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Water pollution from pharmaceutical use in livestock farming: Assessing differences between livestock types and production systems

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Abstract

Livestock production is a major source of pharmaceutical emissions to the environment. The current scientific discourse focuses on measuring and modeling emissions as well as assessing their risks. Although several studies corroborate the severity of pharmaceutical pollution resulting from livestock farming, differences in pollution between livestock types and production systems are largely unknown. In fact, there is no comprehensive analysis of factors influencing pharmaceutical use—the emission's source—in the diverse production systems. To address these knowledge gaps, we developed a framework to investigate pharmaceutical pollution from different livestock production systems and applied it in a first pilot assessment to compare pollution from organic and conventional cattle, pig, and chicken production systems on selected indicator substances, covering antibiotics, antiparasitics, hormones, and nonsteroidal anti-inflammatory drugs (NSAIDs). Given the lack of statistics, for this article we retrieved novel qualitative information about influential factors for pharmaceutical use and pollution from expert interviews and combined this with quantitative data on, among other factors, the environmental behavior of specific substances from the literature. Our analysis reveals that factors across a pharmaceutical's entire life cycle influence pollution. However, not all factors are livestock type or production-system dependent. The pilot assessment furthermore reveals that differences in pollution potential between conventional and organic production exist, but for antibiotics, NSAIDs, and partially for antiparasitics, some factors lead to greater pollution potential in conventional systems, and others in organic systems. For hormones, we identified a comparatively greater pollution potential from conventional systems. Among the indicator substances, the assessment over the entire pharmaceutical life cycle illustrates that flubendazole in broiler production has the greatest per unit impact. The framework and its application in the pilot assessment generated insights useful to identifying which substances, livestock types, production systems, or the combination thereof have great or little pollution potential, informing more sustainable agricultural management practices. *Integr Environ Assess Manag* 2023;19:1495–1509. © 2023 The Authors. *Integrated Environmental Assessment and Management* published by Wiley Periodicals LLC on behalf of Society of Environmental Toxicology & Chemistry (SETAC).

KEYWORDS: Environmental assessment framework; Livestock production systems; Organic livestock; Veterinary pharmaceuticals; Water pollution

INTRODUCTION

Pharmaceuticals in the environment have gained increasing attention over the past decades as they pose ecotoxicological risks, appear in drinking water and food products, and are associated with antimicrobial resistance development (Aus Der Beek et al., 2015; Boxall et al., 2006; Hoelzer et al., 2017; Leung et al., 2013; Singh et al., 2019). Global antibiotic use in livestock farming is estimated to be thousands of tons per year, revealing an increasing trend (Van Boeckel et al., 2015). Although the EU prohibited the use of veterinary antibiotics as growth promoters in 2006 and overall sales in Europe declined, the purchase of more than 6000 tons was reported in 2018 (European Commission, 2005; European Medicines Agency, 2020). In Germany and the Netherlands (the geographical setting of this study), antibiotic use has been decreasing due to different policies (Mevius & Heederik, 2014; Wallmann et al., 2018). Yet, antibiotic use in livestock remains substantial, amounting to hundreds of tons per year (SWAB, 2021; Wallmann et al., 2018). Information about the application of other pharmaceuticals (e.g., antiparasitics or hormones) in livestock remains largely undetermined as there are no comprehensive

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datasets available (Di Guardo & Finizio, 2017). Additionally, comprehensive information is lacking on veterinary pharmaceutical use that differentiates between livestock types or farm characteristics (Wöhler et al., 2020).

Several attempts to assess pharmaceutical (mostly antibiotic) environmental pollution from livestock animals have been made over the past decades. These cover risk assessment methods (Kools et al., 2008; Menz et al., 2015), modeling approaches (Bailey, 2015; Wöhler et al., 2021), and experimental studies (Jaffrézic et al., 2017; Kay et al., 2005; Kivits et al., 2018), and aim mostly to evaluate the environmental status and impact of pharmaceutical emissions. Despite the evidence of pharmaceutical pollution from livestock production demonstrated by these studies, none differentiates pharmaceutical pollution between alternative livestock production systems. Gaining insight into the influence of production system characteristics on pharmaceutical pollution is, however, crucial to determining if and how pollution from the various livestock types and production systems differ.

In the EU, all agricultural activities are regulated by the Common Agricultural Policy (CAP), independent of production system or livestock type. Launched in 1962, the CAP had the primary goals of securing food provision to EU citizens and fair living standards for farmers (European Commission, 2020a). This policy focus, along with the development of artificial fertilizers, has led to an intensification of Europe's agricultural systems (Van Zanten et al., 2014). Agricultural intensification and farm expansion have developed further as a result of CAP reforms and a competitive global market for agricultural goods (Van Zanten et al., 2014). However, several environmental impacts such as greenhouse gas emissions, land use degradation, and water pollution have been associated with intensive (livestock) farming over the past decades (Ilea, 2009). To tackle these, recent policy reforms aim for the sustainable development of the agricultural sector. This includes a "greening" of CAP and the adoption of the farm to fork strategy as part of the EU's green deal (European Commission, 2019; Nazzaro & Marotta, 2016). The farm to fork strategy specifically mentions the goal to reduce antibiotic use to combat antimicrobial resistance; other pharmaceutical substance groups are not mentioned. The "greening" development of agricultural policies goes hand in hand with a growing societal demand for sustainable animal products (Lebacq et al., 2013) and increasing organic production (European Commission, 2020b). Organic farming is classified by EU Council Regulation (EU) 2018/848 on organic production and labeling of organic products (European Commission, 2020c) and aims to combine food supply with environmental preservation, whereby pollution prevention of freshwaters is specifically addressed. Veterinary pharmaceutical use is not prohibited but is restricted in organic livestock farming.

Policies regulating veterinary pharmaceutical use and pollution are the EU strategic approach to pharmaceuticals in the environment, the EU regulation 2019/06 on veterinary medicinal products and EU regulation 2019/04 on the manufacture, placing on the market, and use of medicated feed. Although the former recognizes livestock as a source of pharmaceutical pollution, proposing different areas of action, the two latter focus mostly on the veterinary pharmaceutical market and supply chain. The environmental relevance of pharmaceuticals is only mentioned as a side aspect, for example, the required environmental risk assessment for authorization of medicinal products. None of the policies relates pharmaceutical pollution to different livestock production systems.

