UNIVERSITY OF COPENHAGEN
FACULTY OF HEALTH AND MEDICAL SCIENCES

Improving quantification and understanding of patterns in antimicrobial use in Danish cattle

Analyses of data from rosé veal farms

PhD Thesis

Jeanette Kristensen

This thesis has been submitted to the Graduate School of Health and Medical Sciences, University of Copenhagen on August 4th, 2025

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University of Veterinary Medicine, Vienna, Austria

Contents

Preface

Dear reader, thank you for picking up this thesis. I hope you find it an enjoyable or at least interesting read. I have added a bit of information on my professional background and experiences with cattle, farmers, medicine, and legislation. The background for the initiation of the project is also briefly described. I hope, this will add transparency and give you a better basis for critically approaching the content presented in the following chapters and manuscripts.

I graduated with a Master of Science in Veterinary Medicine (DVM) from the University of Copenhagen in 2017 and started working as a veterinary practitioner in a small 4-veterinarian practice later that spring. I mainly worked with acute work on cattle, but I also substituted for my boss on some routine advisory service visits to cattle farms. Cattle or cattle related tasks took up around 80% of my work time with the remaining time divided on primarily pigs, dogs, cats and horses with the occasional exotic animal thrown in. During my two years in practice, I gained insights into many aspects of medicine use for cattle. I prescribed, dispensed and used medicine for cattle, and billed, documented, and recorded this. I discussed medicine use and documentation with farmers and obtained a level of understanding regarding their different attitudes towards and challenges with this. In the summer 2019, I joined the Danish Veterinary and Food Administration as an Official Veterinarian. Primarily, I carried out different routine tasks related to control and transport of live animals. This required collaborating and efficiently communicating with farmers, workers, chauffeurs, colleagues, and transport companies; and sometimes overcoming language barriers. I experienced working actively with many different types of legislation. And finally, I obtained a general understanding of the system and work processes in the Danish Veterinary and Food Administration.

The Danish Veterinary Consortium (DK-VET) is a collaboration between the University of Copenhagen (UCPH) and the Statens Serum Institut (SSI) for the performance of the veterinary public service agreement. This agreement was signed by the Ministry of Food, Agriculture and Fisheries (FVM) and the University of Copenhagen (UCPH). The work done by DK-VET is often referred to as veterinary contingency work. One of the aims with this thesis was to build competence in working with VetStat data on cattle, which is relevant for future contingency work and scientific research. The project was part of a series of projects conducted by the VetStat-cluster at UCPH working towards evidence-base use of VetStat data. Previously, VetStat work on UCPH focused primarily on pigs. The need for cattle-oriented research in this area, including improved understanding of VetStat data and its validity, was recognised, which led to this project being proposed.

Funding

Kvægafgiftsfonden (in English: The Danish Cattle Levy Fund) (KAF) funded a third of the expenses over a three-year period; originally from 2020 to 2022 but extended due to leave of absence. KAF funding was used to cover salary expenses and other project relevant expenses such as payment for data extracts from the Danish Cattle Database (DCDB) and expenses during the field study for travel and equipment. KAF approved the project but did not have any influence on the studies planned, their realisation, or the decision to publish.
The remaining funding for the projects was covered by the University of Copenhagen and included expenses for salary, travel, conference participation and publication fees.

Acknowledgements

I would like to thank **Kvægafgiftsfonden** and the **University of Copenhagen** for their interest in and financial support of this project.
My deepest gratitude goes to my main supervisor, **Liza**, who proposed this project and has been a constant source of both professional and personal support. Her hands-on approach and availability—always just an email or a zoom call away—have been invaluable. Liza consistently brings fresh perspectives and alternative approaches to our discussions, enriching the depth and direction.
I am sincerely thankful to my co-supervisors, **Alice** and **Amanda**. Alice's thoughtful nature has been a steady presence, and her insights are always carefully considered and deeply meaningful. Her expertise in data management and analysis, as well as her structured and cohesive input on writing, have been a source of inspiration. Amanda's advocacy for work-life balance have reminded me of the importance of personal well-being alongside academic progress. Her ability to see the bigger picture has frequently reminded me to stay focused, when I tend to get lost in the details. Though not involved in daily supervision, **Helle** has been a supportive member of our VetStat-cluster, consistently encouraging and reminding me to prioritize well-being.

During my research stay at **SEGES Innovation P/S**, department for Livestock, I had the pleasure of working with **Henrik**, whose deep knowledge of Danish rosé veal production and generous feedback greatly enriched my fieldwork. I also thank **Anne Mette** for her insightful methodological input and enjoyable conversations during our daily carpooling. The **Statistics & Analyses** team in the department provided valuable feedback on an early version of the study presented in Manuscript II, which led to significant improvements in the statistical approach. I also wish to thank **Malene**, who was instrumental in selecting and extracting the data used in Manuscript III. Thank you to **Mogens** from the department, who kindly shared his office space and engaged in several helpful discussions about my project.
I am grateful to **SEGES Innovation P/S** for access to data and for fostering a collaborative environment.

Special thanks to the **rosé veal farmers** who participated in the study—your openness and engagement were essential to this research.
I also appreciate the support from the **Danish Veterinary and Food Administration**, particularly **Laura**, for guidance in accessing and understanding VetStat data during the early phases of the study.

Thanks to my **VetStat-cluster** colleagues for inspiring discussions and a strong sense of community. I'm especially grateful to **Anne-Sofie**, who initially encouraged me to apply for the position. In the early years, our many walks provided space to share both professional frustrations—often about data—and personal reflections. Her support has meant a great deal to me.
Alongside Liza, Alice, Amanda, Helle, Anne-Sofie, **Kimmie, Leo**, and **Maya**, the cluster has grown into a vibrant group and valuable academic and social community during my thesis work.

