The utility of quality indicators for antimicrobial stewardship from human medicine for antimicrobial stewardship implementation in companion animal practices in the Netherlands

Writing Assignment

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Mariken van Wessel

Supervisor

Dr. E.M. (Els) Broens

Utrecht University

Faculty of Veterinary Medicine

Department Biomolecular Health Sciences

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Abstract

Antimicrobial Resistance (AMR) is currently among the biggest threats to healthcare. To reduce AMR, it is necessary to limit the selective pressure of antimicrobial usage (AMU) leading to AMR. To achieve this, there is an emerging interest in Antimicrobial Stewardship Programs (ASPs). Research in human medicine has yielded positive results in the design and implementation of ASPs. To help implement, improve and evaluate the effectiveness of ASPs, Quality Indicators (QIs) that measure the quality of AMU are used in human medicine. Companion animal medicine also contributes to the development of AMR and therefore there is an emerging interest in ASPs for this sector. Currently, ASPs are not routinely implemented and QIs are not developed for companion animal practices. Therefore, this literature review investigates which QIs for antimicrobial stewardship, derived from human medicine, can contribute to the implementation of ASPs in companion animal practices in the Netherlands.

To address this research gap, literature research was conducted using the PubMed and Web of Science databases. This has led to an overview of QIs and associated themes for ASPs used in hospitals and general practices (GPs) in human medicine. In addition, core elements for ASPs with associated challenges in companion animal practices have been identified.

Subsequently, QIs were identified that can contribute to the implementation of ASPs in companion animal practices. There are currently no QIs that are directly applicable to companion animal practices in the Netherlands. However, QIs that have the most potential to be applied first in companion animal practices, are drug- and disease-specific QIs that are used in GP. Other QIs are too advanced or complex or not applicable in companion animal practices. Future research should focus on ways to take the hurdles that currently hinder the adaptation and implementation of the drug- and disease-specific QIs into ASPs for companion animal practices.

Plain Language Summary

Antimicrobials are medications that help fight infections caused by small organisms such as bacteria, fungi and parasites. However, sometimes these medications no longer work because these organisms have become resistant. This phenomenon is called antimicrobial resistance and it is a major problem facing healthcare systems around the world, because it reduces the effectiveness of antimicrobial treatments.

Antimicrobial resistance occurs when antimicrobial medications are used too often or incorrectly. So, it is important that doctors and patients are aware of this problem. To increase awareness on antimicrobial resistance and to promote correct use of antimicrobials, Antimicrobial Stewardship Programs (ASPs) are developed and used. These programs are already implemented in hospitals and general practices and have led to less and better antimicrobial treatments in human medicine. ASPs contain different elements like education and feedback for doctors. One element that is used to provide feedback are the so-called quality indicators (QIs). These QIs measure for instance how many antimicrobial treatments a doctor prescribes or whether the correct drug is prescribed according to guidelines. QIs can be used to compare different doctors and in that way they help increase awareness and improve antimicrobial treatment.

Antimicrobials are not only used in human medicine, they are used in veterinary medicine as well. Pets also get antimicrobial treatments when they go to the veterinarian with an infection caused by small organisms. In veterinary medicine there is also attention for antimicrobial resistance, but in pet practices, which include pets such as dogs, cats and rabbits, ASPs and QIs are less common. There are some smaller studies done in different countries, but antimicrobial stewardship in veterinary medicine is still in the early stages of its development.

In this writing assignment I looked at the different QIs that are used in human medicine, to see if these can be used in pet practices as well, to increase awareness and improve antimicrobial treatment in this setting. I selected a few QIs from general practice that seem very suitable for pet practices. Other QIs need to be adjusted or are not suitable for pet practices at all. The selected QIs can be included in ASPs for veterinary medicine to increase awareness among veterinarians and pet owners. This will lead to less and better antimicrobial treatments in our pets. The ultimate goal is to maintain the effectiveness of antimicrobial treatments in both humans and animals.

1. Introduction

The emergence of antimicrobials was groundbreaking for the development of medicine, reshaping the ability to effectively manage and treat numerous infectious diseases. For example, antibiotics have enabled the successful execution of invasive medical procedures such as open-heart surgeries and organ transplantations. However, there has been an increasing amount of microorganisms exhibiting resistance to antimicrobials. This phenomenon, known as Antimicrobial Resistance (AMR), ranks among the worst threats to healthcare to date, posing the risk of treatment failures and subsequent increased morbidity and mortality (Huemer et al., 2020). To highlight the magnitude of AMR's consequences; it is estimated that antibiotic-resistant bacteria alone will lead to over 10 million deaths worldwide per year (O'Neill, 2016). The problem of AMR is further complicated by the lack of development of new antimicrobials (Garau et al., 2018).

Given the limited development of new antimicrobials and the fact that numerus studies show that AMR is associated with antimicrobial use (AMU), it is important to use antimicrobials adequately and responsibly to limit the selective pressure of AMU leading to AMR (Septimus, 2018). To achieve this, there has been an emerging interest in Antimicrobial Stewardship (AMS) (Dyar et al., 2017). AMS refers to a collaborative and multidisciplinary approach to measure and improve antimicrobial prescribing, by choosing the most appropriate drug, dosing, duration, and route of administration. The objective is to reduce AMR by ensuring to only use antimicrobials when needed and by using antimicrobials responsible (Dyar et al., 2017; Septimus, 2018). Typically, these AMS interventions are combined into overarching antimicrobial stewardship programs (ASPs).