Although several studies aim to elucidate how livestock production systems differ in their sustainability performance and what causes these differences (e.g., Boggia et al., 2010; Clark & Tilman, 2017; De Vries et al., 2015; Pirlo & Lolli, 2019; Van Der Linden et al., 2020), these assessments neglect pharmaceutical pollution altogether. Consequently, we propose that research on pharmaceuticals in the environment overlooks the interrelationship with production systems, whereas studies presenting sustainability assessments of production systems do not include pharmaceutical pollution. To address this research gap, the present study aims to identify if and how differences in livestock production systems affect pharmaceutical pollution. This is done by developing a framework through the systematic identification and compilation of factors that influence pharmaceutical pollution in its different life cycle stages and by applying that framework in a pilot assessment. Specifically, we first select different livestock types and production systems. Next, we develop the framework to assess pharmaceutical pollution from these livestock types and production systems along the consumption-related pharmaceutical life cycle (excluding pollution occurring before pharmaceutical administration, that is, from manufacturing). Finally, we apply the framework in a pilot assessment to gain first insights on differences in pharmaceutical pollution among livestock types and production systems. Both the framework development and the pilot assessment are based on expert interviews conducted in Germany and the Netherlands and on a literature review. We specifically use information from expert interviews where other data are not available. For the framework development, this is specifically the case for the pharmaceutical administration. In addition, we search for major differences among livestock types and production systems in this life cycle stage, which is why our investigations focus on this in particular. As mentioned above, veterinary pharmaceutical pollution has been investigated previously, and therefore knowledge and quantitative data on parts of the pharmaceutical life cycle are readily available (e.g., a pharmaceutical's degradation rates). Although we fill in this quantitative information in the pilot assessment wherever possible, we follow a qualitative approach that comparatively indicates pollution potential based on information from the interviews when quantitative data is lacking. The study's findings may serve as grounds for policy recommendations relating to agriculture and sustainability, ultimately leading to less pharmaceutical pollution from livestock production.

METHODS AND DATA

Selection of livestock types and production system categories

To arrive at a categorization of livestock types and production systems that can be applied to our framework, we define a set of desirable categorization properties. First, they need to differentiate livestock types and production systems in their use of and practices concerning veterinary pharmaceuticals. Second, ideally, the categories would be sufficiently homogeneous in aspects relevant to veterinary pharmaceuticals to characterize with modest ambiguity. Third, the categories need to be sufficiently traceable in statistics to allow an operationalization of the assessment. For the selection of categories, we conducted a literature review.

For livestock types, Eurostat (2021) describes beef cattle, dairy cattle, pigs, broiler chickens, and laying hens as the most dominant livestock types in the German and Dutch context (Eurostat, 2021). These categories (largely) overlap with those published on antibiotic use in Germany and the Netherlands (Van Geijlswijk et al., 2018; Wallmann et al., 2018). We therefore consider this livestock type categorization suitable for our assessment. A detailed description of livestock sectors in the EU, Germany, and the Netherlands providing background information is given in the Supporting Information.

For selecting livestock production systems, many categorizations exist in the literature. For example, intensive (Ilea, 2009) and extensive (Delattre et al., 2020) livestock farming, precision livestock farming (Hartung et al., 2017), multispecies livestock farming (Martin et al., 2020), and integrated crop-livestock farming (Moraine et al., 2014) are represented. These categories are not, however, based on any regulatory indicators and are mostly defined for individual studies, fitting the research purpose and setup. A categorization scheme frequently used for statistical analysis of farming structures in the EU is farm typologies. The approach has its roots in pure economic reasoning because it originates from the time where EU's agricultural policies targeted profitable production (Andersen et al., 2007). Andersen et al. (2007) argue that an environmentally based extension to farm typologies is essential to environmental assessments that should give grounds for today's and future policies. One legally certified difference in production systems exists in the EU: between organic and conventional (non-organic). Organic farming is regulated by the EU's Council Regulation (EU) 2018/848 on organic production and labeling of organic products (European Commission, 2020c). Various standards for livestock production are set out in the regulation. These cover the origin of the animal, husbandry practices and housing conditions, breeding, feed, disease prevention, and veterinary treatment as well as cleaning and disinfection. The overall focus of best environmental practices, protecting natural resources and high animal welfare standards, is reflected in these standards. Pharmaceutical use is mentioned in the criteria for breeding and disease prevention and veterinary treatment. In breeding, the use of hormones and other substances to control reproduction is prohibited. The criteria for disease prevention and veterinary treatment regulate the use of allopathic medicinal products, which is only permitted for the treatment of sick animals. Restrictions and accompanying measures, such as an extended withdrawal time, apply in this case and are defined in EU regulation 889/2008 on rules governing organic production, labeling, and control (European Commission, 2020c). To assure consistency among member states, national legislation defining organic farming is not permitted (Früh et al., 2014). Every farming type not covered by this regulation is considered conventional.

To summarize, in this research, we differentiate between the five different livestock types: beef cattle, dairy cattle, pigs, broilers, and laying hens as the dominant livestock types in the countries of investigation. Given that a proper categorization between production systems that meets the abovementioned requirements is lacking, we select the distinction between organic and conventional production systems as an existing, legally defined classification to be used in our environmental assessment focusing on pharmaceutical pollution. For each combination of the five livestock types and the two production systems, we investigate factors that influence pharmaceutical pollution.

Framework development

To develop a framework for assessing pharmaceutical pollution from different production systems, we followed the logic of the consumption-related pharmaceutical life cycle (see e.g., Slana & Dolenc, 2013). This means that we distinguish pollution phases along the pharmaceutical life cycle from administration in livestock to the environmental impact (excluding pharmaceutical manufacturing before administration in different livestock production systems), as illustrated in Figure 1.

For the administration of each of the life cycle stages, metabolization and consequent excretion, pharmaceuticals in manure, pharmaceutical application to agricultural land, pharmaceutical environmental behavior, and pharmaceutical environmental impact, we outline what factors influence the pharmaceutical load and pollution, and whether these factors differ among livestock types and production systems. By definition, some of the life cycle stages are purely substance dependent and therefore independent of their source.