I would especially like to acknowledge **Søren** and **Matt** from our section, **Animal Health and Welfare** at the University of Copenhagen, for facilitating access to VetStat, CHR, and DCDB data. Søren handled legal aspects, while Matt managed the technical implementation. Despite many barriers and frustrations, they managed to achieve what at one point seemed almost impossible. **Maj**, a fellow PhD student and co-author, brought great energy and crucial insights into DCDB data. And thank you to **Jeanne** for being an always cheerful and practical help with travel and expenses. Thank you to all my colleagues from our section at the University of Copenhagen for your engagement, support, and for making the workplace a stimulating and enjoyable environment.

Lastly, a big heartfelt thank you to my wonderful family and friends.
Thank you, **Benjamin**, for your unwavering support throughout this process, for putting up with me in these last months, and for holding everything together.
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And thank you to my **parents,** and my **sister** and her **fiancé**, for your continuous support in daily life—your help has been invaluable.

Publications included in the PhD thesis

Manuscript I

Kristensen, J., Skarbye, A. P., Kruse, A. B., Nielsen, L. R. (n.d.). On-farm Antibiotic Management, Use and Recording Practices: Questionnaire-based interviews in 36 Danish Rosé Veal Farms (Unpublished, planned submission for peer-review in *Acta Veterinaria Scandinavica*)

Manuscript II

Kristensen, J., Kruse, A. B., Kjeldsen, A. M. H., & Nielsen, L. R. (2025). Key farm characteristics associated with the level of antimicrobial use in rosé veal production – A Danish database study. *Preventive Veterinary Medicine*, *235*. https://doi.org/10.1016/j.prevetmed.2024.106406

Manuscript III

Kristensen, J, Kruse, A. B., Skarbye, A. P., Nielsen, L. R. (n.d.). Evaluation of the accuracy of a standard metric (ADD200) to monitor on-farm use of antibiotics for Danish rosé veal calves less than one year old (Unpublished, planned submission for peer-review in *Preventive Veterinary Medicine*)

Other scientific work

Scientific article:
Henningsen, M. B., **Kristensen, J.**, Kirkeby, C. T., & Nielsen, S. S. (2024). A registry-based comparative analysis of antibiotic usage reporting for adult cattle on Danish dairy farms. *Acta Veterinaria Scandinavica*, *66*(1). https://doi.org/10.1186/s13028-024-00763-9

> Contributions to manuscript: Contributed significantly to the conceptualization, choice of methodology, data curation, formal analysis, visualization, investigation, and validation of the study.

Posters
A Register-based Study of Antibiotic Use in Danish Veal Farms - Which farm characteristics affect antibiotic use?, Society for Veterinary Epidemiology and Preventive Medicine (SVEPM), annual conference 2023

Benchmarking af dyrlægers antibiotikaordinationer til svin og kvæg (Benchmarking of veterinarians' prescriptions of antibiotics in pig- and cattle herds), Den Danske Dyrlægeforening, Årsmøde 2023 (The Danish Veterinary Association, Annual Meeting 2023)

Presentations
Kendetegn ved slagtekalveproduktioner med højt og lavt antibiotikaforbrug - Et feltstudie i 36 bedrifter (Characteristics of veal calf productions with high and low antibiotic use - A field study in 36 farms). Kvægkongressen, 2024 (The Danish cattle sector annual congress, 2024)

Improving quantification and understanding of patterns in antimicrobial use in Danish cattle herds. VetStat seminar 2024 (Local seminar for relevant stakeholders planned by the VetStat-cluster at the University of Copenhagen, 2024)

Other work:

Leave of absence to participate in contingency work in the Danish Veterinary Consortium. Two reports were requested by the Danish Veterinary and Food Administration from the University of Copenhagen:

Stege, H., **Kristensen, J.**, Kruuse, A. B., & Nielsen, L. R. (2021) *Deskriptiv analyse af dyrlægers ordinationer af antibiotika i svine- og kvægbesætninger* (Descriptive analysis of veterinarians' prescriptions of antibiotics in pig- and cattle herds). URL: https://dkvet.dk/rapporter/Deskriptiv_analyse_af_dyrl_gers_ordinering_af_antibiotika_i_svine-_og_kv_gbes_tninger_31-03-2021.pdf [Accessed 27/7/2025]

> Contributions to report: Contributed significantly to the conceptualization, choice of methodology, data curation, formal analysis, visualization, investigation, validation of the study, and writing of original draft.

Stege, H., **Kristensen, J**., Skarbye, A. P., & Nielsen, L. R. (2022) *Benchmarking af dyrlægers ordination af antibiotika til svin og kvæg* (Benchmarking of veterinarians' prescriptions of antibiotics in pig- and cattle herds). URL: https://dkvet.dk/rapporter/Benchmarking_af_dyrl_gers_ordination_af_antibiotika_til_svin_og_kv_g_31.08.2022.pdf [Accessed 27/7/2025]

> Contributions to report: Contributed significantly to the conceptualization, choice of methodology, data curation, formal analysis, visualization, investigation, validation of the study, and writing of original draft.

