=9), *Responsibility* (n=7) and *Veterinarian-client relationship* (n=6), whilst in the pig sector barriers related to *Disease epidemiology & outcomes* (n=5) were most common. For the generic food-producing animals on the other hand, barriers were related to *Veterinarian-client relationship* (n=4) *External pressures (n=3), Disease epidemiology & outcomes* (n=3) and *Economic factors (n=3)*. (Figure 2).

**Significant facilitators and barriers to veterinarians' prudent antimicrobial prescribing**

Significant facilitators (n=10) and barriers (n=8) to prudent AMP were identified in only two studies with one focusing on the cattle sector (Espetvedt et al., 2013) and one on the pig sector (Visschers et al., 2016). Below, we present significant facilitators and barriers to veterinarians' prudent AMP per livestock sector.

*Cattle sector*

A survey of veterinarians using the theory of planned behaviour in four Nordic countries (Espetvedt et al., 2013) focused on factors influencing veterinarians' intention to prescribe antimicrobials for mild clinical mastitis in dairy cattle. The study identified significant facilitators to prudent AMP for mild clinical mastitis were related to *Disease epidemiology & outcomes* (n=5), including availability of diagnostic test results, the ability to physically examine an animal and clinical history of the animal or herd, and one *Economic factor*,

297 namely veterinarians' consideration of treatment costs to the farmer. Significant barriers to
298 veterinarians' initiating treatment for mastitis on the other hand, were mainly related to
299 *Knowledge* (n=6), and included beliefs that initiating treatment on the same day as
300 diagnosing mild clinical mastitis produced the best outcomes. Remaining barriers included
301 *Veterinarian-client relationship* (n=1), with farmer influencing veterinarians' AMS and
302 *Responsibility* (n=1), namely related to veterinarian's prescribing behaviour being influenced
303 by other veterinarians.

304 *Pig sector*

305 A cross-sectional survey conducted within the pig livestock sectors in six European
306 countries, reported factors influencing veterinarians' self-reported reduction in AMU
307 (Visschers et al., 2016). These were found to be facilitated by factors related to *Knowledge*
308 (n=4), including veterinarian's perceived need for antimicrobial treatment, perceived
309 feasibility of AMU reduction, veterinarian attending additional courses and having greater
310 experience in pig practice. No significant barriers to veterinarians' prudent AMP were
311 identified in the pig sector.

312

313 **Summary of significant facilitators and barriers to veterinarians' prudent antimicrobial**
314 **prescribing**

315 Significant facilitators to veterinarians' AMP focused on European countries and
316 veterinarians with practices involving cattle and pigs. In these particular populations, the
317 evidence suggested strategies to improve their AMP could include education, addressing
318 veterinarians' knowledge and perceptions about AMU, and improving diagnostic processes.

319

## All facilitators and barriers to farmers' prudent antimicrobial use

There were also 39 non-intervention studies that identified factors influencing farmers' AMU in all livestock sectors, including n=95 facilitators and n=129 barriers. Facilitators related to *Agricultural factors* were the most common in all livestock sectors (n=13 in cattle, n=12 in pigs, n=7 in poultry, n=3 in aquatic sector (shrimp), n=8 in food-producing animals), with the exception of the lamb livestock sector in which *Disease epidemiology & outcomes* facilitators were most common (n=4). Furthermore, in the cattle sector, facilitators related to *Disease epidemiology & outcomes* were also frequently reported (n=11), while for food-producing animals, facilitators related to *Knowledge* were also relatively common (n=5), (Figure 2).

Like facilitators, barriers from the *Agricultural factors* category were most frequently identified for the majority of the livestock sectors, including pigs (n=12), poultry (n=7), aquatic (n=8) and food-producing animals in general (n=12). For cattle sector, barriers related to *Responsibility* (n=8) were most frequent, followed by *Agricultural factors* (n=7) and *Veterinarian-client relationship* (n=6), while for lamb sector only 3 barriers were identified. These related to one facilitator in *Drug-related factors*, *Responsibility* and *Knowledge* (Figure 2).

## Significant facilitators and barriers to farmers' prudent antimicrobial use

Amongst identified factors to farmers' prudent AMU, 51 significant facilitators and 64 barriers were identified in 24 studies.

*Cattle sector*

In the cattle sector, there were n=17 significant facilitators to farmers' prudent AMU. Most commonly, these were related to *Agricultural factors* (n=7) and included practices used when introducing new animals to the farm or herd, duration of the veal fattening period, geographical location, size of the farm or participation in a herd management program. Five

345 *Disease epidemiology & outcomes* facilitators were also identified. These were related for
346 example to the use of selective or alternative to AMU treatments for mastitis, and
347 preventative measures, such as vaccines or examination of the animals upon arrival to the
348 farm. Other significant facilitators to AMU in cattle sector were the *External pressures* (n=3)
349 from social referents, consumers and breeders' association, *Responsibility* (n=1), namely
350 farmers feeling that they should use antimicrobials prudently because of their responsibility
351 to preserve them or human health, and *Knowledge* (n=1) of inappropriate use of 3rd and 4th
352 generation cephalosporins.

353

354 With regards to significant barriers identified in the cattle sector (n=19), the most common
355 categories were *Agricultural factors* (n=9), including the size of the farm, poor housing
356 conditions, type of herd and farm management practices, such as timely replacement of teat
357 cup liners. Barriers related to *Knowledge* (n=4) included farmer's knowledge on
358 antimicrobials, perceptions on the importance of AMU in food production, causes of mastitis,
359 and farmers' level of education (high school diploma or equivalent). Other barriers included
360 *Responsibility* (n=2), namely keeping treatment records and the blanket use of antimicrobial
361 for mastitis, *Drug-related factors* (n=2) for the treatment of mastitis, *External pressures* (n=1)
362 resulting from the impact of regulations, and *Disease epidemiology & outcomes* (n=1)
363 related to the use of mastitis diagnostic test.

364

365 *Pig sector*

366 A total of 14 significant facilitators to farmers' prudent AMU in pig farming were identified
367 with facilitators related to *Agricultural factors* (n=7), such as good management practices in
368 general, good biosecurity, good general health of animals, type of farm (specialized sow
369 farms), presence of changing facilities and stockmanship. Five *Knowledge* facilitators were
370 also identified. These related to farmers' perceptions of AMR risks, efficacy for AMU

reduction and perceptions of AMU and AMR on the farm. Remaining facilitators to farmers' prudent AMU included *Veterinarian-client relationship* (n=1), in particular receiving support from the veterinarian, and *Responsibility* (n=1), in administering antimicrobials only after consulting a veterinarian.

With regards to barriers to prudent AMU in pigs (n=18), these were predominantly related to *Agricultural factors* (n=12), such as, geographical location, farm type, shorter farrowing rhythm, poor biosecurity measures and farm size. With regards to the latter, for fattening pig farms smaller farm size, while for farrow-to finish farms larger farm size was associated with increased AMU. Other barriers were related to *Knowledge* (n=3), including farmer's lower perceived risk of AMU, perceived need for AMU and higher level of farmer's education; *Disease epidemiology & outcomes* (n=2) related to the number of pathogens the animal was vaccinated against and not using homeopathic treatments; and *Drug-related factors* (n=1), such as using routine antimicrobial prophylaxis.

*Poultry sector*

In the poultry farming sector 10 significant facilitators were identified, including seven *Agricultural factors*, such as cleanliness, infection prevention measures and all-in-all-out production system. Examples of agricultural factors also included the use of growth promoters and controlled feeding regimens, and obtaining chicks from more than one hatchery. However, on farms using more than one chicks-supplying hatchery, AMU to treat infections increased; hence obtaining chick from more than one hatchery could be both, a facilitator and a barrier to prudent AMU. The remaining facilitators were from the *Disease epidemiology & outcomes* category (n=3) and all related to the use of bacterial flora to establish a protective gut flora in the animals and prevent digestive disorders.

Amongst 16 significant barriers to prudent AMU in poultry farms, most common were barriers related to *Agricultural factors* (n=7) and *Disease epidemiology & outcomes* (n=5). With regards to the former, the type of farm (meat rather than egg or mixed chicken farms and household rather than small-to-medium farms) use of whole-wheat feed, greater slaughter weight, geographical location of the farm and more than one full-time job devoted to production were associated with increased AMU. For *Disease epidemiology & outcomes*, increased AMU in broiler chickens was associated with certain diseases, namely: necrotic enteritis, respiratory disease, coccidiosis and wet litter disease. Furthermore, the use of vaccines against infectious bursal disease was significantly associated with increased therapeutic AMU. Other identified barriers to prudent AMU in poultry sectors included *Drug-related factors* (n=2) concerning prophylactic AMU; *Veterinarian-client relationship* (n=1), namely lack of support from the veterinarian; and *Responsibility* (n=1) that is not involving veterinarian in making decision to medicate flocks.

*Lamb sector*

For the lamb sector, n= 6 significant facilitators and n=3 barriers to farmers' prudent AMU were identified. Four of the facilitators were assigned to the *Disease epidemiology & outcomes* category. These factors indicated that AMU was commonly associated with certain types of disease in lambs. One *Agricultural factor* that was related to three or more lambing periods per year was also associated with decreased AMU. Interestingly, with regard to farmers' use of antimicrobials overall, having more than 20 years of practice in farming (*Knowledge* category) was associated with increased AMU on lamb-producing farms; however, farmers having 20-29 years of experience was found to be a facilitator, specifically for the use of non-licensed antimicrobials. Other significant barriers to prudent AMU included *Drug-related factors* (n=1), such as group treatment; and *Responsibility* (n=1), concerned farmer rather than the veterinarian making a decision to treat.

*Aquatic animals sector*

For AMU in the context of aquatic animal farming, only one study focusing on shrimp farms was identified, with three significant facilitators related to *Agricultural factors* (stocking density, time of harvest & farm density in the area). With regards to barriers, all were also related to *Agricultural factors* (n=8), such as the use of water fertilizers, disinfectants, feed supplements and probiotics and geographical location of the farm.

*Generic*

Only one significant facilitator to prudent AMU in generic food-producing animals was identified. This was farmers' greater *Knowledge* in relation to antimicrobials and AMR. No significant barriers were identified for the generic group of farmed animals.

**Summary of significant facilitators and barriers to farmers' prudent antimicrobial use**

For farmers, regardless of the livestock category, studies suggest that facilitators to prudent AMU predominantly relate to good farm management practices. In addition, in the pig and generic food-production sectors farmers' knowledge, and for the cattle sector factors related to disease prevention, diagnosis and mastitis treatment were influential.

# Discussion

This review of the evidence on veterinarians' prudent AMP and farmers' prudent AMU in food-producing animals found that the evidence base for effective interventions is limited and we believe the field is ripe for implementation of intervention studies across all livestock

sectors. Robust evidence of some effect is restricted to an educational intervention in European cattle farmers and the Yellow Card scheme for Danish pig farmers. There is a need to build a strong knowledge base on effective approaches for improving AMS in livestock farm animal management, health and well-being. To achieve it, further intervention studies are required in all livestock sectors, focusing on both farmers and veterinarians and using more robust experimental designs. Improved research design requires use of randomised controlled trials, non-randomised controlled trials, controlled before-after studies and interrupted time series and repeated measures studies (EPOC, 2017). Future studies should also clearly detail the active elements of the content of the intervention and the local contexts in which the intervention is to be implemented should be considered.