The framework was developed based on the rationale of cause–effect, investigating for each stage of the life cycle what factors cause (or inversely avoid) pharmaceutical loads and consequently pollution. Cause–effect relationships are a common rationale to ground frameworks for environmental assessments (see e.g., Cormier & Suter, 2008; Mourhir et al., 2016; Niemeijer & De Groot, 2008; Rugani et al., 2019). Understanding the dynamics between social and

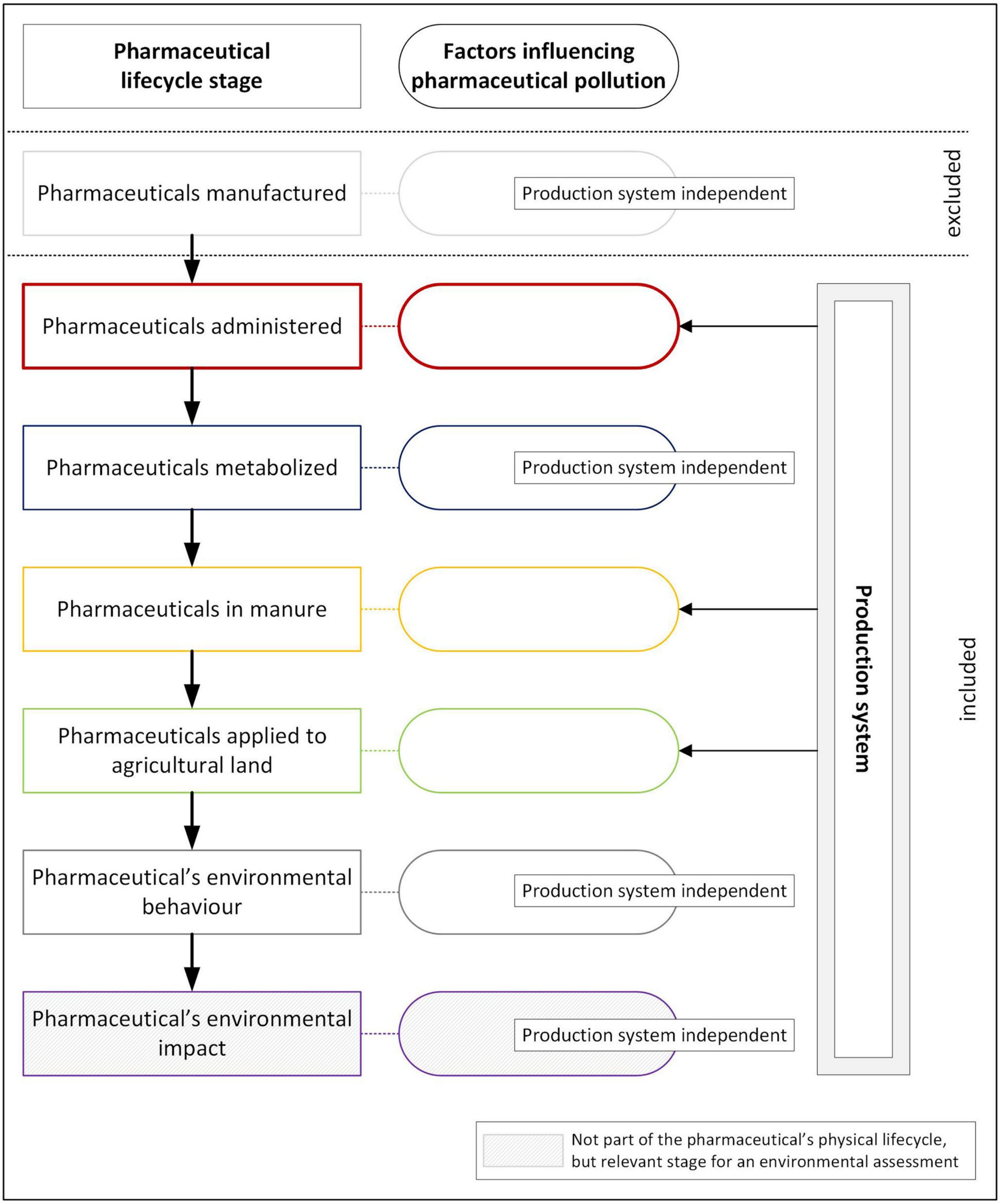

FIGURE 1 Conceptual setup of the framework development following the consumption-related pharmaceutical life cycle

environmental systems is pivotal for environmental assessments that often aim to serve environmental policies (Binder et al., 2013; Bodde et al., 2018; Kelly et al., 2013). One of the most prominent frameworks including cause–effect relationships is the Driver-Pressure-State-Impact-Response Framework established by the European Environmental Agency (Kristensen, 2004). We used these existing frameworks and their rationale as an inspiration to create the first framework to assess pharmaceutical pollution from different livestock types and production systems.

Although the identification of factors relating to the pharmaceutical administration are retrieved from expert interviews, factors concerning the other life cycle stages are obtained from the literature. Compiling this information leads to a framework that can be used to cross-check which causes apply in different livestock types and production systems. If possible (i.e., if available data allow), the individual elements of the framework can be filled with quantitative data as well.

Pilot assessment

For contextualization of the German–Dutch case adopted in the pilot study, we first give an overview of pharmaceutical use in German and Dutch livestock production systems, focusing on purposes and common practices of pharmaceutical application. Following this overview, the pilot assessment is conducted. In this article, we fill the framework with information using data that are retrieved from both interviews and the literature. First, we present a qualitative comparison of pollution potential—a tendential comparison for the degree of pollution—from pharmaceutical administration between conventional and organic production per substance group. A qualitative approach was chosen because quantitative data on pharmaceutical use differentiating production systems are not available. So, the qualitative descriptions give novel insights where quantitative data are lacking. Second, we conduct substance-specific pilot assessments for a set of indicator substances assessing all life cycle stages of the framework. Indicator substances (most relevant to quantity and/or frequency used) per substance group and livestock type are retrieved from the interviews. For the life cycle stage administration, pharmaceuticals in manure and pharmaceuticals in manure applied to agricultural land, the pollution potential resulting from each of the identified factors is (qualitatively) indicated per production system. The substance-specific rates for excretion, degradation in manure, the environmental behavior expressed as degradation in soil, and the environmental impact threshold for predicted-no-effect-concentration (PNEC) are indicated in quantitative terms (Supporting Information).