Kruuse, A. B., Skarbye, A. P., & **Kristensen, J**. (2024). Benchmarking af danske dyrlægers ordination af antibiotika (Benchmarking of Danish veterinarians' prescriptions of antibiotics in pig- and cattle herds). *Dansk Veterinærtidsskrift, 3*. URL: https://dvt.ddd.dk/bladarkiv/2024/nr-3/benchmarking-af-danske-dyrlaegers-ordination-af-antibiotika/ [Accessed 28/7/2025]

> Contributions to manuscript: Contributed significantly to the conceptualization and review and editing.

Summary

Projections attribute 10 million deaths annually to antimicrobial resistance (AMR) by 2050. To address the challenge of AMR, several international and national efforts have been initiated to mitigate its development and spread in both humans and animals since the 1990s. Despite this, AMR remains a global concern. Antimicrobial use (AMU) and injudicious AMU is recognised as one of the main drivers of AMR, though the mechanisms of AMR development are complex and not yet fully understood.
Use of antibiotics has become an integral and routine component of the intensive livestock production highlighting the need for monitoring to discover and mitigate injudicious AMU practices. Monitoring of veterinary AMU is widely implemented, and Denmark was among the first with the implementation of the Danish Veterinary Medicines Statistics Program (VetStat). In VetStat, prescription medicine sales data for animals with identification of receiving livestock herd have been continuously and mandatorily recorded since 2000. This makes it a valuable source of information on AMU in livestock. Research on AMU with VetStat data has mainly been centred on pigs, due to the large industry compared to cattle. A knowledge gap remains in the monitoring and quantification of AMU in Danish cattle. This project was initiated with the dual goals of improving quantification and understanding of patterns in antimicrobial use in Danish cattle and building competences in working with VetStat data on cattle. Funding came from Kvægafgiftsfonden (in English: The Danish Cattle Levy Fund) and the University of Copenhagen (UCPH), and the project was affiliated with the UCPH VetStat-cluster which specialises in evidence-based VetStat research. Rosé veal farms were selected as the study population in this thesis due to their relatively high levels of AMU compared to dairy farm calves, and because previous research had identified a potential for AMU reduction here.

The aim of this thesis is to promote prudent AMU in cattle by improving AMU quantification and understanding of patterns in AMU in VetStat. When quantified and monitored AMU does not accurately reflect on-farm practices, it can lead to misinterpretations and biased assumptions. These, in turn, may compromise the integrity and effectiveness of initiatives intended to promote prudent AMU. To identify where misinterpretations can occur an overview of both on-farm AMU and the associated monitoring is necessary. This led to the choice of this approach: "From cattle to computer – and back again". In this approach, AMU is viewed as a series of events following this timeline: Veterinary prescription of antimicrobials for a farm, recording of sale in VetStat, on farm general management of antibiotics, actual AMU and the associated treatment practices and diagnostics, treatment

documentation, and finally, a treatment record of the individual treatment carried out. The thesis is built around three manuscripts covering these steps.

The first manuscript reports on a questionnaire field study in 36 professional Danish rosé veal farms. Here, the on-farm events related to AMU were addressed in a series of frequency analyses of identified on-farm conditions and practices supplemented with qualitative answers. This highlighted some main challenges for interpretation of on-farm AMU when using VetStat monitoring. Monitoring describes amounts of antibiotics, but it does not address the on-farm efficacy nor the necessity of treatment. A consequence of this may be that two farms with the same level of AMU in monitoring can have vastly different risks of developing AMR. One may have practices leading to an optimal efficacy of treatment targeting only calves in need of treatment while the other may have several practices leading to injudicious AMU and thereby increased risk of AMR. Another challenge is related documentation and recording practices. Generally, farms had a systematic approach minimising the risk of errors and bias in treatment records, but identified practices led to the conclusion that errors highly likely occur, though the extent could not be determined. In addition, not all farms carried out digital recording resulting in these data being incomplete for the population.

The second manuscript reports on a register study on recorded sale of antibiotics and quantified level of AMU per farm in VetStat. Hence, this study focuses on the events prior to the actual AMU. In this study, the association between farm characteristics that could be identified for 119 Danish rosé veal farms in existing digital monitoring and monitored level of AMU in VetStat were investigated with a Multivariable Linear Regression. The key findings were that increasing farm-size and/or number of suppliers was associated with an increase in level of AMU, while a higher proportion of crossbred calves among the bulls was associated with lower AMU. The latter effect could, however, not be separated from the effect on-farm composition of the sexes. The challenge to interpretation of AMU monitoring resulting from these findings is that current monitoring does not account for farm characteristics. In a benchmarking setting, not accounting for farm characteristics may skew the ranking of farms and reduce the relevance to the individual farmer.

The third manuscript reports on a register study converting the recorded used doses per treatment to VetStat standard doses. This was done to determine the accuracy of the standard doses. The used doses were generally higher than the standard doses which affects interpretation of AMU monitoring by overestimating the number of daily treatments carried out with VetStat data. Additionally, reported sold amounts were higher than reported used amounts also leading to an overestimation. To investigate factors influencing the relationship between used and standard doses a

Linear Mixed-Effects Model was build. The converted used doses were used as outcome, calf age at treatment and antibiotic class of the product used for treatment were introduced as explanatory factors and the model was corrected for the effect of farm. The model found increasing calf age at treatment, which can be used as a proxy of weight increase, associated with higher used doses. An estimated average weight of calves at treatment was 142kg, which corresponds poorly with the 200kg used as average weight at treatment in VetStat. This should theoretically have led to an underestimation of daily treatments in VetStat, which was the opposite of what was observed. Some of this can likely be attributed to the effect of antibiotic class on the converted used doses, where differences were seen between antibiotic classes. Especially macrolides had high predicted converted doses leading to an overestimation in VetStat. The most frequently used macrolide had a prolonged effect, which the standard doses only partially corrected for. For improved transparency in monitoring, such corrections should be clearly stated.