The dearth of research in low income countries found in this review, despite no restriction being placed on language of publications, may be a reflection of the development state of low and middle income countries in managing AMU in animals reared for food. However, as seen in the introduction, Governments and countries are taking action. The use of antimicrobials in animals is now part of AMR strategies worldwide (The White House, 2015; World Health Organization, 2015; HM Government, 2019). The World Organization for Animal Health and the European Union through the Surveillance of Veterinary Antimicrobial Consumption (World Organization for Animal Health, 2020) are supporting low- and middle-income countries to collect data on AMU in animals reared for food. It is possible that such initiatives do not include funding to research and evaluate the effects of these new systems. Funding to do so should be considered by research funders. Furthermore, perhaps these initiatives do not lend themselves particularly well to traditional academic publications as they are not necessarily led by academics or academic institutions, rather by industry or the veterinary profession. It is therefore essential that development and evaluation of new AMS initiatives in animals reared for food sector are performed in partnership with industry, practitioners and academics.

It is also noteworthy that the outcome of choice in the reviewed studies was overwhelmingly reduction in AMU. Reduction in the use of antimicrobials in food-producing animals is a laudable aim. A recent meta-analysis, of the effectiveness of interventions in reducing AMR in food-producing animals and humans, has demonstrated that restricting AMU led to a 15% reduction in antibiotic-resistant bacteria and 24–32% reduction in prevalence of multidrug-resistant bacteria in animals (Tang et al., 2017).

However, AMU derived from prescription data, is not necessarily the most appropriate outcome to use or for use on its own. Although, prescription data on AMU as an outcome measure may have some benefits, in that it is quantifiable, may be readily available as part of routine practice, and could be considered reliable. Validity of such measures may be affected by prescriptions not being recorded (Pinto Ferreira, 2017), courses of antimicrobials not being completed (Chan et al., 2012), antimicrobials being purchased online (Morgan et al., 2011) or over the counter in some countries (Om and McLaws, 2016) and AMU in animal feed not requiring a prescription.

Another problem is a lack of consistency in the use of metrics for AMU reporting (Mills et al., 2017; Pinto Ferreira, 2017), despite efforts to standardise the measure and reporting of AMU. The European Medicines Agency established standardised units of measurement for reporting antimicrobial consumption at the European level: 'defined daily dose' (DDDvet) and 'defined course dose' (DCDvet). However, these metrics use fixed daily dose (DDDvet) or fixed course dose (DCDvet) defined per active substance and administration route rather than per individual product, and are based on the mean dose of all veterinary medicine products documentation from nine European countries (European Medicines Agency, 2015). Therefore, does not account for different course lengths. Furthermore, such measures can

only be used in countries with established AMU surveillance systems, and as this review demonstrated, are not being used consistently across the studies. Thus, further efforts are required to improve standardised reporting.

Furthermore, to engage farmers and veterinarians in AMS it may be necessary to consider other outcomes. It would be worth considering the desire of both farmers and veterinarians to rear healthy food-producing animals in the most cost effective and time efficient manner. It is acknowledged that the primary outcomes examined in this review were related to AMU but only two of the included studies had secondary animal health and well-being outcomes (Speksnijder et al., 2017). It is possible that using antimicrobials prudently and complementing this approach with implementation of interventions promoting animal health could contribute towards reduction in AMU. Appreciating the drivers of farmers' and veterinarians' AMS and the requirement for valid outcomes, it would seem that outcome measures related to prudent use of antimicrobials in food-producing animals along with outcomes related to the health status of the animals would be appropriate when evaluating the effectiveness of approaches for improving AMS. If this was the case then prudent AMU, rather than total use of antimicrobials, as defined by type, dose and duration as appropriate for the animal given the presenting condition and context (Mills et al., 2017) would be the outcome of choice. This could be used alongside those measuring the cost of implementation of the intervention and health status of the animals.

The strengths of this systematic scoping review are that it was conducted in a systematic and rigorous manner and that, to the best of our knowledge, this is the first review assessing the body of evidence on interventions for improving AMS and facilitators and barriers to prudent AMU and AMP in livestock farmers and veterinarians. The search comprised an extensive range of appropriate index terms and free-text words and spanned five major databases. Furthermore, the use of PRISMA-ScR checklist (Tricco et al., 2018) helped to enhance rigour and improved the quality of review reporting. The results demonstrate the

need to enhance the evidence base from low-income countries and a larger range of livestock sectors. However, it should be acknowledged that our review did not assess the quality of the included studies so findings should be considered with these two limitations in mind.

This scoping review summarises for the first time the extent, range, and nature of global research activity on approaches for improving AMS in farmers and veterinarians involved in livestock farm animal management, health & well-being. It sets the agenda for future research as it describes a scarcity of robust study designs and recommends improvements in research designs for studies in this area. Furthermore, it provides a new direction for outcome measures in the research agenda suggesting, that in addition to those related to AMU, secondary outcomes regarding animal health and well-being need to be considered. Finally, this evidence synthesis summarises the current evidence to guide strategies to improve AMS in farmers and veterinarians.

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## Declaration of Competing Interest

None.


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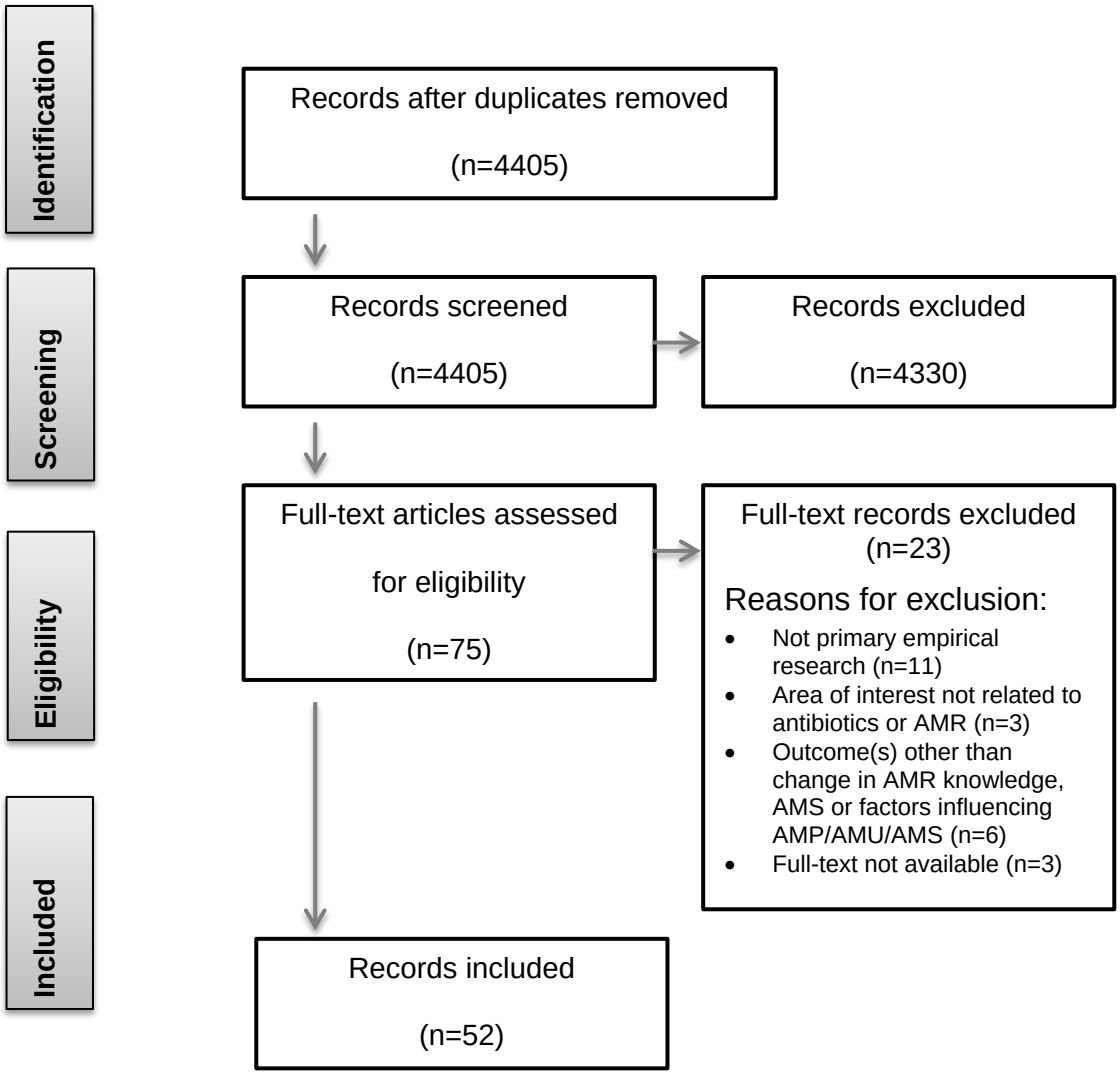
# Appendix A

## Supplementary materials

1. Search strategy applied in MEDLINE database
2. Data extraction tool
3. Characteristics of studies included in the review

Supplementary material related to this article can be found, in the online version, at [insert http address]

680 Figure 1. Study selection flowchart

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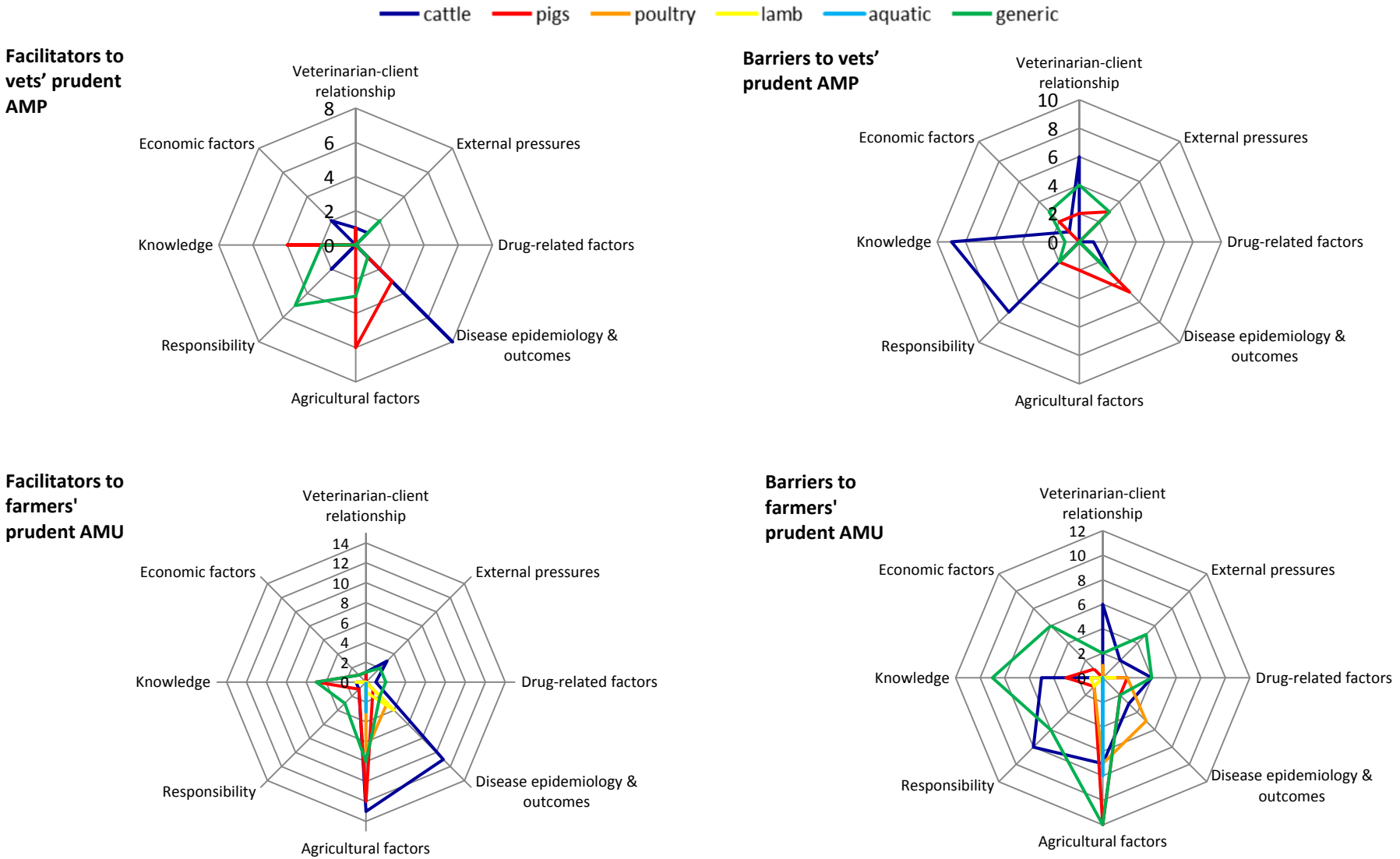
683 Figure 2. The number of identified facilitators and barriers to vets' prudent AMP and farmers' prudent AMU per category in livestock sectors