Data collection

Data for both the framework development and the pilot assessment were collected in two ways: (1) reviewing pertinent literature and (2) conducting expert interviews. For the literature review, peer-reviewed publications, gray literature, and policy documents were thematically scanned for each of the life cycle stages as well as for the description of livestock sectors and the overview of pharmaceutical use in Germany and the Netherlands. Expert interviews were conducted in a semistructured format with German and Dutch livestock veterinarians. This choice was made because they have expertise in what influences pharmaceutical use and have a representative overview of different farms and production systems. Through German and Dutch agricultural and veterinary organizations and/or associations, we identified relevant interviewees, namely veterinarians who specialized in different livestock types. After the procedure of snowball sampling, we consolidated the iterative process of interviewee identification and received further contacts. Snowball sampling is an established method to identify stakeholders in qualitative environmental research (Bendtsen et al., 2021). In total, 31 veterinarians were contacted, of whom 14 granted an interview. Half of the interviewed veterinarians are based in Germany; the other half are in the Netherlands. Six interviewees had a specialization in cattle (beef and/or dairy), four in pigs, and four in poultry (layers, broilers, and turkeys). Three of them also worked as policy advisers. It should be noted that not all interviewees had (extensive) experience with organic production systems because of the comparatively small share of organic production. This was specifically the case for the Dutch beef cattle sector. All interviews were conducted through video calls in June and July 2021.

The semistructured interview setup followed a predesigned questionnaire, provided in the Supporting Information. The questionnaire consists of five content-related sections that align with the research aims and method stated above: (1) general aspects of pharmaceutical use in livestock production systems, (2) factors and drivers influencing pharmaceutical use in livestock production, (3) differences in pharmaceutical use among livestock types and production systems, (4) indicator pharmaceuticals, and (5) assessing the pharmaceutical life cycle.

Based on audio recordings, all interviews were transcribed nonverbatim. The transcripts were coded using the atlas.ti software. Codes were created for a thematic analysis, following the questionnaire's setup. For instance, individual codes were created for factors influencing pharmaceutical use per livestock type. To compile the coded text passages, code reports were retrieved. From these reports, information was extracted and analyzed. Following up on the example to thematically analyze influential factors, for instance, we listed all factors named and clustered them systematically. From the veterinarians' judgment about how influential the named factors are in different production systems, the differences in pharmaceutical administration in diverse production systems were qualitatively assessed (in general and specifically for a set of indicator substances listed by the interviewees).

RESULTS

A novel framework to assess pharmaceutical pollution from different production systems

Figure 2 illustrates the framework to assess pharmaceutical pollution from different livestock types and production systems for the following pharmaceutical life cycle stages: administration, metabolization, pharmaceuticals in manure, application to agricultural land, environmental behavior, and environmental impact. Although the factors that fill the framework for the stage of pharmaceutical administration

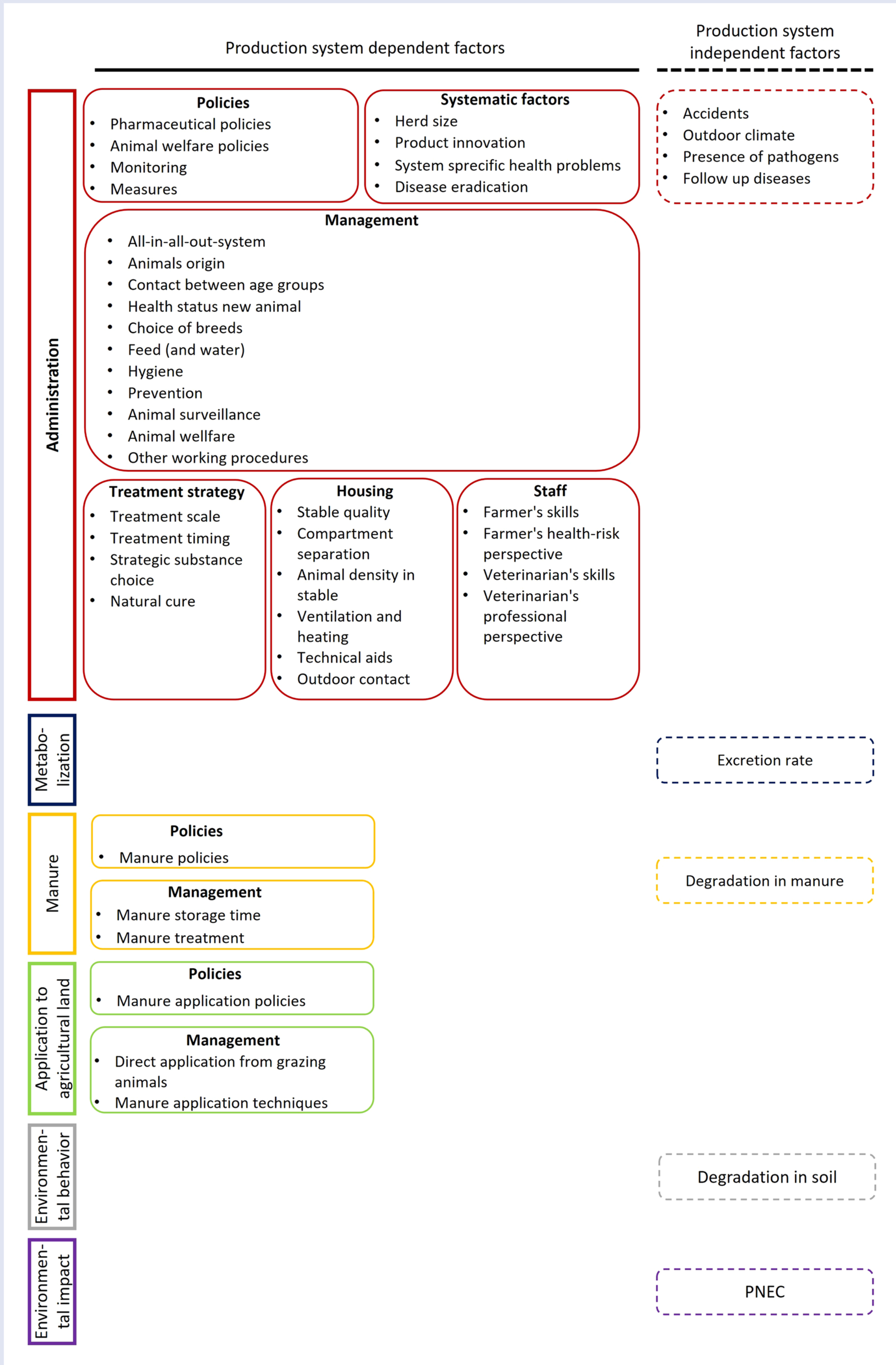

FIGURE 2 Framework illustrating identified factors that influence pharmaceutical pollution

result from the conducted interviews, factors for the other stages were obtained from the literature. We differentiate between factors that potentially differ among livestock types and production systems and factors that are purely substance dependent and thus independent of their source. For the administration, the framework displays collated factors mentioned for any livestock type. Not all factors, however, are relevant to all livestock types; see Supporting Information: Table S2.