Throughout the thesis work, two major challenges for interpretation spanning all studies became apparent. Firstly, the structure of VetStat data presented a challenge, as monitoring is carried out at herd-level, but often farms consist of more than one herd combined into one production under one ownership and with similar practices and conditions. Neither ownership nor production type is currently available in VetStat monitoring. Including these could improve relevance of benchmarking to the farmers and motivate receptive farmers to initiate AMU reduction efforts on the farms. Secondly, the farms exhibited a high degree of heterogeneity with regards to both on-farm practices and in the data. In the third study, farms were found to explain 61% of the variance in the AMU data used for modelling. This highlight the importance of considering the context of the individual farm when planning initiatives to promote prudent AMU. The farmer's motivation and mindset, which were not addressed in this thesis, may play a crucial role. The drivers behind and factors influencing AMU on-farm are complex. Local holistic evidence-based strategies are important for achieving prudent AMU.

The studies conducted in this thesis point to areas where accuracy of monitoring can be improved. This could limit misinterpretations and aid in implementing more effective initiatives promoting prudent AMU in the future. These initiatives should be coordinated and implemented at multiple levels, both locally and nationally, based on sustained communication between stakeholders

Sammendrag

Prognoser tilskriver 10 millioner dødsfald årligt til antimikrobiel resistens (AMR) i 2050. For at imødegå udfordringen med AMR er der siden 1990'erne iværksat flere internationale og nationale initiativer for at begrænse udviklingen og spredningen af AMR hos både mennesker og dyr. På trods af disse tiltag forbliver AMR en global bekymring. Antimikrobielt forbrug (AMU) er anerkendt som en af de vigtigste drivkræfter bag udviklingen af AMR, og uhensigtsmæssigt forbrug er særligt bekymrende, selvom mekanismerne bag er komplekse og endnu ikke fuldt forstået. Brug af antibiotika er blevet en integreret og rutinemæssig del af intensiv husdyrproduktion, hvilket understreger behovet for overvågning for at identificere og begrænse uhensigtsmæssig brug. Overvågning af veterinært antibiotikaforbrug er udbredt, og Danmark var blandt de første med implementeringen af det danske veterinære lægemiddelstatistikprogram (VetStat). I VetStat er salg af receptpligtig medicin til dyr, med identifikation af den modtagende besætning, blevet registreret obligatorisk og løbende siden 2000. Dermed udgør VetStat en værdifuld kilde til viden om antibiotikaforbrug i husdyrproduktionen. Forskning i AMU baseret på VetStat har primært fokuseret på svin grundet branchens størrelse i forhold til kvæg. Der mangler viden om overvågning og kvantificering af AMU i dansk kvægproduktion. Dette projekt blev iværksat med det dobbelte mål at forbedre kvantificeringen og forståelsen af mønstre i antibiotikaforbrug hos dansk kvæg samt at opbygge kompetencer i arbejdet med VetStat-data på kvæg. Projektet blev finansieret af Kvægafgiftsfonden og Københavns Universitet (UCPH), og det var tilknyttet UCPH's VetStat-Klynge som er specialiseret i evidensbaseret VetStat-forskning. Slagtekalvebedrifter blev udvalgt som studiepopulation i denne afhandling på grund af deres relativt høje niveau af AMU sammenlignet med malkekalve, og fordi tidligere forskning har peget på et potentiale for reduktion af AMU her.

Formålet med denne afhandling er at fremme ansvarligt antibiotikaforbrug (AMU) hos kvæg ved at forbedre kvantificeringen af AMU og forståelsen af forbrugsmønstre i VetStat. Når det kvantificerede og overvågede antibiotikaforbrug ikke afspejler de faktiske forhold på bedriften, kan det føre til fejltolkninger og skævvredne antagelser. Dette kan i sidste ende kompromittere integriteten og effektiviteten af initiativer, der har til formål at fremme ansvarligt antibiotikaforbrug. For at identificere hvor fejltolkninger kan opstå, er det nødvendigt med et overblik over både det reelle antibiotikaforbrug på bedrifterne og den tilknyttede overvågning. Dette dannede grundlag for tilgangen: "Fra kvæg til computer – og tilbage igen". I denne tilgang betragtes AMU som en række hændelser, der følger en tidslinje: Veterinær ordination af antibiotika til en besætning, registrering af salget i VetStat, den generelle håndtering af antibiotika på bedriften, den faktiske anvendelse og de tilknyttede

behandlingspraksis og diagnostik, dokumentationen af behandlingen samt den endelige registrering af den konkrete behandling. Afhandlingen er bygget op omkring tre manuskripter, der hver dækker dele af denne proces.

Det første manuskript omhandler en spørgeskemaundersøgelse gennemført som feltundersøgelse i 36 professionelle danske slagtekalvebedrifter. Her blev forhold og praksis omkring antibiotikaforbrug på bedrifterne belyst gennem frekvensanalyser og kvalitative svar. Nogle hovedudfordringer i fortolkningen af VetStat-data blev identificeret. Overvågningen reflekterer mængder af antibiotika, men adresserer ikke nødvendigheden eller effekten af en behandling. Det betyder, at to bedrifter med samme niveau af registreret forbrug kan have vidt forskellig risiko for udvikling af AMR—hvor den ene har ansvarligt antibiotikaforbrug begrænset til syge kalve, og den anden har mindre hensigtsmæssig behandlingspraksis og dermed øget risiko for udvikling af AMR. En anden udfordring relaterer sig til dokumentation og registreringspraksis. Generelt havde mange bedrifter en systematisk tilgang, men der blev identificeret forhold, der med stor sandsynlighed kan føre til fejl i behandlingsregistreringerne. Derudover var det ikke alle bedrifter, der anvendte digital registrering, hvilket gjorde data ukomplette for populationen.