Extensive research has already been conducted on designing and implementing ASPs in the field of human medicine. In fact, ASPs have already been successfully implemented in multiple hospitals in various countries (Garau et al., 2018; Tinker et al., 2021; Hwang et al., 2021). The implementation of ASPs in hospitals has led to a notable reduction in adverse events associated with the use of antimicrobials and therefore might contribute to a decline in AMR. The majority of ASPs implemented in hospitals are based upon the 'seven core elements for ASPs', an ASP guideline established by the Centers for Disease Control and Prevention (CDC) (Septimus, 2018). These core elements consist of: Leadership commitment, Accountability, Involvement of a pharmacy leader, Actions to implement intervention, Tracking prescriptions, Reporting prescriptions and Education for healthcare providers (CDC, 2019). These core elements should be tailored to each unique ASP, given the inherent differences between hospitals in terms of size, staffing, and prescribing practices (Cunha, 2018). Of all the core elements, 'Actions to implement interventions' exhibits the most variety of researched specifications for ASPs, such as performing microbiological diagnostics prior to initiating antimicrobial treatments, choosing drugs and dosing based on clinical evidence-based guidelines, and far more (Septimus, 2018; Tinker et al., 2021; Majumder et al., 2020).

ASPs must not only be tailored to different hospitals but also within each hospital due to the diversity of medical departments. To illustrate, distinct ASPs have been developed for medical departments such as paediatric medicine (Probst et al., 2021) and the intensive care unit (Murphy et al., 2022). Moreover, there is need for tailored ASPs beyond the hospital setting, for example for general practice (GP). GP takes on special significance in the context of AMS, as most antibiotic prescriptions in human medicine originate from this sector. This makes GP a good place to implement ASPs (Hawes et al., 2020a). Therefore, the CDC established core elements for ASPs for outpatient settings, including GP. These outpatient core elements include the following four: Commitment, Action for policy and practice, Tracking and reporting and lastly Education (Sanchez et al., 2016). Furthermore, research on ASPs in

GP has been conducted and important actions for ASPs have been identified e.g. feedback to prescribers, consultation support and delaying prescribing of antimicrobials. Although progress has been made in the early stages of implementing ASPs in GP, it is imperative to highlight the continued need for further research to optimize the outcomes of ASPs (Suttels et al., 2022; Hawes et al., 2020a).

AMR does not only influence human medicine, it extends its influence into veterinary medicine. For example, the American Veterinary Medical Association Committee on Antimicrobials observed an increasing amount of infections caused by antibiotic-resistant bacteria in animals in the United States (Ruzante et al., 2022). Even though multidrug-resistant bacteria have been isolated from farm and companion animals, a total quantification of direct effects of AMR on animal health in veterinary medicine is lacking (Allerton et al., 2023). AMU in animals contributes to the development of AMR in animals and by direct and indirect contact this contributes to AMR in the environment and humans. This interaction characterizes AMR as a 'One Health' problem and veterinarians as crucial players against AMR (McEwen et al., 2018; Allerton et al., 2023). Although AMU in veterinary medicine is more pronounced in farm animals than in companion animals, companion animal medicine plays a crucial role in the context of AMR. This is primarily due to the close relationship between companion animals, their owners, and the extended household (Lloyd et al., 2018).

Due to the close relationship between companion animals and humans, which facilitates the potential transfer of AMR, ASPs have become a point of interest within companion animal practices in the last decade. Theoretical ASPs have been proposed, often inspired by ASPs established within human medicine (Lloyd et al., 2018). Moreover, trials of ASPs in companion animal practices have been conducted, exemplified by studies of Hopman et al. (2019), Richards et al. (2023) and Hardefeldt et al. (2022). Both the theoretical research and trials are contributing to the development of ASPs for companion animal practices. However, the ultimate success of ASPs in companion animal practices depends on their adaptation to unique practices and maintenance of their implementation.

Conventionally, the effectiveness of ASPs is evaluated through the monitoring of AMU. Nonetheless, this quantification of AMU offers an incomplete perspective. To fully measure the impact of ASPs, attention should also be focused on assessing the quality of AMU. In order to assess the quality of antimicrobial prescribing, so-called Quality Indicators (QIs) are used. QIs are “measurable elements of practice performance for which there is evidence or consensus that they can be used to assess the quality of care provided” (O’Riordan et al., 2021, p1). QIs for AMS have been developed and successfully deployed across diverse healthcare settings, including hospitals and GPs. (O’Riordan et al., 2021). Currently there are no QIs defined or implemented in companion animal practices yet. Consequently, this study aims to investigate which QIs designed for ASPs in human medicine can be effectively utilized to support the successful and maintainable implementation of ASPs in companion animal practices in the Netherlands. This leads to the following research question: *‘Which quality indicators for antimicrobial stewardship derived from human medicine can contribute to the implementation of antimicrobial stewardship programs in companion animal practices in the Netherlands?*’.

In order to address the research question, literature searches were conducted using the PubMed and Web of Science databases. The used search terms, applied filters, and search strategy can be found in the Appendix. The subsequent sections of this literature review are organized as follows. Chapter Two provides a concise overview of the QI developed in human medicine. Chapter Three offers an insight into the core elements of ASPs in companion animals practices. Chapter Four discusses which QI from human medicine can be applied to companion animal practices in the Netherlands. The final chapter provides the conclusion and suggestions for future research.

2. Quality Indicators for antimicrobial stewardship in human medicine

Quality Indicators (QIs) in medicine can be defined as "measurable elements of practice performance for which there is evidence or consensus that they can be used to assess the quality of care provided" (O'Riordan et al., 2021, p1). This definition emphasizes that QIs should be evidence based or having a consensus among experts that they can effectively evaluate the quality of care. Therefore, QIs should be based on available scientific evidence whenever possible and otherwise based on consensus of experts opinions. The best way of developing QI would be to base them on both.