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# Supplementary file 1

**Scoping review of approaches for improving antimicrobial stewardship in livestock farmers and vets: search strategy applied in MEDLINE database**

| | |
|---|---|
| *Population* | |
| 1 | MH "Animals, Domestic" |
| 2 | MH “Livestock” |
| 3 | (livestock OR “farm animal*” OR “domestic* animal*” OR “food animal*” OR “food-producing animal*” OR flock* OR herd*):ti,ab |
| 4 | MH "Poultry" |
| 5 | MH "Quail" |
| 6 | (poultry OR fowl* OR chicken* OR chick* OR rooster* OR hen* OR pullet* OR capon* OR pullet* OR “domestic* bird*” OR duck* OR turkey* OR goose OR geese OR quail OR “guinea fowl*”):ti,ab` |
| 7 | MH "Cattle" |
| 8 | MH "Buffaloes" |
| 9 | (cattle OR kine OR cow* OR ox* OR bull* OR bovid* OR bovine OR bullock* OR heifer* OR calves OR calf OR longhorn* OR shorthorn* OR buffalo* OR ruminant*):ti,ab |
| 10 | MH "Sheep" |
| 11 | (sheep OR ewe* OR ram* OR lamb* OR wether*):ti,ab |
| 12 | MH "Goats" |
| 13 | (goat* OR billygoat* OR billy OR billies OR kid* OR nanny OR nannies):ti,ab |
| 14 | MH "Swine" |
| 15 | (pig* OR swine* OR hog* OR boar* OR sow* OR piglet*OR shoat*OR shote*):ti,ab |
| 16 | MH "Salmon" |
| 17 | (salmon OR “farmed fish”):ti,ab |
| 18 | MH "Deer" |
| 19 | (deer OR stag*OR hind*):ti,ab |
| 20 | MH "Farmers" |
| 21 | (farmer* OR agriculturalist*OR agriculturist* OR rancher* OR smallholder* OR breeder* OR grazier* OR farmhand* OR “farm-hand*” OR crofter* OR shepherd* OR cowherd* OR cowhand* OR cowm?n OR herdsm?n OR herder* OR cattlem?n OR stockm?n OR sheepm?n OR worker* OR labo#rer* OR employee* OR staff):ti,ab |
| 22 | MH "Veterinarians" |
| 23 | (veterinarian* OR vet* OR “veterinary surgeon*” OR “veterinary physician*” OR “veterinary practitioner*”):ti,ab |
| 24 | ((MH "Animal Feed") |
| 25 | ((“animal feed” OR “animal food” OR provender OR fodder OR forage OR supplement* OR mineral* OR vitamin* OR nutrient*) N4 (supplier* OR producer* OR provider* OR seller* OR contractor* OR contributor* OR manufacturer*)):ti,ab |
| 26 | OR/1-25 |
| *Area of Interest* | |
| 27 | MH "Anti-Infective Agents” |
| 28 | MH "Anti-Bacterial Agents" |
| 29 | MH "Drug Resistance, Microbial+" |
| 30 | MH "Drug Resistance, Multiple+” |
| 31 | (multiresistant OR multiresistance OR "multi-resistant" OR "multi-resistance" OR MDR OR MDRO* OR pandrug OR “pan-drug” OR PDR OR AMR):ti,ab |
| 32 | ((drug* OR multidrug OR “multi-drug” OR antimicrobial* OR “anti-microbial*” OR antiinfection* OR “anti-infection*” OR “anti-infective” OR antiinfective OR antibacterial* OR “anti-bacterial*” OR antibiotic* OR “anti-biotic*” OR Fluoroquinolone* OR Cephalosporin* OR “beta-lactam*” OR penicillin* OR aminoglycoside* OR Streptogramin* OR Glycopeptide* OR Macrolide*) N4 (resistant OR resistance OR tolerant OR tolerance)):ti,ab |
| 33 | OR/27-32 |
| *Context* | |

| | |
|---|---|
| 34 | MH "Farms" |
| 35 | MH "Animal Husbandry" |
| 36 | MH "Organic Agriculture" |
| 37 | (farm* OR farming OR “food-production*” OR farmstead* OR ranch* OR smallholding* OR farmland* OR grassland* OR pasture*OR “animal feeding operation*” OR AFO OR AFOs OR CAFO OR CAFOs OR “livestock operation*” OR husbandry OR agriculture OR agribusiness*):ti,ab |
| 38 | MH "Fisheries" |
| 39 | MH "Aquaculture" |
| 40 | (fishery OR fisheries OR “fish farm*” OR aquaculture* OR pisciculture* OR aquafarm* OR “salmon farm*”):ti,ab |
| 41 | MH "Dairying" |
| 42 | MH "Eggs" |
| 43 | ((meat OR dairy OR milk OR egg* OR cheese*) N4 (product* OR producing OR supply OR supplie* OR farm* OR provid* OR provision*)):ti,ab |
| 44 | MH "Veterinary Medicine" |
| 45 | MH "Hospitals, Animal" |
| 46 | ((vet* OR veterinary OR animal*) N4 (practice* OR hospital* OR clinic* OR surgery OR surgeries OR centre* OR center* OR medicine)):ti,ab |
| 47 | OR/34-46 |
| *Outcomes* | |
| 48 | ((inappropriat* OR irrational OR imprudent OR unnecessar* OR irresponsibl* OR misuse* OR improper* OR mistake* OR indiscriminat* OR suboptim* OR bad OR overuse* OR excessiv* OR vary OR varied OR variation OR poor OR unsafe*) N4 (antimicrobial* OR "anti-microbial*" OR antiinfection* OR "anti-infection*" OR antibacterial* OR "anti-bacterial*" OR antibiotic* OR "anti-biotic*") N4 (use OR usage OR using OR consumption OR buy* OR purchas* OR acquir* OR obtain* OR sell* OR trad* OR utili?e OR treatment* OR dispos* OR storage OR storing OR sharing OR shared OR expectation* OR request* OR administ* OR dispens* OR demand* OR prescribe* OR prescript*)):ti,ab |
| 49 | ((appropriat* OR rational OR prudent OR judicious* OR optimal* OR correct OR proper* OR responsibl* OR safe* OR good OR decreas* OR limit* OR curb* OR minimi?e* OR minimal* OR lessen* OR curtail* OR abate* OR restrict* OR lower* OR discontinue* OR delay*) N4 (antimicrobial* OR "anti-microbial*" OR antiinfection* OR "anti-infection*" OR antibacterial* OR "anti-bacterial*" OR antibiotic* OR "anti-biotic*") N4 (use OR usage OR using OR buy* OR purchas* OR acquir* OR obtain* OR sell* OR trad* OR utili?e OR treatment* OR consumption OR dispos OR storage OR storing OR sharing OR shared OR expectation* OR request* OR administ* OR dispens* OR demand* OR prescribe* OR prescript*)):ti,ab |
| 50 | ((behavio#r N3 (change* OR changing OR alter* OR modification* OR modify OR modifying OR modifies OR modified)) OR intention*):ti,ab |
| 51 | (attitude* OR belief* OR view* OR opinion* OR expectation* OR "anticipat* regret" OR knowledge OR awareness OR "risk perception*" OR "perceived risk*" OR "perceived susceptibility" OR "treatment perception*"):ti,ab |
| 52 | ((antimicrobial OR “anti-microbial” OR antiinfection OR “anti-infection” OR antibacterial OR “anti-bacterial” OR antibiotic OR “anti-biotic”) N3 (stewardship)):ti,ab |
| 53 | (MH "Infection Control") |
| 54 | (MH "Communicable Disease Control") |
| 55 | ((“infection prevention” OR “infection control” OR “infection prevention and control” OR IPC OR “cross-infection prevention” OR “universal precautions”) N4 (practice* OR practis* OR procedure* OR follow* OR method* OR implement* OR compliance OR adhere* OR routine* OR obedience OR obey* OR conform*)):ti,ab |
| 56 | OR/48-55 |
| 57 | AND/26, 33, 47, 56 |

## Supplementary file 2.

**Scoping review of approaches for improving antimicrobial stewardship in livestock farmers and vets: Data extraction tool**

| Study ID | Country | Study aim(s) | Study design | Type of stakeholder(s) (i.e. farmer/veterinarian) | Type of animals/farms | Sample | Nature of intervention(s)<br><br>(intervention studies only) | Comparator<br><br>(intervention studies only) | Data collection methods | Outcome measures | Relevant findings |
|---|---|---|---|---|---|---|---|---|---|---|---|
| First author, (year) | | | | | | | | | | | |
| | | | | | | | | | | | |
| | | | | | | | | | | | |
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## Supplementary file 3.