Det andet manuskript omhandler et registerstudie baseret på salgsdata fra VetStat. Undersøgelsen fokuserer på hændelser før den faktiske anvendelse af antibiotika på bedriften. I dette studie blev sammenhængen mellem bedriftskarakteristika identificeret i eksisterende overvågningsdata og niveau af AMU i VetStat undersøgt på 119 danske slagtekalvebedrifter ved hjælp af multivariabel lineær regressionsanalyse. Resultaterne viste, at større bedrifter og/eller flere kalveleverandører var forbundet med øget antibiotikaforbrug, mens en højere andel af krydsningskalve blandt tyrene var forbundet med lavere forbrug. Sidstnævnte kunne dog ikke adskilles fra effekten af kønssammensætning på bedriften. Den nuværende overvågning tager ikke højde for bedriftskarakteristika. I en benchmarking sammenhæng, kan dette påvirke relevansen og den opfattede retfærdighed af benchmarkingen hos den enkelte landmand.

Det tredje manuskript rapporterer på et registerstudie, hvor de forbrugte doser blev konverteret til VetStats standarddoser for at evaluere nøjagtigheden af disse. De forbrugte doser var generelt højere end standarddoserne, hvilket kan medføre en overvurdering af det registrerede behandlingsomfang i VetStat. Desuden var det rapporterede salg ofte højere end det rapporterede forbrug, hvilket ligeledes kan føre til en overvurdering. En lineær mixed-effects model blev brugt til at undersøge faktorer, der påvirkede forholdet mellem forbrugte og standarddoser.
De konverterede forbrugte doser blev anvendt som outcome-variabel, kalvens alder ved behandling samt antibiotikaklassen for det anvendte præparat blev introduceret

som forklarende variable, og modellen blev korrigeret for effekt af bedrift. Modellen fandt, at stigende kalvealder ved behandling – som kan anvendes som en proxy for vægtøgning – var forbundet med højere anvendte doser. Den estimerede gennemsnitsvægt ved behandling var 142 kg, hvilket afviger markant fra den standardvægt på 200 kg, der anvendes i VetStat. Dette burde teoretisk set føre til en undervurdering af behandlingsfrekvensen, men det modsatte blev observeret. Noget af dette kan sandsynligvis tilskrives effekten af antibiotikaklassen på de konverterede anvendte doser, hvor der blev observeret forskelle mellem klasserne. Især makrolider havde høje prædikterede konverterede forbrugte doser, hvilket førte til en overvurdering i VetStat. Det mest anvendte makrolid havde en prolongeret effekt, som standarddoserne kun delvist korrigerede for. For at sikre større gennemsigtighed i overvågningen bør sådanne korrektioner angives tydeligt.

Gennem arbejdet med denne afhandling blev to centrale fortolkningsmæssige udfordringer, som går på tværs af alle studier, tydelige. For det første udgør strukturen i VetStat-data en udfordring, da overvågningen sker på besætningsniveau, mens mange bedrifter består af flere besætninger samlet i én produktion under samme ejerskab og med lignende praksis og forhold. Hverken ejerskab eller produktionstype er i øjeblikket tilgængelige i VetStat-overvågningen. Inklusion af disse oplysninger kunne øge relevansen af benchmarking for landmændene og motivere landmænd åbne for forandring til at igangsætte initiativer for reduktion af antibiotikaforbrug på bedriften. For det andet udviste bedrifterne stor heterogenitet både i praksis og i data. I det tredje studie blev det påvist, at bedriften forklarede 61 % af variationen i de AMU-data, der blev anvendt til modellering, hvilket understreger vigtigheden af at tage den enkelte bedrifts kontekst i betragtning ved planlægning af initiativer til fremme af ansvarligt antibiotikaforbrug. Landmandens motivation og mindset, som ikke blev behandlet i denne afhandling, kan spille en afgørende rolle. Drivkræfterne bag og de faktorer, der påvirker antibiotikaforbruget på bedriften, er komplekse. Lokale, holistiske og evidensbaserede strategier er vigtige for at opnå ansvarligt antibiotikaforbrug.

Studierne udført i denne afhandling peger på områder, hvor nøjagtigheden af overvågningen kan forbedres. Dette kan begrænse fejltolkninger og bidrage til implementeringen af mere effektive initiativer, der fremmer ansvarligt antibiotikaforbrug i fremtiden. Sådanne initiativer bør koordineres og implementeres på flere niveauer – både lokalt og nationalt – baseret på løbende kommunikation mellem interessenter.