A wide variety of QIs are already widely employed in assessing care within human medicine. For example, QIs have been used to assess the quality of care in the intensive care unit (ICU), perioperative care and laboratory performances in hospitals (Kumpf et al., 2022; Wacker, 2023; Sciacovelli et al., 2023). Furthermore, QIs have been used to implement, asses and improve antimicrobials stewardship programs (ASPs) in hospitals and general practice (GP) (O'Riordan et al., 2021; Van der Velden et al., 2020).

QI for antimicrobial stewardship programs in hospitals

The majority of QIs for antimicrobial stewardship (AMS) are developed for the hospital setting. They cover a broad spectrum ranging from general QIs to very specific indicators. While some of these QIs have clear methodologies of how they were created, others lack clarity in this regard. This poses a challenge because it becomes difficult to verify if these QIs are based on scientific evidence or consensus of experts, which is important to know following the definition of QIs.

To address this issue, O'Riordan et al. (2021) conducted an extensive literature research about QIs for ASPs in hospitals. They selected QIs for ASPs in hospitals from which the methodology of their development was described. For these selected QIs, the methodology quality was assessed via the 'Appraisal of Indicators through Research and Evaluation' (AIRE) instrument. This is a validated instrument that enables to assess the quality of QIs on different domains, namely 'purpose, relevance and context', 'stakeholder involvement', 'scientific evidence' and 'additional evidence, formulation and usage'. The study of O'Riordan et al. (2021) used the latter three domains to assess the QIs for ASPs (O'Riordan et al., 2021).

O'Riordan et al. (2021) divided the selected QIs in structural QIs, process QIs and outcome QIs. Furthermore, they assigned the individual QIs to themes. Table 1 offers a concise overview of the QI themes with examples for each theme. The process QIs within the theme '*Specific infectious conditions'* contains among others QIs for community-acquired pneumonia, chronic obstructive pulmonary disease (COPD), urinary tract infections and bloodstream infections. For outcome QIs for ASPs in hospitals only one theme was identified. In total, 229 ASP specific QIs for hospitals were identified, which are distributed across the beforementioned themes (O'Riordan et al., 2021).

Table 1. Concise overview of identified themes for Quality Indicators (QI) for Antimicrobial Stewardship Programs (ASPs) in hospitals. (O'Riordan et al., 2021).

QI theme	Example of a specific QI
Structural QI	
AMS governance, leadership and accountability	A multidisciplinary AMS team is created
AMS multidisciplinary expertise and resources	Antimicrobials mentioned on guidelines should always be available in the hospital
AMS policies and programs to improve antimicrobial prescribing	Audit and feedback is given to prescribers of antimicrobials
Antimicrobial prescription guidelines	Antimicrobials guidelines are present
AMS education	AMS education is provided to prescribers
Microbiology laboratory standards, AMR surveillance and feedback	Antibiograms are used when prescribing antimicrobials
Process QI	
Infection diagnosis	Results of bacteriological sensitivity tests are documented
Pharmacy-supported interventions	Allergies for antimicrobials are documented
Important elements for good antimicrobial prescribing practice	Documentation of each antimicrobial treatment plan is present
Specifically for certain infectious conditions	Duration of pyelonephritis therapy not longer than 10 days
Outcome QI	
Clinical outcome	Clinical outcomes of patients who had an antimicrobial treatment are monitored

AMS = Antimicrobial Stewardship

All but one (QIs for AMU in ICU) QIs scored high on methodology quality. The scores on 'stakeholder involvement', 'scientific evidence' and 'additional evidence, formulation and usage' domains varied substantially among QIs. The lowest scores were observed in the 'additional evidence, formulation and usage' domain, indicating that QI are frequently lacking validation in practical application (O'Riordan et al., 2021).

QI for antimicrobial stewardship programs in general practice

The vast majority of antimicrobials prescriptions in the human medicine take place in primary care. Meaning that GP contributes to AMR substantially. Therefore, QIs that assess AMU in GP are very relevant. However, the organization of care in GP is significantly different from the hospital setting what makes the utility of QIs designed for hospitals in GP questionable (Pulcini et al., 2013).

ESAC drug-specific Quality Indicators

The first set of QIs designed for ASPs in GP are the 'QIs for outpatient use in Europe', established by the European Surveillance of Antimicrobial Consumption (ESAC). To improve AMU in GP, these twelve QI are developed by a multidisciplinary team, therefore they are based on consensus of expert opinions. The QIs are assessed on the possibility of reducing AMR, improving patient health benefits, costs and alignment with public health policy makers (Coenen et al., 2007). The QIs are focused on total AMU expressed in Defined Daily Dose per 1000 patients per day (DID), on the total (DID) and relative (in percentage) consumption of certain antimicrobial classes and on the seasonal variation (Coenen et al., 2007). An overview of these drug-specific QIs of the ESAC can be found in Table 2.

Table 2. Overview of the drug-specific Quality Indicators developed by the European Surveillance of Antimicrobial Consumption for antibiotic use in outpatient settings (Coenen et al., 2007).