**Characteristics of studies included in the review**

Table of content

## Table 1. Characteristics of the intervention studies

| *Farming sector* | Study ID | Country | Study aim(s) | Study design | Type of stakeholder(s) | Sample | Nature of intervention(s) | Comparator | Data collection methods | Outcome measures |
|---|---|---|---|---|---|---|---|---|---|---|
| *Dairy cattle farms* | Kuipers et al. (2016) | Netherlands | To examine the variation in AMU and the effects of external factors on trends in antibiotic use at the herd level | Case control study | Farmers | N=94 dairy herds | Actively guided use of antibiotics, biannual meetings with project team members and a veterinarian; provision of AMU feedback reports | Lack of active guidance | Data collected from antimicrobials purchase invoices and veterinary visits records | AMU (ADDD) |
| *Dairy cattle farms* | Raymond et al. (2006) | USA (Washington state) | (1) to describe AMU and biosecurity practices among dairy producers; and (2) to evaluate the effectiveness of a collaborative approach to promoting prudent AMU on dairy farms | Non-controlled before-after study | Farmers | N=381 dairy farms | Educational intervention (letters, newsletters, press release on the colostrum management and calf immunity testing and the use of antibiotic-medicated milk replacer); kits for testing colostrum and calves' immunity; a reference manual on disease management and AMU and dictionary of terms | Pre-intervention | Postal questionnaires | AMU (percentage of farmers who report using particular type of antimicrobial); use of medicated milk replacer and infection prevention and control practices |
| *Dairy cattle farms* | Speksnijder et al. (2017) | Netherlands | To evaluate the main effects of an animal health planning program | Randomized controlled trial | Dairy farmers | N= 35 dairy farmers | Animal health planning program | None | The quality of the animal health planning process assessed during farm visits; farm-level AMU reports | AMU (ADDD); animal health & production parameters; compliance with animal health programme objectives |
| *Piglets & fattening pigs farms* | Arnold et al. (2004) | Switzerland | To find out whether the ban on nutritive antimicrobial growth promotion introduced in Switzerland in 1999 had caused an increase in the therapeutic AMU given orally to piglets and fattening pigs. | Retrospective secondary data analysis | Farmers & veterinarians | N=6427 medicated feed prescriptions | Ban on nutritive antimicrobial growth promotion | Pre-intervention | Veterinary prescribing data | Therapeutic AMU given orally (PDD and amount of active antimicrobial ingredient) |
| *Sow &* | Dupont et | Denmark | To (1) investigate | Retrospective | Farmers | N= 179 farmers | Yellow card scheme | Pre- | Questionnaires & | AMU (amount of |

| *Farming sector* | Study ID | Country | Study aim(s) | Study design | Type of stakeholder(s) | Sample | Nature of intervention(s) | Comparator | Data collection methods | Outcome measures |
|---|---|---|---|---|---|---|---|---|---|---|
| *piglets, weaners & finishers pig farms* | al. (2017) | | which measures had been implemented to reduce the antimicrobial consumption according to farmers and veterinarians and (2) investigate if said measures were reflected in antimicrobial purchase data | secondary data analysis & cross-sectional survey | | & N=58 veterinarians | (AMU thresholds) | intervention | Danish national database on prescribed veterinary medicine (antimicrobial purchase data) | active antimicrobial ingredient per pig, ADD per 100 pigs per day & ADDD); measures implemented to reduce AMU |
| *Weaner & finisher pig farms* | Jensen et al. (2014) | Denmark | To investigate the potential effects of the Yellow Card on AMU in the Danish pig production | Retrospective secondary data analysis | Farmers | Antimicrobial prescription from January 2002 to December 2012 (N not provided) | Yellow card scheme (AMU thresholds) | Pre-intervention | Danish national database on prescribed veterinary medicine (antimicrobial prescription data) | AMU ($ADDD_{25}$ per pig produced) |
| *Farrow-to-finish pig farms* | Rojo-Gimeno et al. (2016) | Belgium (Flanders) | To assess the economic impact of substituting improved management practices, particularly biosecurity strategies, for AMU | Quasi-experimental study | Farmers | N=117 farms | Tailored management intervention plan (consisting of measures to improve biosecurity, general management, vaccination and AMU) | None | Farm visits involving completion of questionnaires & face-to-face surveys | Economic impact |

AMU = antimicrobial use; PDD = Prescribed Daily Doses; ADD = Animal Daily Doses; ADDD = Animal-Defined Daily Doses; $ADDD_{25}$ = the standard dose for treatment of 25 kilograms of body weight

**Table 2. Characteristics of all studies that identified facilitators and barriers to veterinarians' prudent antimicrobial prescribing**

| *Farming sector* | Author and year | Country | Study aim(s) | Study design | Sample | Data collection methods | Relevant outcome measures | Identified significant facilitators to prudent AMP | Identified significant barriers to prudent AMP |
|---|---|---|---|---|---|---|---|---|---|
| *Dairy cattle farms* | **Espetvedt et al. (2013)*** | Denmark, Finland, Norway & Sweden | To (1) investigate whether Nordic veterinarians, on a between country-level, vary in their intention to start medical treatment of a dairy cow with mild clinical mastitis, on the same day as making the diagnosis; and to (2) study the underlying behavioural components of the intention score within each country | Cross-sectional survey | N=543 veterinarians with cattle treatment records | Postal questionnaire | Intention scores for initiating treatment for mild clinical mastitis on the same day as making the diagnosis | **Disease epidemiology & outcomes (n=5)**<br>Lack of knowledge about the bacterial pathogens involved in the mild clinical mastitis case ($p<0.05$); lack of knowledge about the history of bacterial pathogens involved in mastitis within the herd ($p<0.05$); ability to examine the cow with mild clinical mastitis in conjunction with other work during a farm visit ($p<0.05$); diagnostic/ sensitivity test results: finding the Bulk milk somatic cell count status on the farm to be good ($p<0.05$); clinical history - the cow with mild clinical mastitis having high somatic cell count or repeated mastitis events in the same lactation ($p<0.05$)<br>**Economic factors (n=1)**<br>Veterinarian's consideration of treatment costs to the farmer of treating the cow ($p<0.05$)<br>**Uncategorised (n=1)**<br>Country of origin: veterinarians in Finland had the lowest mean intention score for initiating the treatment for mild clinical mastitis on the same day as making the diagnosis in comparison with other countries ($p<0.05$) | **Veterinarian-client relationship (n=1)**<br>Farmers influencing veterinarian's behaviour on starting treatment on the same day as making the diagnosis ($p<0.05$)<br>**Responsibility (n=1)**<br>Other veterinarians influencing veterinarian's behaviour on starting treatment on the same day as making the diagnosis ($p<0.05$)<br>**Knowledge (n=6)**<br>Veterinarian's beliefs that: initiating treatment on the same day as diagnosing mild clinical mastitis gives the best results compared to delaying treatment ($p<0.05$); prevents blind teats ($p<0.05$); ensures more milk in the bulk tank on a long term ($p<0.05$); contributes to reduced somatic cell count in a herd ($p<0.05$); prevents further spread of mastitis bacteria in a herd ($p<0.05$); and will make the farmer more satisfies ($p<0.05$)<br>**Uncategorised (n=1)**<br>Country of origin: veterinarians in Denmark had the highest mean intention score for initiating the treatment for mild clinical mastitis on the same |

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| | | | | | | | | | day as making the diagnosis in comparison with other countries ($p<0.05$) |
| ***Dairy cattle farms (no details provided)*** | **Gibbons et al. (2013)** | UK (Ireland) | To determine if (1) non-clinical issues influence the veterinary surgeons' decision to prescribe antimicrobials; and if (2) a range of pharmacological and non-pharmacological issues influence the veterinary surgeons' choice of antimicrobials prescribed | Cross-sectional survey | N=118 veterinary surgeons working in cattle practice | Questionnaire (distributed at veterinary society meetings) | Factors influencing AMP | None | **Veterinarian-client relationship (n=2)** Farmers' pressure/demands (57.5% of respondents); blame if antimicrobials later prove necessary (55.8% of respondents)<br>**Disease epidemiology & outcomes (n=1)** Lack of confidence in their diagnosis (40.2% of respondents)<br>**Responsibility (n=1)** Being called again if animal does not improve (49.5% of respondents) |
| ***Dairy cattle farms*** | **Higgins et al. (2017)** | UK (England) | To explore how veterinarians rationalised their prescribing decisions for mammary treatments at drying off, and the barriers and motivators they perceived to implementing selective dry cow therapy | Qualitative study | N=20 veterinarians with clinical large animal experience | Face-to-face interviews | Factors influencing AMP; barriers and facilitators to implementing Selective Dry Cow Therapy | **Veterinarian-client relationship (n=1)** Rising farmers' awareness<br>**External pressures (n=1)** Legislation and guidelines pressure<br>**Disease epidemiology & outcomes (n=1)** Availability of diagnostic tests<br>**Responsibility (n=2)** Veterinarians' united commitment to implementation of selective dry cow therapy; veterinarian (rather than farmer) administering the treatment<br>**Economic factors (n=1)** Economic incentives for the implementation of selective dry | **Veterinarian-client relationship (n=2)** Conflicts of interests; difficulties when engaging with the farmers<br>**Disease epidemiology & outcomes (n=2)** Concerns over adverse outcomes with teat sealants versus antibiotics; lack of reliable data that would allow for the identification of uninfected cows<br>**Responsibility (n=3)** Concerns over farmer's ability to administer internal teat sealants; |

| *Farming sector* | Author and year | Country | Study aim(s) | Study design | Sample | Data collection methods | Relevant outcome measures | Identified significant facilitators to prudent AMP | Identified significant barriers to prudent AMP |
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| | | | | | | | | cow therapy | veterinarian's seniority; concerns over the SDCT treatment complexity<br>**Knowledge (n=1)**<br>Limited knowledge and awareness surrounding selective dry cow therapy |
| ***Dairy cattle farms*** | **McDougall et al. (2017)** | New Zealand | To determine the factors associated with the selection of antimicrobials by dairy veterinarians, and the attitudes of those veterinarians and dairy farmers to AMU and AMR | Mixed methods study | N=22 dairy farmers & N=206 dairy cattle veterinarians | Facilitated focus groups (veterinarians and farmers) & online survey ( veterinarians) | Factors influencing AMP | **None – reported factors influencing selection of antimicrobials, but no barriers or facilitators** | |
| ***Dairy cattle farms*** | **Redding et al. (2013)** | Peru (Cajamarca) | To (1) obtain the perspectives of antibiotic providers on current AMU and its appropriateness by dairy farmers in Cajamarca; (2) to determine which factors influence a provider's prescribing practices; and (3) to compare these 2 aims between veterinarians and feed-store vendors | Qualitative | N=20 veterinarians and feed store vendors | Focus groups and semi-structured face-to-face interviews | Factors influencing AMP | **Disease epidemiology & outcomes (n=2)**<br>Understanding the importance of the clinical situation; ability to examine an animal | **Veterinarian-client relationship (n=1)**<br>Farmer's preferences<br>**Drug-related factors (n=1)**<br>Widespread availability of drugs /prescriber's inventory<br>**Responsibility (n=2)**<br>Farmer's habits and practices of using particular drugs; competition from other prescribers<br>**Knowledge (n=2)**<br>Concerns over farmer's low level of education; concerns over farmer's poor understanding of the drug indications<br>**Economic factors (n=1)**<br>Awareness of farmers' economic pressures |