Pilot assessment

Purposes and common practices of pharmaceutical use in Germany and the Netherlands. In the EU, veterinary pharmaceuticals are defined as veterinary medicinal products under directive 2001/82/EC and describe substances or a mixture of substances that diagnose, prevent, or treat diseases, or that restore, correct, or modify physiological functions in animals. The interviews revealed that, for different livestock types, pharmaceuticals with various functions are applied for diverse purposes. For prevention (especially for viral infections) vaccines were considered of exceptional importance. Preventive treatment with antibiotics is restricted in both Germany and the Netherlands (Köper et al., 2020; Speksnijder et al., 2015). Most of the veterinarians interviewed highlighted this but explained that a metaphylactic use is possible. Especially in beef cattle (veal), pigs, and poultry, metaphylactic treatment is a common practice due to typical housing situations of large herds. For veal and pigs, veterinarians described the aim of treating the smallest unit possible, whereas this is hardly possible for poultry where herds typically consist of tens of thousands of animals (for nontransmittable diseases, affected poultry are generally selected for killing). To restrain disease entry and spreading, a synchronized all-in-all-out system per stable, farm, or even region has been established in the pig and poultry fattening sectors. For all animal types (including dairy cattle), herd treatment exists for antiparasitic therapy.

Despite these practices, the interviewees explained that most pharmaceutical use is to treat diseases once they have occurred. They outlined that veterinary stock controls are conducted for early disease detection. Although in the Netherlands a veterinary-herd contract is mandatory (Bondt & Kortstee, 2016), it is common to have frequent veterinary stock controls in Germany as well. Yet, some farmers prefer to call veterinarians on demand only. According to the interviewed veterinarians, pertinent health issues occur across livestock's diverging life stages and body functions. In the dairy sector, most pharmaceuticals are used for calving and udder health. Here, generally individual cows are treated. Veal calves are specifically vulnerable to infections in the first weeks of their life. For pigs, the breeding and piglet sectors are the most challenging for health management. Depending on the livestock type, the occurring diseases differ and, consequently, also the applied substances. Table 1 presents an overview of commonly treated diseases by livestock type. A pharmaceutical substance group (that is seldom used to treat diseases but is used mostly to modify physiological functions, namely the reproductive cycle) is hormones. To understand the relevance of different substance groups for the diverse livestock types, we also include an overview of such (based on the information from interviewees) in Table 1.

Over the past years, limiting the use of antibiotics has been a priority for the EU as well as German and Dutch national policies. In addition to the 2006 EU-wide prohibition against antibiotics as growth promoters (European Commission, 2005), a harmonized monitoring of veterinary antibiotic sales in European countries was requested by the European Commission in 2010 (European Medicines Agency, 2021). Köper et al. (2020) indicate that the implementation of a monitoring scheme alone has led to the reduction in antibiotic use in Germany. In 2014, a benchmarking system with consequent actions was the first mandatory measure to reduce antibiotic use in fattening farms (noting that the dairy livestock is excluded from this system). Between 2011 and 2018, antibiotic sales decreased by 58% in Germany (Köper et al., 2020). The Netherlands implemented stepwise antibiotic reduction targets from 2008 onward; the latest goal is to reduce antibiotic use by 70% with reference to 2009 (Mevius & Heederik, 2014). This target was first reached in 2019, whereby reductions differ per livestock type (Groot et al., 2021). Antibiotics are not only regulated as a substance group, but also per substance which interviewees mentioned as potentially relevant to environmental pollution. One example are the categories of antibiotic use in livestock in the Netherlands (first, second, third choice, and prohibited substances; Werkgroep Veterinair Antibiotica Beleid, 2021). The interviewed veterinarians mentioned that the preference to apply certain substances differs in the two countries as well.

Pharmaceutical pollution from different livestock types and production systems

Comparing administration of different substance groups. For the pilot assessment we first analyzed the conducted interviews to retrieve information about where the pollution potential for the various pharmaceutical substance groups differs between conventional and organic production per livestock type. We did this for each factor identified for the life cycle stage of pharmaceutical administration and present these qualitative outcomes in Supporting Information: Tables S5–S9. The results presented are described as tendencies for pharmaceutical pollution and result from interviewees' precise statements or from combining logics of different interviews and assuming that some general statements about production systems apply to all livestock types. Yet, we were not able to fill in information for all factors. To interpret the results, it is necessary to emphasize that several interviewees pointed out that, even if there is a tendency, exceptions exist in all production systems with respect to most of the factors.

TABLE 1 Commonly treated diseases and applied substance groups for different livestock types (data based on interviews with veterinarians)

Livestock type	Cattle	Pig	Chicken
Commonly treated diseases	• Respiratory diseases (especially in calves; e.g., bovine respiratory disease, pneumonia) • Diarrheal diseases (especially in calves) • Parasites (e.g., worms, lice, cryptosporidium) • Metabolic diseases (e.g., ketosis in dairy cows) • Lameness and claw problems • Udder infections, especially mastitis (in dairy cows) • Fertility problems (e.g., ovary-related diseases; in dairy cows) • Milk fever (in dairy cows) • Abomasum displacement (in dairy cows) • Uterus infections (e.g., caused by *Trueperella pyogenes* or *E. coli*) • Diverse disease-causing pathogens that occurred as secondary infection after a primary viral infection	• Respiratory diseases (e.g., pneumonia, bronchitis) • Diarrheal diseases (especially in piglets) • Diseases of the central nervous system (e.g., meningitis caused by *Streptococcus suis*) • Wound infections (especially in piglets) • Glässer's disease • Parasites (e.g., *Ascaris suum*, Coccidia, Sarcoptes) • Fertility problems • Urinary tract infections • Diverse disease-causing pathogens that occurred as secondary infection after a primary viral infection (e.g., influenza, cicovirus)	• Bacterial infections of especially the respiratory tract or intestines (by e.g., Pasteurella, *E. Coli*, Enterococcus, Staphylococcus, *Ornithobacterium rhinotracheale*) • Parasites (e.g., worms, coccidia) • Clostridiosis • Lameness • Footpad dermatitis • Erysipelas • Polyserositis • Diverse disease-causing pathogens that occurred as secondary infection after a primary viral infection (e.g., avian rhinotracheitis, Marek's disease, infectious bursal disease)
Applied substance groups	• Antibiotics • Antiparasitics • Nonsteroidal anti-inflammatory drugs (NSAIDs) • Hormones (in dairy cows)	• Antibiotics • Antiparasitics • Nonsteroidal anti-inflammatory drugs (NSAIDs) • Hormones	• Antibiotics • Antiparasitics