Abbreviations and definitions

Abbreviations:

ADD: Animal Daily Dose defined in VetStat either per animal or per kg body weight

ADD100: Animal Daily Doses per 100 animals per day (separate calculations for age groups)

ADD200: Animal Daily Dose per 200 kg animal (Danish standard weight for calves aged less than one year)

AMU: Antimicrobial use

AMR: Antimicrobial resistance

Besætningsnr.: Danish unique identification of herds in CHR

CHR: The Danish Central Husbandry Register

CKR-nr.: Danish unique identification of cattle individuals in CHR

CVR: The Danish Central Business Register

CVR-nr.: Danish unique identification of businesses in CVR

DCDB: The Danish Cattle Database

DVFA: The Danish Veterinary and Food Administration

EU: The European Union

VASC: Veterinary Advisory Service Contracts

VetStat: The Danish Veterinary Medicines Statistics Program

Definitions:

Adult cattle: Cows and cattle aged more than 2 years (adult cattle)

Animal-days: Summarised number of days an animal within an age group is present on a herd

Calves: Cattle aged less than one year

Farm: One whole production under one ownership identified by unique identification of the owner or business responsible for the animals

Herd: A group of animals in the same production type

Site: A defined geographical location housing one or more herds

Youngstock: Heifers, bulls and steers between 1 and 2 years of age

1. Introduction

Antimicrobial resistance (AMR) and its implications for health and health care in the future has long been a concern in the scientific community, but during the 1990s the worry truly began to spread to policymakers. In 1998, a European Union (EU) conference titled the “The Microbial Threat” was held in Copenhagen, Denmark. If actions should be taken to prevent or limit further spread of AMR transparency in the area and policy changes were needed and fast (Frimodt-Møller, 2004). During the conference consensus amongst stakeholders and experts was that AMR, its development and spread, was a complex process but that antimicrobial use (AMU) had a significant effect on it and should be addressed when searching for a solution to the problem (Frimodt-Møller, 2004; Mevius et al., 1999; Stege et al., 2003). The conference included stakeholders from various countries, sectors, industries, and organisations and centred around 5 central topics: Implications of AMR for human health, monitoring of AMR microorganisms, recording of human and veterinary AMU, good AMU practice, and future research to prevent AMR development and spread (Frimodt-Møller, 2004, Mevius et al., 1999). The need for a common global strategy was recognised as AMR neither respect borders nor species. Almost 27 years later, AMR remains a global concern, and the topics discussed in 1998 remain relevant. A report from 2016 projected 10 million deaths annually attributable to AMR by 2050, which would surpass even cancer (O’Neill, 2016). In the report as well as during the 1998 conference, reduction of injudicious AMU in agriculture was amongst the main topics.

AMU has become an integrated part of intensive livestock production systems around the globe. When a production system relies on use of antibiotics to maintain productivity it is indicative of injudicious AMU or overuse. This is evident in how studies point to interventions which could decrease AMU such as, biosecurity, implementation of herd health plans, education of farmers, and alternative production types like organic production (Redman-White et al., 2023). In the current livestock production phasing out AMU is likely not feasible. And with risk of injudicious AMU, it is essential to ensure monitoring that is both accurate, up-to-date, and continuous. Such monitoring enables stakeholders to track the current status and observe developments over time. This insight is crucial for conducting risk assessments for AMR development and for planning and implementing targeted efforts and initiatives that support and promote prudent AMU.

AMU monitoring systems aimed at veterinary medicine has been widely implemented, especially within the EU (AACTING, n.d.a.). Denmark has long been a frontrunner in the fight against AMR and monitoring efforts have been a central part of the Danish strategy. Information on Danish AMU monitoring in livestock is accessible from two major sources: the Danish Integrated Antimicrobial Resistance Monitoring and Research Programme (DANMAP) and the Danish Veterinary Statistics Program (VetStat). DANMAP reports include national monitoring on AMR and AMU in humans and animals and have been published annually since 1997; all reports are available from the official webpage (www.danmap.org) (DTU National Food Institute & Statens Serum Institute., n.d.). VetStat is a national database owned by the authorities containing mandatory continuously collected records of all sale of prescription medicine for animals since 2000 (Stege et al., 2012). Other Danish efforts mitigating AMR and promoting prudent AMR initiated by the authorities and the Danish livestock industry include: non-profit for veterinarians on sales of antimicrobials (1995), AMU guidelines (1996), total ban of antimicrobial growth promoters (2000), restrictions on fluoroquinolones for food animals (2002), action plans for reduction of AMU in food animals (2005), 10% AMU reduction for farm animals (2010), cattle industry target of 20% AMU reduction (2014), and a One Health Strategy (2017) (Aarestrup et al., 2010; DANMAP, 2023). Evaluating the success of some of these mentioned initiatives depend on the monitoring. Another Danish initiative dependent on monitoring is the Yellow Card Scheme, which was introduced in VetStat in 2010. The Yellow Card Scheme utilises data on sale of antibiotics at herd-level to benchmark herds against each other and against national averages for AMU (Jensen et al., 2014). Benchmarking is carried out for pigs and cattle, respectively, and for predefined age groups. Thresholds are incorporated into the benchmarking for each species age group and if a herd exceeds the threshold, a Yellow Card is issued, and reduction of AMU becomes mandatory (Jensen et al., 2014). Currently, this is only enforced for pig herds.

In addition to monitoring efforts by authorities, VetStat is also a valuable data source in research. In Denmark, antibiotics prescribed for pigs constitute by far the largest proportion of AMU for animals. In 2023, pigs received 84% of the prescribed amount of antibiotic active compound, while cattle only accounted for around 9% (DANMAP, 2023). This likely explains why monitoring of AMU in Danish cattle has received little attention compared to pigs in research, where studies with VetStat data have been carried out for many years (Dupont et al., 2017a). However, in 2023 DANMAP reported an AMU of almost eight tons of antibiotic compound in cattle, which is a considerable amount in itself. A key challenge with using VetStat data described for pigs is that sale of antibiotics is used as a proxy of AMU (Dupont et al., 2017a). This challenge also applies to cattle highlighting the relevance of research on VetStat AMU monitoring and quantification and its relationship with actual AMU in cattle herds. Krogh et al. (2020), reported on level of AMU in Danish dairy calves from 2015 to 2018 and herd-level the treatment incidence was found to be markedly lower than the treatment incidence reported by Fertner et al. (2016) for Danish herds producing veal calves and young bulls. This difference is likely attributable to the differences in production types. Fertner et al. (2016) found that rosé veal starter herds generally had the highest level of AMU. They also estimated that 51% of the antibiotics reported sold for calves in VetStat in 2014 were used in large veal calf and young bull producing herds with 99% being prescriptions and 1% being veterinary use and dispensing. A potential for significant reduction in AMU in Danish veal production has been proposed making it a highly relevant study population (Carmo et al., 2018a). This thesis will focus on VetStat monitoring and quantification of AMU for cattle with analyses of data from rosé veal farms.