| *Farming sector* | Author and year | Country | Study aim(s) | Study design | Sample | Data collection methods | Relevant outcome measures | Identified significant facilitators to prudent AMP | Identified significant barriers to prudent AMP |
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| ***Pig farms (types not specified)*** | **Coyne et al. (2014)** | UK | To investigate the drivers and motivators behind the AMU and AMP patterns in the pig industry | Qualitative study | N=26 farmers & veterinarians | Focus groups | Drivers and motivators of AMP | **Disease epidemiology & outcomes (n=2)**<br>Use of diagnostic tests; vaccines<br>**Agricultural factors (n=3)**<br>Good farming practices in general; improved farm facilities; good health status of the herd | **Veterinarian-client relationship (n=1)**<br>Farmers' pressure/demands<br>**Disease epidemiology & outcomes (n=1)**<br>Disease epidemiology in general |
| ***Pig farms (types not specified)*** | **Coyne et al. (2016)** | UK | To explore the attitudes, motivations and reasoning behind AMP decisions by pig veterinary surgeons | Qualitative study | N= 21 pig veterinary surgeons | Qualitative, semi-structured interviews | Drivers and motivators of AMP and dispensing decisions; barriers to reducing AMU for both prophylaxis and treatment | **Veterinarian-client relationship (n=1)**<br>Acknowledging a mutual relationship and shared responsibility for AMU between veterinarian and a farmer<br>**Disease epidemiology & outcomes (n=1)**<br>Vaccines<br>**Agricultural factors (n=3)**<br>Good farming practices in general; good stockmanship; improved farm facilities | **Veterinarian-client relationship (n=1)**<br>Farmers' pressure/demands<br>**External pressures (n=3)**<br>Importation pressure; pressure from food retailers; poor public perception<br>**Disease epidemiology & outcomes (n=4)**<br>Disease consequences; lack of confidence in diagnosis; time delay when waiting for diagnostic test results; short, or lack of withholding period<br>**Agricultural factors (n=2)**<br>Old, poorly managed buildings; poor health status of animals<br>**Responsibility (n=2)**<br>Concerns over farmer's compliance with the treatment; veterinarian feeling professional responsibility for animal health & well-being<br>**Economic factors (n=2)**<br>Low cost of the drug; awareness of farmer's economic pressure |

| *Farming sector* | Author and year | Country | Study aim(s) | Study design | Sample | Data collection methods | Relevant outcome measures | Identified significant facilitators to prudent AMP | Identified significant barriers to prudent AMP |
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| ***Pig farms (all types)*** | **Visschers et al. (2016)*** | Denmark, Belgium, France, Germany, Sweden, Switzerland | To (1) investigate pig farmers' and veterinarians' perceptions of AMU and reducing AMU; and (2) to identify the demographic and perception variables associated with the intention to reduce AMU among pig farmers and reduction behaviours among veterinarians | Cross-sectional survey | N=1,294 pig farmers & N=334 veterinarians with a reported pig practice | Postal questionnaire (farmers) & online questionnaire (veterinarians) | Factors influencing veterinarians' intentions to reduce AMU | **Knowledge (n=4)** Veterinarian attending more types of additional courses ($p<0.001$); less than 50% of time spent in pig practice ($p<0.001$); veterinarian's lower perceived need for antimicrobials ($p<0.05$); higher perceived feasibility of reducing antimicrobials ($p<0.001$) **Uncategorised (n=1)** Veterinarian being from France, Sweden or Switzerland ($p<0.05$) | None |
| ***Generic (Food producing animals, companion animals, equines)*** | **Briyne et al. (2013)** | 25 European countries | To identify factors and information sources used to decide prescribing behaviour, influencers for seeking antimicrobial sensitivity testing and the frequency of use of such services | Cross-sectional survey | N= 3004 practitioners Food-producing animals' veterinarians N=1766 (58.8% of the total sample) | Online questionnaire | Factors and information sources influencing AMP | **None – reported factors influencing selection of antimicrobials, but no farriers or facilitators** | |
| ***Generic (types of farms not stated)*** | **Hockenhull et al. (2017)** | UK | To investigate what is currently known about AMU in food-producing animals, encompassing their use at farm level, the practices and perceptions of the stakeholders involved in their administration, and the availability and validity of data on their use in practice | Rapid assessment literature review | N= 48 peer-reviewed papers | Research on AMU published in peer-reviewed journals between 2000 and 2016 | Factors influencing veterinarians' AMP | **Disease epidemiology & outcomes (n=1)** Use of diagnostic/sensitivity tests **Responsibility (n=1)** Feeling responsibility for public health | None |
| ***Generic (types of farms not stated)*** | **Magalhães-Sant'Ana et al. (2017)** | Ireland | To provide a value-based reflection on the constraints and possible opportunities for responsible use of | Qualitative case study | N=8 experts (a dairy farmer, national regulatory body representatives, | Focus groups | Barriers and constrains to responsible AMU and AMP | **External pressures (n=1)** Improved regulations **Responsibility (n=2)** Implementing a 'one farm, one vet' policy where a single | **Veterinarian-client relationship (n=1)** Farmers' pressure/demands **External pressures (n=2)** External pressures in |

| *Farming sector* | Author and year | Country | Study aim(s) | Study design | Sample | Data collection methods | Relevant outcome measures | Identified significant facilitators to prudent AMP | Identified significant barriers to prudent AMP |
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| | | | veterinary antimicrobials in Ireland | | veterinarians) | | | veterinarian holds responsibility over the particular farm; electronic prescribing/centralised recording<br>**Knowledge (n=2)**<br>Veterinarian attending additional courses; improving veterinarians' knowledge and awareness surrounding antimicrobials and AMR | general; lack of good regulations<br>**Disease epidemiology & outcomes (n=1)**<br>lack of sensitivity testing<br>**Knowledge (n=1)**<br>Lack of reliable farm-level data on AMU |
| ***Generic (types of farms not stated)*** | **Postma et al. (2016)** | Flanders & Netherlands | To quantify opinions of veterinarians from the Netherlands and Flanders regarding AMU and resistance issues in farm animals | Cross-sectional survey | N=611 veterinarians | Online questionnaire | Factors influencing AMU reduction and AMP | **Responsibility (n=1)**<br>Motivation for conserving veterinary antimicrobials in the future | **Veterinarian-client relationship (n=1)**<br>Farmers' pressure/demands<br>**Responsibility (n=1)**<br>Professional responsibility for animal health and well-being<br>**Economic factors (n=1)**<br>Financial incentives for the veterinarian |
| ***Generic (poultry, pig, dairy cattle and veal calf farms)*** | **Speksnijder et al. (2015a)** | Netherlands | To identify determinants influencing farm animal veterinarians' AMP | Qualitative study | N=11 farm animal veterinarians | Semi-structured interviews | Factors influencing AMP | **Agricultural factors (n=1)**<br>Farm visits to identify and avoid risks<br>**Responsibility (n=1)**<br>Feeling responsibility for public health | **Veterinarian-client relationship (n=1)**<br>Farmers' pressure/demands<br>**External pressures (n=1)**<br>Pressure from advisors<br>**Disease epidemiology & outcomes (n=2)**<br>Fear of alternative therapy treatment failure; time delay when waiting for diagnostic test results<br>**Responsibility (n=1)**<br>Professional responsibility for animal health & well-being<br>**Economic factors (n=2)**<br>Cost control; awareness of farmers' economic pressures |

| *Farming sector* | Author and year | Country | Study aim(s) | Study design | Sample | Data collection methods | Relevant outcome measures | Identified significant facilitators to prudent AMP | Identified significant barriers to prudent AMP |
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| ***Generic (poultry, pig, dairy cattle and veal calf farms)*** | **Speksnijder et al. (2015b)** | Netherlands | To (1) explore differences in attitudes towards AMU and reduction opportunities in farm animals; (2) and the interaction of veterinarians with farmers in improving animal health and reducing AMU between categories of veterinarians | Cross-sectional survey | N=377 completed questionnaires from veterinarians | Online questionnaire | Factors influencing AMP; factors influencing solutions for high AMU | **External pressures (n=1)** Benchmarking of AMU and AMP prescribing<br>**Agricultural factors (n=2)** Improved feed quality; improvements in housing and climate and benchmarking | **Veterinarian-client relationship (n=1)** Farmers' pressure/demands |

*Study reported significant facilitators and/or barriers to veterinarians' prudent antimicrobial prescribing; AMP = antimicrobial prescribing; AMR = antimicrobial resistance; AMU = antimicrobial use

**Table 3. Characteristics of all studies that identified facilitators and barriers to farmers' prudent antimicrobial use**

| *Farming sector* | Study ID | Country | Study aim(s) | Study design | Sample | Data collection methods | Relevant outcome measures | Identified facilitators to prudent AMU | Identified barriers to prudent AMU |
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| ***Veal calf and young bull farms*** | **Fertner et al. (2016)*** | Denmark | To (1) describe the total amount of antimicrobials registered for all large Danish herds with a veal calf and potentially young bull production in 2014; and to (2) identify risk factors influencing the amount of antimicrobials registered at herd level in large Danish herds which purchased calves and raised them to slaughter (full-line production) | Secondary analysis of data | N= 325 large veal calf and young bull producing herds<br><br>(N=183 herds included in risk factor analysis) | Danish Cattle database & National Danish database on drugs for veterinary use (VetStat) | Risk factors influencing the amount of antimicrobials registered at herd level | **Agricultural factors (n=1)**<br>Introducing calves at a young (12-28 days) or older (35-240 days) age, rather than medium (29-34) age (p<0.001) | **Agricultural factors (n=4)**<br>Shorter (<291 days) length of time an animal was present in the herd (p<0.001); type of herd (starter herds, p<0.001); larger (>61) number of purchased calves per year (p=0.004); large number of introduced calves (p<0.001) |
| ***Dairy cattle farms*** | **Habing et al. (2016)*** | USA (Michigan and Ohio) | To (1) measure farmers' disease severity treatment threshold for antimicrobial treatment of calf diarrhoea a, (2) to identify predictors of more selective application of antimicrobials among conventional dairy producers; and to (3) describe the usage frequency and perceptions of efficacy of common antimicrobial alternatives among conventional and organic producers | Cross-sectional survey | N=634 conventional (N=459) and organic (N=175) dairy farmers | Postal questionnaire | Influences on treatment thresholds | **Responsibility (n=1)**<br>Perceptions that AMU in farming has an impact on human health (p=0.017) | **External pressures (n=1)**<br>Higher concern about the impact of AMU regulations (p=0.022)<br>**Knowledge (n=1)**<br>Believe that AMU is essential in food production (p=0.007) |
| ***Dairy cattle farms*** | **Jones et al. (2015)*** | UK (England & Wales) | To (1) look into the extent to which recommended | Cross-sectional survey | N=71 dairy farmers | Postal questionnaire | Factors influencing decision-making | **External pressures (n=2)**<br>Farmer's decrease in concern over consumer | None |