Comparing the possibility of pollution for different livestock types reveals that major differences exist in applied substance groups, that is, no administration of hormones and nonsteroidal anti-inflammatory drugs (NSAIDs) for chickens. Also, hormones are not considered relevant in the beef cattle sector because all interviewees explained that beef cattle originate from dairy farms. However, the sector description (Supporting Information) demonstrates that bovine meat is also produced in primary production and therefore in these systems hormone use might also exist. Furthermore, differences between livestock types exist for specific factors that relate to livestock type-specific production characteristics. One example of this is the feed quality and composition (that is influential to the animal health and thus pharmaceutical use) where interviewees specifically mentioned a difference between conventional and organic systems in pig and chicken production, but not in cattle.

When comparing the conventional with the organic production systems, we can summarize that, depending on the factor, both production systems can have more or less pollution potential. Although, for example, hygiene practices lead to less pollution potential in conventional systems, disease prevention measures have the same tendency in organic systems. For other factors, we did not identify differences. Here the production system is not primarily influential; for example, accidents can happen in all production systems with similar consequences for pollution. For some factors, no difference between production systems resulted from the fact that there was no difference mentioned in the interviews, for example, for the factor "animal origin," stating that more animal origins on one farm led to higher likelihood of disease outbreaks.

Another observation is that, for each livestock type and each substance group (or a combination thereof), several influential factors do not apply. This is specifically the case for the substance group hormones. Hormones are given for reproduction purposes or to cure diseases that relate to fertility and reproduction. Consequently, all factors that influence infectious diseases do not influence the use of hormones. When comparing production systems, we see a clear tendency that pollution potential for hormones is larger in conventional production systems than in organic ones. This is because the use of hormones in organic production is limited to disease treatment, meaning that hormone administration for fertility management is only practiced in conventional systems.

The pollution potential of antiparasitics is influenced by a variety of factors but, in beef and dairy cattle, we identified only one factor where it differs between production systems: outdoor contact. Due to the regulation that all organically raised animals (independent of the livestock type) are required to have outdoor contact, the tendency for pollution resulting from antiparasitic use is greater in organic livestock farming than in conventional farming.

The pollution potential for antibiotics and NSAIDs is mostly analogous for the various factors. Interviewees explained that often these substance groups are administered for the same diseases either in parallel, or enforcing treatment with NSAIDs first, before falling back to antibiotic use. For these substance groups, the most differences among production systems were identified.

It should be noted that some of the factors impact each other. An example of this is the abovementioned restriction of hormone use in organic production systems that leads to greater pollution potential from several factors other than pharmaceutical policy in conventional systems.

Pilot assessment for indicator substances. All indicator substances are listed in Supporting Information: Table S10. For the pilot assessment, we selected one substance per group and livestock type, prioritizing those named by German and Dutch interviewees and those mentioned most often. The results indicate where most pollution potential is expected. In addition to the qualitative comparison among production systems, the excretion rate, degradation in manure and soil, and PNEC evaluate pollution potential quantitatively. Figure 3 presents the pilot assessment for oxytetracycline in dairy cattle production. The pollution potential from the excreted fraction and the degradation (in manure and soil) are high and medium, respectively. The PNEC is comparatively high, indicating a low pollution potential for the life cycle stage environmental impact. Supporting Information: Figures S1–S13 illustrate results for all other indicator substances and livestock types assessed. Comparing these, we identify flubendazole in broiler production as having the greatest per unit impact as the result of a comparatively high excretion rate, slow degradation, and low PNEC. Here, also, qualitative differences among production systems exist: for some factors conventional systems have the tendency for greater pollution, and for others the organic systems. For several substances, we diagnosed the lack of data to conduct a complete pilot assessment. Specifically for the hormone prostaglandin F2α, we were not able to retrieve any information about the excretion, degradation, or environmental impact. Despite these gaps, the assessment gives a starting point to understand differences in pollution from different livestock types and production systems. Moreover, it helps to identify which substances, livestock types, production systems, and the combination of these are likely to have the greatest pollution potential.

DISCUSSION

Results in perspective

No comprehensive analysis that compares pharmaceutical pollution from different livestock types and production systems exists (Sanders et al., 2019). There are, however, studies that compare individual aspects between organic and conventional livestock farming (or production system characteristics thereof) that can affect pharmaceutical pollution. In this section, we reflect on our findings from the pilot assessment (emphasizing factors of pharmaceutical administration that revealed differences between conventional and organic systems) from the perspective of relevant existing studies.

Herd size was identified as a systematic factor during our assessment. Although hormone treatment to synchronize herds and influence littering is prohibited in organic livestock farming, interviewees observed this practice in conventional (cattle and pig) farms with large herds. For dairy farming, Crowe et al. (2018) see the EU's milk quota removal as a major reason for herd size increase and the consequent need for fertility management, where hormone administration is one alternative method. Thus, it is unclear which methods farms with large herds tend to use and how much hormone pollution results from this.

The breeds of livestock were identified to relate to health status and pharmaceutical use. Interviewees explained that breeds designed to maximize production, commonly used in conventional systems, are potentially more disease-sensitive. This finding goes in hand with results by Louton et al. (2019), who conclude that slow-growing broiler breeds generally have better health status. Thus, also pharmaceutical use in slow-growing broilers will be less compared to breeds commonly used in conventional systems, supporting the finding of the present study.

Our results indicate that hygiene standards are less strict in organic systems, especially compared with highly industrialized farms. Therefore, health problems and pharmaceutical use tend to increase with decreasing hygiene. This tendency is reflected in other studies as well. Delsart et al. (2020) describe hygiene difficulties for alternative pig farms (systems differing from the "predominant contemporary structures") due for instance to organic materials used as floor coverage. Also, in organic dairy farming, udder hygiene is less frequently performed than on conventional farms (Orjales et al., 2016).

Animal density in organic farms is lower than conventional production systems. The results of this study indicate that lower animal densities lead to less pharmaceutical use and are supported by Rayner et al. (2020), who conclude that broiler health decreases with higher stocking densities. On the other hand, Tuyttens et al. (2008) could not assign health and welfare differences in organic and conventional broilers to individual factors such as stocking density. Yet, the authors found that overall welfare was better on organic than on conventional farms (Tuyttens et al., 2008).