2. Purpose and outline

2.1. Purpose

The aim of this thesis is to promote prudent use of antibiotics through a better understanding of the on-farm AMU and its related national quantification in VetStat for Danish cattle. It is important to understand how AMU monitoring reflect on-farm AMU when using and interpreting monitoring data. Misinterpretations that lead to flawed or biased assumptions can undermine the effectiveness of initiatives aimed at promoting prudent AMU based on such assumptions. To address the relationship between monitoring and on-farm AMU a comprehensive understanding is crucial. This requires examination of AMU at multiple levels; from on-farm to national level. The approach in this study has been "from cattle to computer - and back again".

The first task was to gain a detailed understanding of the on-farm AMU and related practices including digitalisation of treatment records and their structure. Secondly, quantification methods and AMU monitoring data currently used at the national level in Denmark were examined and later combined with other data sources. Combination with other farm-level monitoring data allowed an initial assessment of farm-level characteristics influencing AMU. Lastly, combination with farm-level treatment data allowed assessment of how, where and when the quantified data could be used to make inferences about the on-farm AMU. The focus was on identifying factors influencing the quantification and challenges with the current quantification methods. With this knowledge, specific precautions and concerns regarding interpretation of VetStat AMU reports can be communicated clearly and suggestions for improvements to quantification methods can be proposed.

With more accurate quantification, patterns indicative of injudicious AMU should become more readily identifiable. This, in turn, could support farmers and other stakeholders in selecting and implementing targeted initiatives that promote prudent AMU.

To aid this approach a series of research questions (RQ) were formulated for studies conducted in the Danish rosé veal population:

RQ1: What happens with antibiotic products from the time when they enter the farm and until their use or disposal?

RQ2: How, when and why are antibiotic products used on-farm?

RQ3: How is AMU documented and recorded on-farm?

RQ4: Which information is available in antibiotic treatment records and how can it be compared and combined with other AMU data?

RQ5: Which information on AMU is available in VetStat and how is it used for quantifying and presenting AMU?

RQ6: Which farm-level characteristics are associated with the quantified level of AMU used in VetStat?

RQ7: How do on-farm AMU treatments correspond to quantified AMU in VetStat?

RQ8: Which factors affect the relationship between on-farm AMU treatments and the corresponding quantified AMU in VetStat?

RQ9: What are the current challenges for interpretation when VetStat monitoring of AMU is used to make inference about on-farm AMU?

Table 2.1. Overview of main and specific objectives and the manuscripts addressing them

	Specific objectives
Manuscript I: *On-farm Antibiotic Management, Use and Recording Practices: Questionnaire-based interviews in 36 Danish Rosé Veal Farms*	
Main objective	Improve the understanding of on-farm antibiotic management, use and recording practices in Danish rosé veal farms
SO1	Describe on-farm general management related to medicine storage and handling
SO2	Identify on-farm treatment strategies and the conditions for initiating treatments including diagnostics performed
SO3	Describe on-farm documentation and recording practices for AMU including storage and digitalisation of treatment records
Manuscript II: *Key farm characteristics associated with the level of antimicrobial use in rosé veal production – A Danish database study*	
Main objective	Investigate how farm characteristics are associated with AMU in calves and youngstock on Danish rosé veal farms
SO6	Identify farm-level characteristics affecting level of AMU in VetStat monitoring based on existing national monitoring data
Manuscript III: *Evaluation of the accuracy of a standard metric (ADD200) to monitor on-farm use of antibiotics for Danish rosé veal calves aged less than one year*	
Main objective	Evaluate the accuracy of the Danish metric ADD200 in describing the doses used for daily on-farm treatments in Danish rosé veal farms
SO7	Compare the doses used and recorded in DCDB for on-farm treatments to the standard doses ADD200 defined for cattle and youngstock in VetStat
SO8	Identify factors affecting the accuracy of the Danish metric ADD200 from VetStat in describing the doses used for daily on-farm treatments in Danish rosé veal farms
Cross-cutting objectives relevant across manuscripts	
SO4	Describe structure and content of antibiotic treatment records available in the Danish Cattle Database, including potentials for merging with data from other sources
SO5	Describe structure and content of VetStat including structure of records, and calculations and variables used for AMU quantification
SO9	Identify current challenges with interpretation when VetStat monitoring of AMU is used to make inference about on-farm AMU and evaluate their potential implications

2.2. Outline

Chapter 1 introduces the topic and knowledge gap addressed in this thesis, while Chapter 2 provides and overview of chosen overall approach to the studies conducted, research questions, and specific objectives. Chapter 3 provides background information on AMU monitoring and quantification in general. Furthermore, Danish cattle population demographics and AMU, and veal production in Denmark is described. Chapter 4 describes the data, databases, and tools used in this thesis, including the pathways and links between data from different sources. Chapter 5 describes the ethical considerations and outlines methods used in this thesis. Chapter 6 lists key findings from the studies conducted and Chapter 7 discusses these under four main themes central to the research questions. Conclusions are provided in Chapter 8, while suggestions for further studies and perspectives are included in Chapter 9. References are listed in Chapter 10. Chapter 11 contains the included three manuscripts. Appendix A contain supplementary material for Manuscript I. Appendix B includes the questionnaire and informed consent form used during the field study in a Danish version. Appendix C includes supplementary material for Manuscript III. For supplementary materials figures and tables are listed with a three-part code referring first to the manuscript number, then supplementary material number, and lastly figure or table number e.g. M1S2T1 (Manuscript 1, Supplementary 2, Table 1) and M3S1F1 (Manuscript 3, Supplementary 1, Figure 1).