| *Farming sector* | Study ID | Country | Study aim(s) | Study design | Sample | Data collection methods | Relevant outcome measures | Identified facilitators to prudent AMU | Identified barriers to prudent AMU |
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| | | | guidance on prudent veterinary AMU in England and Wales is being followed by farmers; to (2) explore reasons why deviations from prudent use by farmers may be occurring; and to (3) identify the factors influencing farmers' decisions on AMU | | | | on AMU | perceptions of milk safety (p=0.029); farmer' beliefs that social referents (e.g. veterinarians, consumers or family members) would approve of them reducing their AMU (p=0.003)<br>**Knowledge (n=1)**<br>Better awareness of inappropriate use of 3rd and 4th generation cephalosporins (p≤0.0168)<br>**Uncategorised (n=2)**<br>Higher proportion of farmer's income derived from milk production (p=0.017); greater likelihood of farmer remaining in milk production (p=0.021) | |
| ***Dairy cattle farms*** | **Kayitsinga et al. (2017)*** | USA (Florida, Michigan, and Pennsylvania) | To assess both the behaviours and social variables related to antimicrobial therapy for clinical mastitis | Cross-sectional survey | N=628 dairy farms | Postal questionnaire | Factors influencing farmers' mastitis management and treatment behaviours | **Disease epidemiology & outcomes (n=2)**<br>The use of natural (organic) treatments to treat clinical mastitis (p<0.001); the use of vaccines to control Staphylococcus aureus mastitis (p=0.038)<br>**Uncategorised (n=1)**<br>Farmer being a member of an Amish community (p<0.001) | **Drug-related factors (n=1)**<br>The use of intramammary antimicrobials at drying off (p<0.001)<br>**Agricultural factors (n=1)**<br>farm size (large farms being more likely to use intramammary and systemic antimicrobials (p<0.001)<br>**Responsibility (n=1)**<br>Keeping treatment records (p<0.001)<br>**Knowledge (n=2)**<br>Farmers' belief that mastitis is caused by "bad luck" (p=0.034); farmer's higher level of education (high school diploma or equivalent (p<0.001) |
| ***Veal farms*** | **Lava et al. (2016)*** | Switzerland | To (1) quantify and describe AMU; and to | Cross-sectional | N=91 veal calf farms | Face-to-face questionnaire; | Risk factors influencing AMU | **Disease epidemiology & outcomes (n=1)** | **Agricultural factors (n=3)**<br>Greater proportion of beef |

| *Farming sector* | Study ID | Country | Study aim(s) | Study design | Sample | Data collection methods | Relevant outcome measures | Identified facilitators to prudent AMU | Identified barriers to prudent AMU |
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| | | | (2) identify the major risk factors associated with AMU and mortality among veal farms rearing own and purchased calves in Switzerland | survey | | copies of veterinary bills and registered antimicrobial treatments; the Swiss national animal movement database | | Presence of clinical examination of the animals upon arrival to the farm (p=0.04)<br>**Agricultural factors (n=3)**<br>Presence of quarantine (p=0.03); longer fattening period duration (p<0.001); geographical location of the farm (mountain zone, p<0.01) | breed calves (for every 10% increase in the proportion of beef breed calves a significant increase of 2.3 treatment incidence in daily doses per animal and year; p<0.01); shared air space for several groups of calves (p<0.01); separate feeding and lying areas (p<0.03) |
| ***Dairy cattle farms*** | **McDougall et al. (2017)** | New Zealand | To determine the factors associated with the selection of antimicrobials by dairy veterinarians, and the attitudes of those veterinarians and dairy farmers to AMU and AMR | Mixed methods study | N=22 dairy farmers & N=206 dairy cattle veterinarians | Facilitated focus groups (veterinarians and farmers) & online survey (veterinarians) | Factors influencing AMU | **None – reported factors influencing selection of antimicrobials , but no barriers or facilitators** | |
| ***Dairy cattle farms*** | **Redding et al. (2014)*** | Peru (Cajamarca) | To assess patterns and determinants of AMU and farmers' knowledge of antimicrobials | Cross-sectional survey | N=156 small dairy farmers | Face-to-face questionnaire | Factors influencing AMU | **Agricultural factors (n=1)**<br>Larger farms (>7 cattle, p=0.016)<br>**Uncategorised (n=1)**<br>Farmer's higher income (p=0.015) | **Disease epidemiology & outcomes (n=1)**<br>Previous use of the California mastitis test on the farm (p<0.0001)<br>**Knowledge (n=1)**<br>Higher antibiotic knowledge score (p=0.033) |
| ***Dairy cattle farms*** | **Scoppetta et al. (2016)*** | Italy (Umbria) | To (1) determine and characterize the AMU on Umbrian dairy farms; and (2) determine the levels of residues in bulk milk and in milk from individual cows on those farms | Cross-sectional survey | N= 30 dairy farms | Face-to-face questionnaire; farm inspections; milk microbiological screening | The influence of farming and milking practices on AMU | **External pressures (n=1)**<br>Regular checks conducted by breeders' association (p<0.05)<br>**Agricultural factors (n=1)**<br>Good management practices in general (p=0.02)<br>**Uncategorised (n=1)**<br>Farmer being ≤53 years old (p=0.003) | None |
| ***Dairy cattle farms*** | **Stevens et al. (2016)*** | Belgium (Flanders) | To evaluate to what extent variations in herd-level antimicrobial | Cross-sectional survey | N=57 dairy cattle herds | "Garbage can audits" (inspection of | Barriers and influencers relating to | **Disease epidemiology & outcomes (n=2)**<br>Use of selective dry-cow | **Drug-related factors (n=1)**<br>Duration of treatment for subclinical mastitis equal |

| *Farming sector* | Study ID | Country | Study aim(s) | Study design | Sample | Data collection methods | Relevant outcome measures | Identified facilitators to prudent AMU | Identified barriers to prudent AMU |
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| | | | consumption can be explained by differences in management practices that are consistently effective in the prevention of (sub)clinical mastitis, and by differences in mastitis treatment strategies | | | empty, disposed drug containers); face-to-face questionnaire | management control practices for mastitis | therapy (p=0.025); use of intramammary homeopathic treatments for clinical or subclinical mastitis (p=0.044)<br>**Agricultural factors (n=1)** Participation in a veterinary herd management program (p=0.001) | to, or longer than 5 days (p=0.05)<br>**Agricultural factors (n=1)** Timely replacement of teat cup liners (i.e. replacement on 2,500 and 5,000 milk traits for rubber and silicone teat cup liners, respectively; p=0.05)<br>**Responsibility (n=1)** Blanket use of antimicrobial for mastitis (p=0.025) |
| ***Dairy cattle farms*** | **Swinkels et al. (2015)** | Netherlands & Germany | To explore the social factors influencing farmers' decision-making on the duration of antibiotic treatment of clinical mastitis | Qualitative study | N=38 dairy farmers | Face-to-face, semi-structured interviews | Factors influencing farmers' decision-making on the duration of antibiotic treatment | None | **Veterinarian-client relationship (n=1)** Extended treatment being recommended by the veterinarian<br>**External pressures (n=1)** Social norms of other farmers<br>**Drug-related factors (n=2)** Persisting or recurrent symptoms at the completion of the drug label protocol; the discrepancy between farmer's perception of cure and claims on the drug label<br>**Agricultural factors (n=1)** Extended treatment being a routine practice<br>**Responsibility (n=2)** Animal welfare perspectives; fear of recurring symptoms |
| ***Dairy cattle farms*** | **Vaarst et al. (2002)** | Denmark | To describe and analyse farmers' perspectives on their own choices regarding decisions to | Qualitative study | N=16 dairy farmers | Semi-structured interviews | Perspectives and influences on decision-making for AMU | **Disease epidemiology & outcomes (n=1)** Blind quarters strategy | **Veterinarian-client relationship (n=1)** Monthly health advisory visits by the veterinarian |

| *Farming sector* | Study ID | Country | Study aim(s) | Study design | Sample | Data collection methods | Relevant outcome measures | Identified facilitators to prudent AMU | Identified barriers to prudent AMU |
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| | | | have cows treated for mastitis | | | | | | **Disease epidemiology & outcomes (n=1)** Somatic cell count goal /the status of the milk quota<br>**Responsibility (n=1)** Farmers' perceived value of the animal<br>**Knowledge (n=1)** Perception that blind quarter strategy indicates bad management |
| ***Dairy cattle farms (organic)*** | **Vaarst et al. (2003)** | Denmark | Not explicitly stated To describe: (1) newly converted organic farmers' choices related to mastitis treatments; (2) their perception of herd management changes during the period of conversion and (3) to identify possible influences of these changes on treatment decisions and disease management | Qualitative study | N=20 newly converted organic dairy farmers | Semi-structured, face-to-face interviews | Influences on decision-making and on treatment for mastitis | **Disease epidemiology & outcomes (n=1)** Blind quarters strategy | **Disease epidemiology & outcomes (n=1)** Somatic cell count/the status of the milk quota<br>**Agricultural factors (n=1)** Making treatment decisions in order to maintain the herd goals and strategies<br>**Responsibility (n=2)** Animals' welfare perspectives; farmers' perceived value of the animal/favouritism for certain animals |
| ***Dairy cattle farms (organic)*** | **Vaarst et al. (2006)** | Denmark | To describe motivations and circumstances under which organic dairy producers had to work when applying an explicit antimicrobial non-use strategy | Mixed-method study | N=12 organic dairy producers who claim that minimized use or non-use of antimicrobials is an explicit goal | Semi-structured interviews & Danish Cattle Database | Factors influencing explicit antimicrobial non-use strategy | **Veterinarian-client relationship (n=1)** Good veterinarian's support to reduce AMU<br>**Drug-related factors (n=1)** Previous disappointing results of AMU<br>**Disease epidemiology & outcomes (n=4)** Somatic Cell Count results/bacteriological culturing; frequent checks of diseased animal; blind quarters strategy; the use of homeopathic or | **Responsibility (n=1)** Farmers' perceived value of the animal/favouritism for certain animals |

| *Farming sector* | Study ID | Country | Study aim(s) | Study design | Sample | Data collection methods | Relevant outcome measures | Identified facilitators to prudent AMU | Identified barriers to prudent AMU |
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| | | | | | | | | alternative treatments<br>**Agricultural factors (n=6)**<br>Good milking routines (e.g. same person milking every day); improving and reflecting on applied control; improvements to nursing period (e.g. old, patient cows staying with calves for longer); ensuring outdoor access or open housing system; regular cleaning of the bedding; prioritising the improvement of the herd health instead of focusing on antimicrobial non-use | |
| ***Fattening pig farms*** | **Arnold et al. (2016)*** | Switzerland | To (1) identify risk factors for regular oral antimicrobial consumption in Swiss fattening pig farms; and (2) to quantify the amount of antimicrobial active substances administered orally to pigs at the farm level | Case control study | N=99 fattening pig farms | Face-to-face questionnaire; farm inventory, treatment records, prescription forms or veterinary invoices | Risk factors for regular oral AMU | **Agricultural factors (n=2)**<br>Analysis of production parameters performed by the farmer, rather than externally (p=0.01); farmer working on other farms (p<0.01) | **Disease epidemiology & outcomes (n=1)**<br>Not using homeopathic treatments (p=0.02)<br>**Agricultural factors (n=4)**<br>Mixing animals from different suppliers (p=0.05); distance to the next farm ≥500 meters (p=0.01); lack of dirty visitor boots (p=0.01); lack of a work protocol to ensure that healthy pigs are treated before sick pigs (p<0.01) |
| ***Farrow-to-finish pig farms*** | **Backhans et al. (2016)*** | Sweden | To (1) investigate the farm, or farmer-related, factors influencing AMU on Swedish farrow-to finish pig farms;<br>and (2) how biosecurity level, farmers' attitudes to antimicrobials and the information provided by the herd | Cross-sectional survey | N=60 farrow-to-finish pig herds | Self-administered questionnaire, treatment records & farm inspections | Factors influencing AMU | None | **Agricultural factors (n=1**)<br>Farm size (greater number of sows, significant for the AMU in fatteners only, p= 0.042)<br>**Knowledge (n=1)**<br>Higher level of farmer's education (significant for the AMU in suckling piglets only, p=0.025) |