According to the results presented, outdoor contact makes animals more vulnerable to infections and parasites. The fact that outdoor contact is a prerequisite in organic livestock production leads to the conclusion that this factor is causing more pharmaceutical use and pollution in organic farming than in conventional production. This phenomenon is described by several studies as well. A review of alternative pig

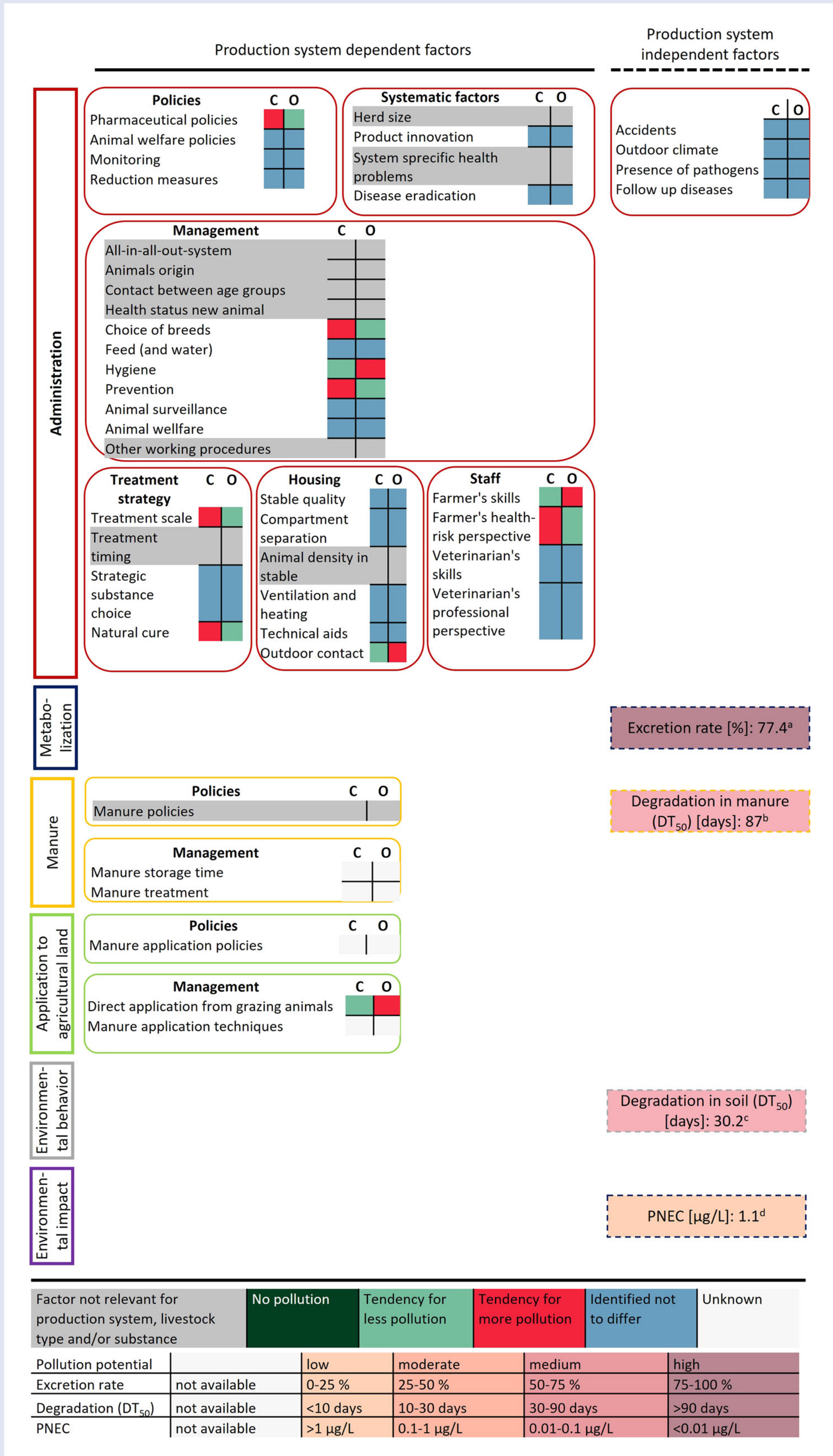

FIGURE 3 Pilot assessment for oxytetracycline pollution from dairy cattle production, comparing conventional (c) and organic (o) systems; data for comparison between production systems from interviews; quantitative data from literature: [a]average excretion rate (Nouws et al., 1985); [b]median DT50 (Berendsen et al., 2018); [c]median DT50 (Aga et al., 2005; Blackwell et al., 2007; Boxall et al., 2006; Chen et al., 2014; L.-L. Li et al., 2010; Wang & Yates, 2008; Y. Li et al., 2016; Yang et al., 2009); [d]predicted no effect concentration (PNEC; Bergmann et al., 2011)

farming systems (including organic) highlights the risks of disease entry (through various pathways such as wild boars, rats, or ticks) and parasites to those production systems that provide outdoor contact (Delsart et al., 2020). Van Wagenberg et al. (2016) conclude that contact with manure and outdoor access are reasons for parasite infections. For other health-related matters such as leg problems, however, outdoor contact has been found health-improving (Van Wagenberg et al., 2016). Interviewees of the present study also mentioned this but judged it to be of minor relevance to pharmaceutical pollution.

For several factors, we identified ambiguities. One example is the natural cure, which we identified to happen more in organic livestock farming than in conventional livestock farming. This comes with the risk that, when natural healing fails, the disease can become more severe and spread to other animals. Orjales et al. (2016) observed equivalent occurrences in a comparative study of conventional and organic dairy cows. Here the nonadministration of antibiotics in a group of organic cows led to chronic infections.

In addition to the comparison of individual factors, we identified one review study that compiles and compares aspects of sustainability between organic and conventional livestock production (Van Wagenberg et al., 2017). Although the study lacks direct statements about pharmaceutical use, it does reach conclusions about animal welfare and public health as indicators of social sustainability. Findings illustrate that sometimes conventional systems (e.g., in cow's udder health) and sometimes organic systems (e.g., less antimicrobial resistances) perform better. This lack of structural bias between conventional and organic production was mirrored in the assessed pharmaceutical pollution potential in this study: For some factors, the conventional system exhibits greater pollution potential (e.g., prevention) and, for other factors, the organic (e.g., hygiene). Palczynski et al. (2021) examine knowledge exchange about good practice in livestock management as a small effort with large potential for animal health. For the findings of the present study, this could indicate that knowledge transfer about practices causing less pollution can lead to less pollution overall (at least when large amounts of pollution are not inherent to the production system).