Drug-specific Quality Indicators
1. Consumption of antibiotics for systematic use expressed in DID
2. Consumption of penicillin's expressed as DID
3. Consumption of cephalosporins expressed as DID
4. Consumption of macrolides, lacosamide's and streptogramins expressed as DID
5. Consumption of quinolones expressed as DID
6. Consumption of beta-lactamase sensitive penicillin's expressed as percentage of the total consumption of antibacterials for systematic use
7. Consumption of combination of penicillin's with beta-lactamase inhibitors expressed as percentage of the total consumption of antibacterials for systematic use
8. Consumption of third and fourth generation cephalosporins expressed as percentage of the total consumption of antibacterials for systematic use
9. Consumption of fluroquinolones expressed as percentage of the total consumption of antibacterials for systematic use
10. Ratio of consumption of broad to the consumption of narrow spectrum penicillin's, cephalosporines and macrolides
11. Seasonal variation of the total antibiotic consumption (winter versus summer)
12. Seasonal variation of the total quinolone consumption (winter versus summer)

DID = Defined Daily Dose per 1000 patients per day (DID)

The most useful QI is the initial one about overall systematic AMU, as this provides a comprehensive picture of the pressure exerted on the selection of resistant bacteria. Furthermore, the QIs about specific antibiotics should always be assessed as a total. For example, if the use of one antibiotic is very low, it can mean that another group of antibiotic has high usage. Therefore the correlation between different QIs should be assessed as well (Coenen et al., 2007).

The clear advantage of these QIs lies in their relative ease of implementation within GP because the data required are often directly available in electronic patient files (Coenen et al., 2007). In a study among French GP these QIs were implemented and the researchers concluded that these QIs can be used as a self-assessment tool for individual GPs. Furthermore, the QIs can create benchmarks for AMU that can serve as a motivational factor for practices to improve their antibiotic prescription habits (Pulcini et al., 2013). A similar study among Dutch GPs concluded that using these QIs can provide valuable insights into the quality of antibiotic prescribing, enabling the identification of future improvement in ASPs. However, they also state that working with the QIs should be with some caution, as still not every prescription is registered (Van der Velden et al., 2016).

When comparing these drug-specific QIs for GP with the overarching QI themes identified for ASPs in hospitals (Table 1), the drug-specific QIs align with the themes '*AMS policies and programs to improve antimicrobial prescribing*' and '*AMS education*' of the structural QI. They align to the first mentioned theme as data regarding AMU can give insights on how antimicrobial prescribing can be improved. Furthermore, these drug-specific QI can be used under the 'AMS education' theme as individual AMU data can help with targeted education regarding prescribing.

ESAC disease-specific Quality Indicators

A disadvantage of the drug-specific QIs is that they only assess the quantification of AMU. However, as emphasized in the introduction, assessing the quality of AMU is also crucial. Hence, the ESAC developed disease-specific QIs for outpatient use of antibiotics in Europe, four years after the introduction of the drug-specific QIs. The objective of the disease-specific QIs is to assess the quality of antimicrobial prescribing via the link between the clinical indication for treatment and the prescribed antimicrobial.

By linking the antimicrobials prescribed to certain indications, it becomes possible to assess the appropriateness and with that the quality of antimicrobial prescribing. However, to assess whether the appropriate antimicrobial agent is being prescribed for a particular indication, antimicrobial prescribing guidelines are needed to determine what the appropriate antimicrobial agent is for a particular indication (Van der Velden et al., 2020).

These disease-specific QIs are developed by a multidisciplinary team with the same assessment methodology as for the drug-specific QI. Eventually a set of seven disease-specific QIs for AMU was created, each comprising three sub-indicators (Adriaenssens et al., 2011). Table 3 shows the QI set and its sub-indicators for acute bronchitis/bronchiolitis. Similar QI sets were developed for six other clinical indications, i.e. upper respiratory infection, cystitis, tonsillitis, sinusitis, acute otitis media and pneumonia (Adriaenssens et al., 2011).

Table 3. Example of a disease-specific Quality Indicator (QI) set by ESAC for outpatient antibiotic use for acute bronchitis/bronchiolitis. 1a shows the first sub-indicator, 1b the second and 1c the third sub-indicator belonging to one QI set (Adriaenssens et al., 2011).

QI set for bronchitis/bronchiolitis
1a. Percentage of patients aged between 18 and 75 years with acute bronchitis/bronchiolitis prescribed antibiotics for systemic use
1b. Percentage of patients aged between 18 and 75 years with acute bronchitis/bronchiolitis prescribed antibiotics for systemic use receiving the recommended antibacterials
1c. Percentage of patients aged between 18 and 75 years with acute bronchitis/bronchiolitis prescribed antibiotics for systemic use receiving quinolones

Assessing these disease-specific QIs on the 'reducing AMR, improving patient health benefits, costs and alignment with public health policy makers' domains showed that the disease-specific QI outperformed the drug-specific QIs in all of these domains. As such, these disease-specific QIs are more effective for checking the quality of antibiotic prescribing for general practitioners (Adriaenssens et al., 2011). Consequently, the disease-specific QIs are the preferred choice as QIs for implementing and improving ASPs in GPs. Like the drug-specific QIs, the disease-specific QIs can also be used for benchmarking. This comparative aspect could be valuable in driving further improvements in antibiotic use within GP, as it allows practices to assess their performance against each other and identify areas for improvement (Adriaenssens et al., 2011).