| *Farming sector* | Study ID | Country | Study aim(s) | Study design | Sample | Data collection methods | Relevant outcome measures | Identified facilitators to prudent AMU | Identified barriers to prudent AMU |
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| | | | veterinarian influence AMU | | | | | | **Uncategorised (n=2)** Farmer being older (significant for the AMU in suckling piglets and weaners only, p≤0.013); farmer being female (significant for the AMU in suckling piglets only, p=0.018) |
| ***Fattening pig farms*** | **Casal et al. (2007)*** | Spain | To (1) examine a number of swine farms in Catalonia, regarding routine mass AMU in fattening units; and (2) to determine the factors related to this use | Cross-sectional survey | N=107 fattening pig farms | Face-to-face questionnaire | Factors associated with the on-farm mass AMU | **Agricultural factors (n=1)** Presence of changing facilities (p=0.024) | **Drug-related factors (n=1)** Routine in-feed or in-water antimicrobial prophylaxis (associated with greater likelihood of using more than one antimicrobial agent for enteric diseases, p=0.003)<br>**Agricultural factors (n=3)** Use of growth promoters (significant effect on AMU for respiratory problems, p=0.001); type of farm (fattening units more likely to use antimicrobials than farrow-to-finish farms, p<0.001), farm being smaller (<1000 animals, p=0.016) |
| ***Pig farms (types not specified)*** | **Coyne et al. (2014)** | UK | To investigate the drivers and motivators behind the use and AMP patterns in the pig industry | Qualitative study | N=26 farmers & veterinarians | Focus groups | Drivers and motivators of AMU | **Disease epidemiology & outcomes (n=1)** Use of vaccines<br>**Agricultural factors (n=3)** Good management practices in general; all-in-all-out (rather than continuous) production system; good health status of the animals<br>**Economic factors (n=1)** Cost of antimicrobial treatment | **Drug-related factors (n=1)** Prophylaxis AMU<br>**Economic factors (n=1)** High production costs |

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| ***Finisher pig farms*** | **Ge et al. (2014)*** | Netherlands | To develop a Bayesian Belief Network model that can be used to estimate the influence of potential causal factors of AMU in livestock production | Secondary analysis of data | N=141 specialised finisher pig farms | The Dutch Farm Accountancy Data Network | Factors influencing AMU | **Agricultural factors (n=2)** Good management practices in general ($p<0.05$); good health status of the animals ($p<0.05$) | None |
| ***Fattening & breeding pig farms*** | **Malik et al. (2015)** | Switzerland | To investigate the influence of attitude and knowledge of pig producers on AMU in pig farms | Cross-sectional survey | N= 220 pig farmers | Questionnaires | The influence of attitude and knowledge on therapeutic and prophylactic AMU | **Agricultural factors (n=1)** Good business practice in general | None |
| ***Farrow-to-finish pig farms*** | **Postma et al. (2016a)*** | Belgium, France, Germany, Sweden | To assess possible associations between the biosecurity level, AMU and farm and production characteristics | Cross-sectional survey | N=227 farrow-to-finish pig herds | Face-to-face interviews, farm inspection, treatment records & veterinary invoices | Associations between management characteristics, production parameters, biosecurity status and AMU | **Agricultural factors (n=2)** Good external biosecurity ($p<0.01$); higher weaning age (not significant: $p=0.06$) | **Disease epidemiology & outcomes (n=1)** Greater number of pathogens the animals were vaccinated against ($p<0.01$) **Agricultural factors (n=1)** Shorter farrowing rhythm ($p<0.01$) |
| ***Fattening pig farms & sow farms*** | **van der Fels-Klerx et al. (2011)*** | Netherlands | To investigate farm-level economic and technical factors that are associated with AMU on pig farms | Secondary analysis of data | N=69 fattening farms and N=63 sow farms | The European Farm Accountancy Data Network | Factors influencing AMU | **Agricultural factors (n=1)** Type of farm (specialized sow farms, $p<0.05$) | **Agricultural factors (n=2)** Greater population density in the area (for sow farms only $p<0.05$); size of the farm (larger farms, $p<0.05$) |
| ***Fattening pig farms*** | **Visschers et al. (2014)*** | Switzerland | To investigate farmers' attitudes and habits related to AMU, their perception of AMR and of policy measures intended to reduce AMU in pig farming | Longitudinal survey | N=66 fattening pig farmers | Postal questionnaire & face-to-face interviews | Factors influencing AMU, and predictors of the perceived impact of policy measures | **Responsibility (n=1)** The habit of only administering antimicrobials after consulting a veterinarian ($p=0.01$) | **Responsibility (n=1)** Recording all drug administrations (not significant: $p=0.06$) **Knowledge (n=1)** Farmer's lower risk perception regarding AMU ($p=0.03$) |
| ***Pig farms (all types)*** | **Visschers et al. (2016a)*** | Denmark, Belgium, France, Germany, | To (1) investigate pig farmers' and veterinarians' perceptions of AMU | Cross-sectional survey | N=1,294 pig farmers & N=334 | Postal questionnaires (farmers) & online | Factors influencing farmers' intentions to | **Veterinarian-client relationship (n=1)** Receiving support of the veterinarian ($p<0.001$ | **Knowledge (n=1)** Farmer's perceived need for AMU ($p<0.001$) **Uncategorised (n=1)** |

| *Farming sector* | Study ID | Country | Study aim(s) | Study design | Sample | Data collection methods | Relevant outcome measures | Identified facilitators to prudent AMU | Identified barriers to prudent AMU |
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| | | Sweden, Switzerland | and reducing AMU; and (2) to identify the demographic and perception variables associated with the intention to reduce AMU among pig farmers and reduction behaviours among veterinarians | | veterinarians with a reported pig practice | questionnaires (veterinarians) | reduce AMU | **Knowledge (n=4)** Farmer's higher perceived efficacy to lower their AMU (p<0.001); higher AMR incidence experienced by the farmer (p<0.001); higher self-reported (perceived) AMU (p<0.001); farmer's higher perceived risks of antimicrobials (p<0.001) | Farmer being Swedish (p<0.001) |
| ***Farrow-to-finish pig farms*** | **Visschers et al. (2016b)*** | Belgium, France, Germany, Sweden | To (1) investigate how accurate farmers' estimations of their own AMU are compared with the actual AMU; (2) to investigate farmers' perceptions of the benefits, need and risks of antimicrobials and of their relationship with their veterinarians and to what extent pig farmers from four different European countries differ in these perceptions; and (3) to quantify to what extent psychological factors are related to pig farmers' AMU in the four investigated countries | Cross-sectional survey | N= 215 farrow-to-finish pig farmers | Self-administered questionnaire & farm visit | Factors influencing AMU | **Knowledge (n=1)** Farmer's higher perceived risks of antimicrobials (p<0.01) **Uncategorised (n=1)** Farmer being Swedish (p<0.05) | **Agricultural factors (n=1)** Farm size (greater number of sows, p<0.01) **Uncategorised (n=1)** Farmer being German (p<0.05) |
| ***Meat, egg and mixed chicken farms*** | **Carrique-Mas et al. (2015)*** | Vietnam (Mekong Delta) | To (1) describe and quantify levels of AMU, both in terms of usage per unit time as well as per chicken produced, in farms in the Mekong Delta; and to (2) identify factors associated with usage | Cross-sectional survey | N=208 chicken farms | Questionnaire | Factors influencing AMU | **Agricultural factors (n=1)** Production system (all-in-all-out type, p<0.001) | **Agricultural factors (n=3)** Geographical location of the farm (Cho Gao and Chau Thanh districts in Vietnam, p<0.001); type of the chicken farm (meat farm, rather than layer or mixed farms, p=0.04); household farms (rather |

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| | | | | | | | | | than small-to-medium farms, p=0.014)<br>**Uncategorised (n=1)**<br>Farmer being male (p<0.001) |
| ***Turkey broiler farms*** | **Chauvin and Madec (2004)*** | France | To (1) assess and compare the variation in AMU across turkey broiler production units; and to (2) explore putative factors which could explain the variation in antibiotic utilisation | Cross-sectional survey | N=130 turkey broiler farms | Face-to-face questionnaire & antibiotic purchase invoices | Factors influencing AMU | **Disease epidemiology & outcomes (n=1)**<br>Administration of bacterial flora for prevention of digestive disorders (p=0.0003)<br>**Agricultural factors (n=2)**<br>Thorough cleaning of the facility floor between flocks (p=0.04); changing clothes at the entrance of the facilities (p=0.03) | **Drug-related factors (n=1)**<br>The use of prophylactic antimicrobials (p=0.004)<br>**Responsibility (n=1)**<br>Lower level of technical and veterinarians 'involvement in decision making to medicate flocks (p=0.03) |
| ***Turkey broiler farms*** | **Chauvin et al. (2005)*** | France | To (1) assess the homogeneity of AMU between flocks on the same farm; and to (2) identify possible relationships between the level of AMU and farm, farmer and flock characteristics | Cross-sectional survey | N=246 turkey broiler flocks from 131 farms | Face-to-face questionnaire & antibiotic purchase invoices | Factors influencing AMU | **Disease epidemiology & outcomes (n=1)**<br>Administration of bacterial flora for prevention of digestive disorders (p=0.01)<br>**Agricultural factors (n=1)**<br>Changing clothes at the entrance of the facilities (p=0.02) | **Veterinarian-client relationship (n=1)**<br>Veterinarians' antimicrobial prescription meeting the farmers' expectations (rather than antimicrobial prescription not being expected by the farmer, p=0.01)<br>**Drug-related factors (n=1)**<br>The use of prophylactic antimicrobials (p=0.02)<br>**Agricultural factors (n=1)**<br>More than one full-time job on the farm devoted to production unit (p=0.004) |
| ***Broiler chicken farms*** | **Hughes et al. (2008)*** | UK | To determine risk factors for the use of prescription antibiotics | Cross-sectional survey | N=497 chicken broiler farms | Postal questionnaire | Risk factors influencing AMU | **Disease epidemiology & outcomes (n=1)**<br>Administration of bacterial flora for prevention of digestive disorders (significantly associated with decreased preventative AMU p=0.003) | **Disease epidemiology & outcomes (n=5)**<br>Type of the disease (all significantly associated with increased therapeutic AMU: necrotic enteritis, p<0.001; respiratory disease, p=0.01; coccidiosis, p=0.001; wet |