Limitations and reflections

We identified several limitations for our study that relate to the research method. The first set of limitations concerns the conducted interviews. The number of interviews is limited. However, all interviewed veterinarians were responsible for a large and diverse set of farms. Some of them worked for practices that have contracts with most farms with a specific livestock type in a region or even a country. So, we judge that, specifically for the factors that influence pharmaceutical pollution, findings from the interviews are robust. For the pilot assessment, interview data might be less representative, especially because of the small number of organic farms and, thus, not all interviewees were experienced with organic farming. Yet, we argue that the pilot assessment is a valuable first step in assessing differences in pharmaceutical pollution among production systems and should be seen as an exploratory study. Moreover, we aim for comprehensiveness at the various steps where data from the interviews are used, but we do not claim that the assessment is complete as veterinarians' insights, experiences, and viewpoints might differ. Although the interviewee selection followed an established and transparent method, there is potential bias in only interviewing veterinarians that were willing to participate. Furthermore, the interviews were conducted in Germany and the Netherlands and, as a consequence, outcomes (especially those of the pilot assessment) might not be directly transferable to other regions because production systems' characteristics such as housing can differ among countries (Früh et al., 2014). Livestock types were classified in a way that falls short in capturing differences in production steps of animals; for example, for pigs, differences in pharmaceutical administration exist between sows, piglets, and the fattening stages. Also, the categorization of production systems comes with limitations. Wallenbeck et al. (2019) demonstrate that the characteristics of organic farms with the same livestock type can differ and so can medicine use. The cause for this, however, was not discussed in detail (Wallenbeck et al., 2019). Moreover, interviewees emphasized that, for both the conventional and the organic production systems, labels that guarantee certain production characteristics (e.g., the prohibition of specific substances) exist. Considering these subcategories would potentially result in different outcomes.

We identified further limitations that may have affected the research outcomes. The identified factors are exclusively those linked directly to the pharmaceutical life cycle. For instance, manure application is considered, but interlinked aspects such as soil treatment practices potentially affecting pollution are not accounted for. Also, factors that depend on a multitude of variables (such as sorption or potential decay in surface waters) are not included. If the purposes require, for example, when using the framework for a specific case study, the framework can be extended by these parameters. Due to nonavailability of data, a quantitative assessment of administered amounts per production system is lacking in the pilot assessment, although considered relevant to a complete evaluation of the pollution potential. Consequently, we relied on qualitative results that are displayed as tendencies. Several interviewees emphasized the ambiguity in their qualitative descriptions attributable to the heterogeneity of farms within one production system category. Furthermore, substance-specific indicators come with limitations as well; for example, the excretion rate does not account for topical administration of antiparasitics. We also do not consider metabolites in the assessment, despite their pollution potential (Celiz et al., 2009).

Reflecting on the results of the pollution potential, we judge that the qualitative comparison of production systems is rather robust in the German–Dutch context due to the high degree of agreement between interviewees' responses. As a first indicative assessment for pharmaceutical pollution potential comparing different livestock types and production systems, it represents a basis for policymaking. Nevertheless, quantitative data on pharmaceutical administration in the different production systems should be collected to substantiate the pilot assessment's results and assess if the findings of our assessment hold. In contrast to the qualitative outcomes, the quantitative comparison of the pollution potential between the indicators' excretion rate, degradation, and PNEC is considered rather sensitive.

CONCLUSION

The research presents a novel framework to assess pharmaceutical pollution from different livestock production systems, covering the entire pharmaceutical life cycle from administration to environmental impact. Along each life cycle stage, we were able to identify factors that influence pharmaceutical pollution. Many of these factors, especially those for the life cycle stage of pharmaceutical administration, can differ among livestock types and production systems. Other factors, such as the degradability in manure or soil, are determined purely by the substance and thus are independent of their source.

One objective of this article was to develop a framework to assess pharmaceutical pollution of different livestock production systems. A remaining challenge identified is the lack of production system categories that are useful to environmental assessments, specifically including pharmaceutical pollution. Furthermore, we emphasize the lack of usefulness of current public databases such as Eurostat to proceed to a quantitative assessment using our framework in the future.

In the pilot assessment, we took an in-depth look at differences in pollution potential between production systems for the stage of pharmaceutical administration in the German–Dutch context. This analysis revealed that, for several factors, a difference between production systems is not expected. Yet, for other factors, we were able to identify tendencies for pollution potential to differ between conventional and organic production. For the substance groups antibiotics and NSAIDs for some factors, the conventional system has a greater tendency to pollute; for other factors, it is vice versa. This is the same for antiparasitic substances except for cattle where tendencies for greater pollution was observed only in organic livestock farming. Overall, pollution with hormones is more likely to result from conventional livestock.

Comparing the pollution potential among indicator substances and livestock types revealed that flubendazole used in broiler production has the greatest per unit substance impact. This results from a high excretion rate of flubendazole in broilers combined with slow degradation in manure and soil and a low PNEC. Differences between organic and conventional production were identified, yet, depending on the influential factor, the tendency for less (or inversely more) pollution was found in both systems.

Using the presented framework, the pollution potential can be identified across substances, livestock types, and production systems. So, the framework is a useful tool to identify where most pollution is expected and thus is a relevant addition to existing environmental assessments that currently neglect pharmaceutical pollution. Based on insights from applying our framework, policy recommendations can be formulated, potentially leading to less pollution overall. Results of the pilot assessment can already support scrutinizing assumptions that are currently made for modeling and risk assessment approaches to evaluate pharmaceutical pollution due to the scattered and incomplete data available.

AUTHOR CONTRIBUTION

Lara Wöhler: Conceptualization; data curation; formal analysis; investigation; methodology; writing—original draft. **Rick J. Hogeboom**: Conceptualization; methodology; writing—review and editing. **Markus Berger**: Conceptualization; methodology; writing—review and editing. **Maarten S. Krol**: Conceptualization; methodology; writing—review and editing.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data are provided in the Supporting Information.

SUPPORTING INFORMATION

Methods and data, data collection details, and results. Tables illustrate an overview of interview questions, results about factors that influence pharmaceutical administration and pollution, and the pollution potential for influential factors in pharmaceutical administration. Figures depict results of the pilot assessment for different substances, livestock types, and production systems.

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