The ESAC QIs are based upon the internationally established Anatomical Therapeutic Chemical (ATC) code for medicines and the internationally established International Classification of Primary Care (ICPC) codes for clinical information (WHO, 2018; WICC, n.d.). These international coding standards facilitate the widespread implementation of the QIs and enable comparisons of AMU among GPs across different countries. However, a challenge is that not all antibiotic prescription data are already linked to ICPC and ATC codes, making it difficult to calculate the QIs in every GP. Therefore, it should be encouraged to general practitioners to collect patient data linked to ICPC and ATC codes and to collect the data in electronic health records (Adriaenssens et al., 2011). Another challenge is that guidelines might differ in various countries which can lead to problems when comparing the outcomes of the disease-specific QIs between different countries (Tyrstrup et al., 2017). Nevertheless, a study in the Netherlands, Belgium and Sweden showed that the disease-specific QIs for outpatient care of the ESAC can be successfully calculated for GPs in these three countries (Tyrstrup et al., 2017). Moreover, a study among Dutch GPs using QIs showing strong similarities with the ESAC QIs, showed that general practitioners preferred the disease-specific QIs over the drug-specific QIs. Furthermore, 70% of the interviewed

general practitioners believed that antibiotic prescription QIs could positively influence their prescription habits. Therefore this trial of antibiotic prescription QIs in GP demonstrates that the QIs can help with implementing and improving ASPs in GP (Van der Velden et al., 2020).

When comparing these disease-specific QIs of GP with the overarching QI themes identified for ASPs in hospitals (see Table 1), the disease-specific QI align with the themes '*AMS policies and programs to improve antimicrobial prescribing', 'AMS education'* and '*Antimicrobial guidelines'* of the structural QI. The rationale for the alignment of the first two themes mirrors that of drug-specific QIs, as mentioned previously. However, the disease-specific QIs also align with the '*Antimicrobial guidelines*' theme as the presence of guidelines is necessary for developing and using these disease-specific QIs.

3. Quality Indicators for antimicrobial stewardship in veterinary medicine

While research and trials have been conducted for developing Antimicrobial Stewardship Programs (ASPs) in companion animal practices, its development lags significantly behind human medicine (Lloyd et al., 2018). ASPs are not routinely implemented in companion animal practices and there are no quality indicators (QIs) defined for companion animal practices (Hardefeldt et al., 2022). However, the demand for ASP QIs in companion animal medicine is evident, as these QIs can help with implementing and improving ASPs in practices. Especially in this incipient state of ASPs development in companion animal practices, QIs can play a role in implementing tailored ASPs, as they provide data and insights on improvement areas.

Multiple theoretic and trial ASPs have been developed and implemented in companion animal medicine. These independent studies offer different ASPs, yet certain elements exhibit notable similarities and overlapping features indicating a shared consensus about their importance. These elements will be further addressed as 'core elements'. In this chapter these core elements, associated QI themes and its applicability in companion animal practices will be described.

Structural QI themes

AMS governance, leadership and accountability

A core element of ASPs often mentioned in reports on AMS in companion animal practices is the presence of an AMS team. Comparing this to the QI themes for ASPs in hospitals, this corresponds to the theme '*AMS governance, leadership and accountability'*.

The importance of a collaborative team within the companion animal practice that communicates with all stakeholders, including the owners of companion animals was discussed by Lloyd et al. (2018) and Vercelli et al. (2022). A trial study implementing ASP in a university hospital for companion animals established an AMS team consisting of clinicians, faculty staff, students and pharmacists (Feyes et al., 2021) and a study that evaluated an ASP in Dutch companion animal practices also had a team with experts that was available for advice and questions remotely (Hopman et al., 2019). Furthermore, the role of veterinary technicians in an AMS team has been researched (Redding et al., 2023). Lastly, assigning a single veterinarian responsible for AMS was reported as one of the success factors for implementing an ASPs on trial basis in companion animal practices (Hardefeldt et al., 2022; Richards et al., 2023). Overall, the presence of an AMS team or responsible person within a practice is repeatedly identified as a core component in ASPs for companion animal practices. Even though there is no consensus about the composition of the AMS team, the importance of having an AMS team in place is highlighted, demonstrating that this QI theme is relevant for companion animal medicine.

AMS policies and programs to improve antimicrobial prescribing

The most recurring core element in ASPs for companion animal practices is the need for 'Tracking and reporting antimicrobial prescriptions' demonstrating that the QI theme '*AMS policies and programs to improve antimicrobial prescribing*' is relevant for companion animal medicine. All ESAC QIs developed for GP also fall under this IQ theme.

Interviews with Australian veterinarians showed that many veterinarians admitted to antimicrobial overuse and that only 35% of respondents were aware of the amount of antimicrobials sold in the practice. This indicates a lack of awareness on AMU in companion animal practices and underscores the need for a structured system to monitor AMU (Hardefeldt et al., 2018). All studies conducted on

AMS in veterinary medicine recommend or implement monitoring of AMU in some way. However, methods to quantify AMU vary between studies. Few studies use the incidence of antimicrobial prescription per 100 consultations or the number of antimicrobial prescriptions during a certain period to monitor AMU (Hardefeldt et al., 2022; Feyes et al., 2021). Another study quantifies AMU by calculating the Defined Daily Dose Animal (DDDA). DDDAs corrects for dosing differences between different antimicrobials and between species and enables comparison over time and between clinics. This method is also used for monitoring AMU in food producing animals and is established by the European Surveillance of Veterinary Antimicrobial Consumption group (ESVAC) (Hopman et al., 2019). These examples show initially the need for a standardised way to quantify AMU and after that a shift of focus towards the use of critically important antimicrobials and the quality of AMU (Lloyd et al., 2018).

In addition to monitoring prescriptions, other components of the element 'Tracking and reporting antimicrobial prescriptions' have been reported repeatedly in companion animal medicine, in particular feedback to veterinarians. Evaluation of and feedback on antimicrobial prescription habits of veterinarians can lead to a decrease in AMU and is an effective and valuable approach for changing antimicrobial prescribing habits (Lloyd et al., 2018; Dunn and Dunn, 2012; Hopman et al., 2019).