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| | | | | | | | | **Agricultural factors (n=3)** The number of hatcheries supplying the farm with chicks greater than 1 (significantly associated with decreased therapeutic AMU p=0.04); use of growth promoters (significantly associated with decreased preventative AMU only, p=0.02); the use of controlled feeding regiments (significantly associated with decreased preventative AMU p=0.004) | litter, p<0.001); use of vaccines against infectious bursal disease (significantly associated with increased therapeutic AMU, p=0.03) **Agricultural factors (n=3)** The use of feed containing whole wheat (significantly associated with increased therapeutic AMU, p=0.004); greater slaughter weight (significantly associated with increased preventative AMU, p=0.005); the number of hatcheries supplying the farm with chicks > 1 (significantly associated with increased preventative AMU, p=0.04) |
| ***Lamb-producing sheep farms*** | **Moon et al. (2011)*** | USA (Ontario) | To (1) calculate antimicrobial and extra-label exposure rates; and to (2) determine treatment-level and farm-level factors associated with AMU and extra-label drug use | Longitudinal survey | N=49 lamb farms | Face-to-face questionnaire, treatment records & inventory records | Factors associated with AMU | **Disease epidemiology & outcomes (n=4)** Type of the disease: (respiratory, p<0.01; treatment of a wound or injury, p<0.01; mastitis p=0.01; post-lambing ewe - treatment of systemic infection signs, p<0.01) **Agricultural factors (n=1)** Three or more lambing periods per year (α=0.05) **Knowledge (n=1)** 20-29 years of practice in farming (associated with decreased use of non-licensed antimicrobials only, p=0.02) | **Drug-related factors (n=1)** Group treatment (p<0.01) **Responsibility (n=1)** Farmer's, rather than veterinarians' decision to treat (p=0.05) **Knowledge (n=1)** Years of practice in farming 20 years or more (associated with increased antimicrobial exposure rates in adult sheep only, p<0.01) |
| ***Aquatic farms*** | **Munasinghe et al. (2012)*** | Sri Lanka | To identify high-risk areas and farm-level risk factors for AMU to inform the core messages and strategic | Prospective Survey | N=603 shrimp farms | Face-to-face questionnaire | Farm-level risk factors for AMU | **Agricultural factors (n=3)** Stocking density <60,000 post larvae/acre (OR=0.60, 95%CI: 0.36-0.99); harvest before the end of 4th | **Agricultural factors (n=8)** Use of fertilizers (depending on the type of fertilizer, OD ranged from OD=2.2, 95% CI: 1.2-4.1 to |

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| | | | placement of extension programs to help farmers develop best management practices for AMU | | | | | month (OR=0.44, 95%CI: 0.25-0.76); higher farm density in the area (mean density 15/km², p=0.018) | OD=7.8, 95% CI: 2.8-21.5); water treatment (OD=2.3, 95% CI: 1.1-4.5); use of disinfectants or pesticides (depending on the type of agent used OD ranged from OD=2.0, 95% CI: 1.2-3.2 to OD=3.0, 95%CI: 1.7-5.1); use of feed supplements (depending on the type of supplement OD ranged from D=1.7, 95%CI: 1.1-2.6 to OD=4.1, 95%CI: 2.1-8.3); the use of probiotics (depending on how probiotics were used OD ranged from OD=2.4, 95%CI: 1.5-3.7 to OD=4.3, 95%CI: 2.6-7.2); nearer distance to streams (p=0.039); distance to water reservoirs (p=0.026); lower farm density in the area (mean density 11/km², p=0.018) |
| ***Generic (poultry, small animals, large animals and mixed farms)*** | **Eltayb et al. (2012)** | Sudan | To investigate the knowledge and practices of farmers' regarding AMU and AMR | Mixed methods study | N=81 farmers | Structured interviews | Knowledge, practises and drivers related to AMU | None | **Drug-related factors (n=1)** Poor quality of locally manufactured antimicrobials<br>**Disease epidemiology & outcomes (n=1)** Lack of accurate diagnosis<br>**Agricultural factors (n=1)** Initiating treatment to keep animals looking healthier and avoid symptoms appearance<br>**Responsibility (n=1)** Administering antimicrobials without consulting a veterinarian |

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| | | | | | | | | | **Knowledge (n=1)** Lack of knowledge on drug instructions<br>**Economic factors (n=2)** Shortening treatment duration to reduce treatment costs; concerns over productivity |
| ***Generic (types of farms not stated)*** | **Hockenhull et al. (2017)** | UK | To investigate what is currently known about AMU in food-producing animals, encompassing their use at farm level, the practices and perceptions of the stakeholders involved in their administration, and the availability and validity of data on their use in practice | Rapid assessment literature review | N= 48 peer-reviewed papers | Research on AMU published in peer-reviewed journals between 2000 and 2016 | Factors influencing farmers' AMU & motivation for its reduction | **Agricultural factors (n=2)** Good biosecurity in general; implementation of health strategies<br>**Responsibility (n=2)** Farmer's greater concern for the public health; ethical factors (not specified)<br>**Economic factors (n=1)** Farmer's desire to reduce the cost of production | **External pressures (n=1)** Extending treatment duration being a social norm amongst farmers<br>**Drug-related factors (n=1)** antimicrobials being readily available<br>**Agricultural factors (n=1)** Poor housing conditions<br>**Responsibility (n=2)** Administering antimicrobials without consulting a veterinarian; animal welfare perspectives<br>**Knowledge (n=2)** Perception of what constitutes "good farming"; perception that reducing AMU results in additional labour<br>**Economic factors (n=1)** Concerns over productivity and profitability |

| *Farming sector* | Study ID | Country | Study aim(s) | Study design | Sample | Data collection methods | Relevant outcome measures | Identified facilitators to prudent AMU | Identified barriers to prudent AMU |
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| ***Generic (dairy cattle, veal calves and pig farms)*** | **Kramer et al. (2017)*** | Netherlands | To (1) characterize farmers' motivating and enabling factors towards AMU and AMR in three major livestock production sectors (dairy cattle, veal calves and pigs); and (2) to explore the impact of these psychological factors on their on-farm AMU | Cross-sectional survey | N=457 dairy, veal and pig farmers | Online questionnaire | Factors influencing AMU and AMR; determinants for on-farm AMU | **Knowledge (n=2)** Farmer's better knowledge on antimicrobials and AMR (p=0.0004); higher perceived risk towards AMR (not significant: p=0.06) | **External pressures (n=1)** Undesired attitude to regulations (not significant: p=0.06) |
| ***Generic (types of farms not stated)*** | **Magalhães-Sant'Ana et al. (2017)** | Ireland | To provide a value-based reflection on the constraints and possible opportunities for responsible use of veterinary antimicrobials in Ireland | Qualitative case study | N=8 experts (a dairy farmer, national regulatory body rep, veterinarians) | Focus groups | Opportunities and constrains to responsible AMU | **External pressures (n=1)** Retailers and processors increasing their quality assurance standards<br>**Disease epidemiology & outcomes (n=2)** Improving vaccinations; development of on-farm diagnostic tests<br>**Agricultural factors (n=2)** Improving farming practices in general; improving biosecurity measures<br>**Knowledge (n=1)** Improving farmers' awareness of their role in combating AMR and human health issues | **External pressures (n=1)** Poor surveillance and control of on-farm AMU regulations<br>**Responsibility (n=1)** Farmer's perceptions of own limited role in AMR |

| *Farming sector* | Study ID | Country | Study aim(s) | Study design | Sample | Data collection methods | Relevant outcome measures | Identified facilitators to prudent AMU | Identified barriers to prudent AMU |
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| ***Generic (various types, including chicken, turkey, guinea fowl, geese, duck, cattle sheep, goat, rabbit and quail farms)*** | **Ojo et al. (2016)** | Nigeria | To (1) assess the range of available antimicrobial agents and level of AMU in animal production in Oyo and Kaduna States of Nigeria; and (2) to evaluate the practices of livestock producers in relation to AMU | Mixed methods study | N=454 livestock farmers | Interviews, questionnaires & focus group | Farmers' practices and factors influencing AMU | **Agricultural factors (n=1)** Improved hygiene in general | **Drug-related factors (n=1)** Prophylaxis AMU<br>**Disease epidemiology & outcomes (n=1)** Severe symptoms<br>**Agricultural factors (n=1)** Use of growth promoters<br>**Knowledge (n=3)** Farmer's past experience on using particular antimicrobial; farmer's assumption of low active ingredients in some brands of the drugs; farmer's desire for urgent outcomes |
| ***Generic (broiler chickens, broiler ducks, pig farms)*** | **Om and McLaws (2016)** | Cambodia | To explore opinions and antibiotic practices on the farms | Qualitative study | N=19 commercial farmers, feed retailers & veterinarians | Face-to-face interviews | Farmers' practices, attitudes and factors influencing AMU | **Drug-related factors (n=1)** Fear of undesired or negative outcomes following antimicrobial treatment<br>**Responsibility (n=1)** Fear of the consequences of AMU in farming on human health | **External pressures (n=1)** Poor AMU monitoring and control system<br>**Drug-related factors (n=1)** Antimicrobials being available for purchase without prescription<br>**Agricultural factors (n=1)** Use of growth promoters<br>**Responsibility (n=1)** Farmer being unable to read drug labels that are not translated into their native language<br>**Knowledge (n=1)** Poor knowledge and awareness on antimicrobials and diseases |

| *Farming sector* | Study ID | Country | Study aim(s) | Study design | Sample | Data collection methods | Relevant outcome measures | Identified facilitators to prudent AMU | Identified barriers to prudent AMU |
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| ***Generic (types of farms not stated)*** | **Postma et al. (2016b)** | Flanders & Netherlands | To quantify opinions of veterinarians from the Netherlands and Flanders regarding AMU and resistance issues in farm animals | Cross-sectional survey | N=611 veterinarians | Online questionnaire | Factors influencing AMU and AMU reduction | **External pressures (n=1)** Benchmarking of AMU, including sanctioning of high users<br>**Drug-related factors (n=1)** Restricting treatments only for diseased animals<br>**Agricultural factors (n=3)** Improving biosecurity measures; improving the quality of animal feed; improving housing conditions<br>**Knowledge (n=1)** Increasing education for farmers on infection prevention | **Agricultural factors (n=4)** Poor management in general; insufficient biosecurity measures; poor housing conditions; insufficient immunity status of young animals<br>**Knowledge (n=1)** Farmers' mentality to easily use antimicrobials<br>**Economic factors (n=2)** Antimicrobial treatment being more economically beneficial than implementation of preventative measures; prioritising animals' growth and production |
| ***Generic (poultry, pig, dairy cattle and veal calf farms)*** | **Speksnijder et al. (2015a)** | Netherlands | To identify determinants influencing farm animal veterinarians' AMP | Qualitative study | N=11 farm animal veterinarians | Semi-structured interviews | Factors influencing AMP and AMU | **Veterinarian-client relationship (n=1)** Regular veterinary supervision<br>**Knowledge (n=1)** Improving farmer's education on caretaking of animals | **Agricultural factors (n=4)** Poor feed quality; poor housing conditions; poor health status of young animals; minimizing the amount of hired labour<br>**Responsibility (n=1)** Farmers' poor motivation to change bad habits<br>**Knowledge (n=1)** Farmers' insufficient skills to detect risk factors for diseases or early signs<br>**Economic factors (n=1)** Higher tariffs for veterinary consultations |

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| ***Generic (poultry, pig, dairy cattle and veal calf farms)*** | **Speksnijder et al. (2015b)** | Netherlands | To (1) explore differences in attitudes towards AMU and reduction opportunities in farm animals; (2) and the interaction of veterinarians with farmers in improving animal health and reducing AMU between categories of veterinarians | Cross-sectional survey | N=377 completed questionnaires from veterinarians | Online questionnaire | Factors influencing solutions for high AMU; reasons for farmers decisions not to implement veterinary advices | None | **Veterinarian-client relationship (n=2)** Farmer's perception that implementation of veterinarian's advice is too expensive, time consuming or too difficult; lack of belief that implementing veterinary advices will result in better outcomes **External pressures (n=1)** Conflicting advices from the veterinarian and other stakeholders |

*Study reported significant facilitators and/or barriers to farmers' prudent AMU; AMP = antimicrobial prescribing; AMR = antimicrobial resistance; AMU = antimicrobial use

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