Antimicrobial prescription guidelines

While attention has been on quantification of AMU, it has been lacking for qualification. To assess the quality of AMU, there has to be consensus on what the right antimicrobial is for a certain indication. Therefore, uniform antimicrobial prescription guidelines are essential. This has also been identified as a core element for ASPs in companion animal practices and it falls under the QI theme '*Antimicrobial prescription guidelines'*, suggesting that this QI theme is relevant for companion animal medicine.

Various studies identify development and use of antimicrobial prescription guidelines as important measures to reduce AMU. Most studies on ASP implementation in companion animal practices use or adapt national guidelines as an intervention to increase awareness or to provide feedback on antimicrobial prescription (Lloyd et al., 2018; Feyes et al., 2021; Richards et al., 2023).

Few guidelines for antimicrobial treatment of animals exist, e.g. those developed by the International Society for Companion Animal Infectious Diseases (ISCAID, n.d.). These international guidelines are valuable but cannot replace national or regional guidelines, which take into account important local factors such as resistance patterns, availability of drugs, and national legislation. Only a few European countries have national guidelines on responsible AMU. These guidelines are often developed without a structured approach and are mostly based on expert opinion (Allerton et al., 2021). It is important that the development of antimicrobial prescription guidelines is independent from pharmaceutical companies, because interviews with veterinarians shows that this leads to scepticism regarding the guidelines (Hardefeldt et al., 2018).

Antimicrobial stewardship education

The final core element identified for companion animal practice is AMS education, that aligns with the '*Antimicrobial stewardship education'* QI theme, demonstrating that this QI theme is relevant for companion animal practices. Hardefeldt et al. (2018) identified a lack of AMS education as a major barrier regarding the implementation of ASPs in companion animal practices. In their online survey conducted among Australian veterinarians, they found that 96% of the respondents of the survey considered additional education on AMS a valuable idea and that 97% of the veterinarians were willing to change their antimicrobial prescription habits based on AMS education.

Most studies included education on AMR and AMU in their ASPs (Feyes et al., 2021; Hopman et al., 2019). Not only veterinary personal was educated regarding AMR and responsible AMU, students were also educated. Few studies also focused on informing companion animal owners or the general public (Hopman et al., 2019; Vercelli et al., 2022). Lastly, given the interest in AMS education but with time- and costs constrains of education in mind, Allerton et al. (2023) examined for various online resources developed for AMS education if they are applicable for companion animal practices.

Discussion

This literature study aimed to identify which quality indicators (QIs) for antimicrobial stewardship (AMS) derived from human medicine can contribute to the implementation of antimicrobial stewardship programs (ASPs) in companion animal practices in the Netherlands. ASPs and corresponding QIs are already widely available and implemented in hospitals. In contrast, the implementation of ASPs in general practice (GP) and companion animal practices is rather new. Having QIs in this initial state can be very useful, as it allows to assess the impact of the ASPs and identify areas of improvement right from the outset. Consequently, QIs can help with the initial implementation and development of ASPs in companion animal practices. The core elements of ASPs in companion animal practices seem to correspond to QI themes identified in human medicine (Table 1). This suggest that these specific and quality checked QIs derived from human medicine could also be applicable in veterinary medicine. This chapter discusses per QI theme whether and how QIs from human medicine can be implemented in companion animal practices, in order of decreasing immediate applicability.

Structural QIs - A pivotal core element for ASPs in companion animal practices is '*AMS policies and programs to improve antimicrobial prescribing'*, with the main focus on monitoring and feedback regarding AMU. Because monitoring and assessing AMU is the most pivotal core element in ASPs for companion animal practices, it is the most significant for initial QIs implementation. For GP drug- and disease-specific QI sets for AMU have been developed. These initial QIs for GP are focussed on AMU, as this is the foremost contributor to AMR in GP, this is also the case in companion animal practices. Due to their direct and profound effect on antimicrobial prescribing, these QIs are ideal initial QIs for GP, but also for companion animal practices.

While literature of companion animal practices currently mainly focuses on collecting quantitative data of AMU, QIs can also facilitate collecting qualitative data. However, there are challenges that need to be addressed before QI implementation for AMU in companion animal practices is possible. First, a standardised unit for expressing AMU is lacking, complicating comparisons between practices and countries. Van der Velden et al. (2016) recommends using 'DDD per 1000 patients per day' for GP, as this enables better comparisons than percentages. Similarly, utilizing DDDA in companion animal practices would be preferred over percentages, although calculating DDDA can be time-consuming.

Second, data required for the calculation of QIs for AMU are often lacking. In the Netherlands, GPs usually have electronic patient files containing the required information, however this is not always the case and also depends on the health report system used. For the companion animal practice, most patient data are collected in electronic health reports, however, monitoring AMU is not mandatory which means that these data are often missing. However, animal practices in European Union (EU) member states will be obligated to collect data on antibiotic sales and usage from 2030 (Regulation 2019/6). Therefore, databases and software to streamline the collection of these data are required. When developing these, it is critical to keep the development of QIs for AMU in mind. Ideally, data collection should encompass AMU for overall systematic use and for specific groups of antibiotics. Moreover, for the qualification of AMU, prescriptions should be related to clinical indications, for example via internationally codes similar to the ICPC codes used in human medicine. Thus, the 2030 obligation for AMU monitoring in animal practices can help prepare data collection for QI calculation.

Given the similarities between GP and companion animal practices regarding AMR and AMU, it is recommended to initiate QI implementation in the latter with the drug-specific QIs from GP. While disease-specific QIs in GPs are deemed more effective for ASPs, they are currently too advanced for initial implementation in companion animal practices, as explained in the following paragraph.

Antimicrobial prescription guidelines are another core element in the companion animal practice. Guidelines can have a direct and profound effect on prescription habits, allow qualification of AMU and are the basis of disease-specific QIs. Therefore, the initial QIs of GP are connected to antimicrobial guidelines. Only a few European countries have national guidelines on responsible AMU in companion animal practices. The challenge with guidelines is establishing suitable guidelines for implementation. EU-wide guidelines present the advantage of allowing comparisons of AMU in companion animal medicine in different countries. Nevertheless, they have the risk of potentially ignoring specific needs of individual countries. In contrast, guidelines tailored to individual practices may hinder comparison between practices and countries. Therefore, there is a need to achieve consensus on nationally grounded, evidence-based antimicrobial prescription guidelines for companion animals. For example, for companion animals practices in the Netherlands, the guidelines of the Royal Dutch Society for Veterinary Medicine are considered to be suitable for implementation as these guidelines are very detailed, species-specific, encompass various diseases and are based on a combination of scientific research and expert opinions (WVAB, 2017). When national guidelines are established, it is possible to develop and implement disease-specific QIs, based on those of the GP, to the companion animal practice.

Furthermore, *AMS education* is a core element within the companion animal practice. The initial QIs of GP are connected to AMS education, as data of the drug- and disease-specific QI can be used as a basis for targeted education on AMU within a practice. For both GPs a companion animal practices it is essential that the whole staff is educated on AMR, AMS, guidelines and QIs, for successful implementation of ASPs. However, several challenges arise with education, including the time constraints staff faces and the financial burden associated with education. Free access online and self-paced AMS education tools are available for companion animal veterinarians, thereby offering an interesting education opportunity. However, education for pet owners is also important as they are often responsible for administering the antimicrobials to the animals, therefore owners are important stakeholders in the context of AMR and AMS. Thus, practical and operational aspects, such as costs, responsibility and content of education must first be considered before it become possible to assess if QIs from human medicine can be implemented for this core element.

Lastly, *AMS governance, leadership and accountability*, particularly in establishing an AMS team, is a core element for ASPs in companion animal practices. Some proposed AMS teams mirror those of hospitals, involving veterinary specialists. However, it is not feasible to adapt this team composition to GPs and first-line companion animal practices, as these settings usually consist of a small team of physicians and technicians. Diverse suggestions for AMS teams indicate the absence of consensus on the composition of an AMS team. Therefore, there is need for further exploration of the composition of an AMS team specifically tailored to GP and companion animal practices. Nonetheless, for both settings it is crucial that all staff in the practice contributes to AMS for maximal effectiveness. When the composition of an AMS team is established, evaluation of suitable QIs from human medicine for this element becomes possible.

QI development for the *AMS multidisciplinary expertise and resources* and *Microbiology laboratory standards, AMR surveillance and feedback* themes is lacking in both GP and companion animal practice. While interest exists for these themes in GP (Hawes et al., 2020a; Suttels et al., 2022; Hawes et al., 2020b; Tonkin-Crine et al., 2023), they are not addressed in companion animal practices. The drug- and disease-specific QIs of GP do not focus on these themes as these have a more indirect effect on prescription behavior and are therefore less suitable as initial QIs. Furthermore, these themes might be too advanced for both the GP and companion animal practice setting. For example, multidisciplinary expertise is not easily accessible for first-line companion animal practices as staff often only consists of

clinicals and technicians. Moreover, the microbiology laboratory theme might not be relevant for companion animal practices, given the limited microbiology laboratory facilities typically available in these settings and the financial barriers associated with additional diagnostic tests.

Process QIs - For process and outcome QI themes, QI development is lacking in both GP and companion animal practices. These QIs seem more relevant in later stages of prolonged ASP implementation. Furthermore, some process QIs are highly specific for the hospital setting and do not seamlessly fit with initial ASP implementation. To illustrate, detailed QIs for specific diseases are not practical to implement, when there is still uncertainty regarding the above-mentioned core elements of ASPs. Moreover, the QIs of the '*Specifically for certain infectious conditions*' theme are often highly specific for hospitals setting, making them unapplicable to GP and companion animal practices.

Outcome QIs - Surprisingly, no reports or studies in GP and veterinary medicine has paid attention to the '*Clinical outcome*' theme. It would be very interesting and informative to evaluate clinical outcome of patients who had an antimicrobial treatment. Dutch guidelines for veterinarians recommend strongly towards the evaluation of clinical outcome and for farm animals this is even legalized (KNMvD, 2015; Ministerie van Economische Zaken, 2013). Although it is obligatory to evaluate these treatments, compliance and enforcement is hard to assess. This poses challenges for implementing this QI theme in practice. Therefore, veterinarians should be more incentivized to collect clinical data on outcomes, for example by implementing this in AMU data to be collected in 2030.

The main contribution of this study is that this literature study is, to the best of the author's knowledge, the first study to analyse the use of QIs for ASPs derived from human medicine for the implementation of ASPs in companion animal practices. Consequently, it offers new insights crucial for the development of ASPs and QIs for companion animal practices. A limitation of this study is that only the Pubmed and Web of Science databases were used, which excludes studies on ASPs and QIs for human and companion animal medicine that are not publicly available and/or present in grey literature. Furthermore, the study used to identify QIs and related themes for hospital medicine dates from 2021 and might miss the most recent QI developments. However, this limitation may not be significant because newer hospital QIs are unlikely to align with the initial stage of ASPs in companion animal medicine due to their specificity.

Conclusion and future perspectives

Antimicrobial Resistance (AMR) is currently one of the biggest threats to healthcare. To reduce AMR, there is an emerging interest in Antimicrobial Stewardship Programs (ASPs). ASPs have already been successfully implemented in hospitals within human medicine. Since AMU in companion animal medicine contributes to the development of AMR as well, there is an emerging interest in ASPs for companion animal practices. To help implement, improve and evaluate the effectiveness of ASPs, Quality Indicators (QIs) are used in human medicine. Currently, QIs are not used for companion animal practices. Therefore, the research question of this literature research was: '*Which quality indicators for antimicrobial stewardship derived from human medicine can contribute to the implementation of antimicrobial stewardship programs in companion animal practices in the Netherlands?*'.

Based on the QI themes for ASPs identified in hospitals and the core elements of ASPs for companion animal practices, various QIs have been identified that can contribute to the implementation of ASPs in companion animal practices. Currently, there are no QIs that can be directly applied in companion animal practices, due to challenges that have to be resolved first.

The QIs with the most potential to be applied first and contribute to the implementation of ASPs within companion animal practices, are the drug-specific QIs of GP (Table 2). These QIs will allow the quantification of AMU to be assessed and create benchmarks within and between companion animal practices. Consequently, these QIs can help implement and improve ASPs, as the data that they provide will help identify areas of improvement within AMU and measure the impact of ASPs. However, to implement these QIs some hurdles have to be cleared. Most important is the establishment of international coding standards for antimicrobial prescription data and consensus on the method to quantify AMU. After the challenges related to a standardised unit for AMU and data collection of AMU are resolved, the drug-specific QIs of the GP can be implemented within companion animal practices.

Next GP disease-specific QIs have the most potential to contribute to the implementation of ASPs within companion animal practices. Once the challenges of collecting AMU data are solved and national guidelines are established, it will be possible to develop and implement disease-specific QIs, based on those of the GP, into the companion animal practice. These QIs allow to assess the quality of AMU, which is essential for implementation and improvement of ASPs within companion animal practices. Main hurdles for the implementation of the disease-specific QIs are again the establishment of international coding standards for clinical information and the integration of these standards into practice management systems. Another important hurdle for these QIs is the shortage of evidence-based guidelines in veterinary medicine.

Furthermore, QIs from the *AMS education* and *AMS governance, leadership and accountability* themes can probably contribute to the implementation of ASPs in companion animal practices. However, currently there are too many challenges associated with these themes to assess which QIs from human medicine can be applied in companion animal practices.

Moreover, regarding the remaining *structural QI, process QI and outcome QI*, these are often too advanced or too complex for the current state of ASPs development in companion animal practices, making them not yet suitable to contribute to the implementation of ASPs in companion animal practices. Some of these QIs are inherently not applicable to companion animal practices, because they are highly specialized and tailored for hospital environments, which are significantly different from those in companion animal practices.

Overall, ASPs and associated QIs appear promising in reducing AMR within companion animal practices. However, for practical implementation of ASPs and QIs within companion animal practices, future research should focus on addressing challenges to the core elements of ASPs. Future research should focus on the development of databases and software tools aimed at efficiently collecting and managing AMU data, an universal unit for AMU and national antimicrobial prescription guidelines. Furthermore, the composition of AMS teams in companion animal practices and the education of staff regarding AMS and AMR should be further examined. Thus, future research should focus on the identified challenges of core elements for further development of ASPs and QIs into companion animal practices.

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Appendix

Literature search strategy

For this literature study, literature research was conducted in the Pubmed and Web of Science databases. The used search terms yielded similar results between the two databases. First, for the introduction the search terms 'antimicrobial resistance' and 'antimicrobial stewardship programs' were used to provide foundational insights and basic information on these topics. This served as the basis for the rest of the literature study. Subsequently, search terms were used to acquire a comprehensive understanding regarding antimicrobial stewardship programs in different settings. To achieve this, the following search terms were used, 'antimicrobial stewardship programs AND hospitals', 'antimicrobial stewardship programs AND general practice', 'antimicrobial stewardship programs AND primary care' and 'antimicrobial stewardship programs AND veterinary medicine'. The selection of articles proceeded in a stepwise manner, first focusing on factors such as the title and the date of publication. The articles were then further selected by examining the abstract, discussion, conclusion and, where necessary, the entire article. Additionally, more literature was found using the references of the selected articles.

Second, for Chapter Two the search term 'quality indicators AND antimicrobial stewardship AND hospital' was used in combination with the filter for article type 'Systematic Review'. This choice was motivated by the sheer number of articles generated by the search term alone, thus a systematic review was used, which provides a structured and comprehensive overview of the available quality indicators for antimicrobial stewardship for hospitals. The systematic review of O'Riordan et al. (2021) was chosen as it not only provides an overview of the present Quality Indicators (QIs), it also quality-checked the development of these QIs, resulting in an overview of high quality QIs. Then the search term 'quality indicators AND antimicrobial stewardship AND general practice' was used. Next, the search term 'quality indicators AND outpatient antibiotics' was used, as general practice sometimes falls under the 'outpatient care' category. For these search terms no additional filters were used.

Lastly, for the third chapter the search terms 'antimicrobial stewardship programs AND veterinary medicine' and 'antimicrobial stewardship programs AND companion animal' were used. The articles were selected with the same method as described in the first paragraph of this section.