3. Background

3.1. Monitoring and quantification of AMU

Guidelines and recommendations for monitoring and quantification of AMU are published by important international organisations such as the World Health Organization (WHO) and World Organisation for Animal Health (WOAH) (WHO, 2022; WOAH,2022). A key scientific phrase cited by WOAH is: "*If you can't measure it, you can't manage it*". While an agreement can be reached about the necessity of monitoring and quantification of AMU, the methods vary around the globe complicating comparisons and limiting transparency (Werner et al., 2018).

It is generally accepted that AMU is reported with a numerator, a denominator, and an indicator. Sanders et al. (2020) provide an overview of the different quantification methods used in a range of countries with established AMU monitoring systems. The numerator expresses the measured AMU, while the denominator relates the AMU to the animal population at risk of treatment, and the indicator quantifies the AMU exposure in the animal population (Sanders et al., 2020). The numerator can be weight-based, dose-based, or count-based. In weight-based or mass-based quantification the numerator is given as weight of active compound used or sold in e.g. mg, kg, or tons. In dose-based quantification the numerator is expressed as number of daily doses, which can be based on either prescribed doses, used doses, or standardised doses. In count-based quantification the numerator is expressed as the number of treatments or treatment courses. The denominator expresses the animal population at risk and is often given as either a measure of animal biomass or the number of animals at risk of treatment. The indicator quantifies the level of exposure within the animal population at risk; for dose-based and count-based numerators this will express a treatment frequency. The choice of quantification metrics can greatly affect the monitoring and associated interpretation of monitoring (Apley et al., 2023; Firth et al., 2024; Sanders et al., 2020). The best quantification method largely depends on what the monitoring is used for and by whom it is used. For large international comparisons like the EU ESVAC reports, comparisons on tons of active compound by population correction unit per country are used (EMA/ESVAC, 2023). Maintaining a high level of details here is difficult due to the differing national monitoring systems. At both national and local levels, increased granularity in monitoring is desirable, as it provides a more detailed understanding of AMU.
In Denmark, both DANMAP and VetStat use VetStat sales data of antimicrobial products for their AMU monitoring, but their quantification methods vary. DANMAP and VetStat both use dose-based quantification with standardised doses, but their

methods vary slightly. Both represent the average daily maintenance dose per day of an antibiotic product used for an indication in each species. DANMAP defines Defined Animal Daily Dose (DADD) for active compounds, route of administration and animal species whereas VetStat defines Animal Daily Doses (ADD) for each product (DANMAP, 2023, Jensen et al., 2004). DANMAP monitoring is carried out at a national level while VetStat monitoring is carried out at both national and herd-level. DANMAP reports DADD by animals, where number of animals is estimated based on weight; they estimate live biomass using average live weights of 10 different sex and age categories in cattle (DANMAP, 2023).
VetStat reports ADD by animals, where number of animals is estimated based on assigned standard weights per species age group (see “4.1.2. VetStat”). For indicator DANMAP uses per 1000 animals resulting in the treatment frequency DAPD. VetStat uses per 100 animals resulting in the treatment frequency ADD100. ADD100 is often used as a proxy for the percentage of animals treated per day (Dupont & Stege, 2012). However, the relationship between the ADD100 and the true percentage of animals treated per day is currently unknown. Additionally, we lack knowledge of the relationship between the standard dose and the used dose for treatment on-farm and the factors influencing this relationship.

3.2. The Danish cattle population

The Danish population has been steadily declining with a 20% reduction over the last more than 20 years (Statistics Denmark, n.d.a). In the second quarter of 2025, the population consisted of 1,409,211 animals in total, of these 86% were female animals with dairy cows representing around 45% of the females, suckler cows representing 5%, and heifers the remaining 50% (Statistics Denmark, n.d.b). The dairy production houses most cows. Based on number of animals beef production can be considered a niche production. For number of male animals, calves less than six months of age accounted for 49%, animals between six months and one year of age 34%, animals between one and two years of age 12%, and the remaining animals were categorised as older than two years of age (Statistics Denmark, n.d.b). This means that most male animals were slaughtered within one year after birth.
The cattle population is located primarily in the western part of Denmark with 94% of the population located west of the Great Belt: 34% of the animals in Southern Jutland, 24% in Northern Jutland, 23% in Western Jutland, and the remaining population in Eastern Jutland (8%) and on Funen (5%) (Statistics Denmark, n.d.b). Many small herds exist and in 2023, 41% of the registered herds in housed 19 animals or fewer, 21% housed between 20 and 49 animals, large herds with more than 200 animals housed accounted for 23% of the cattle, and the remaining herds housed between 50 and 199 animals (DAFC, n.d.). The demographic of the Danish

cattle population based on number of herds per production type is outlined in Figure 1. Below the figure characteristics of the different production types are outlined.

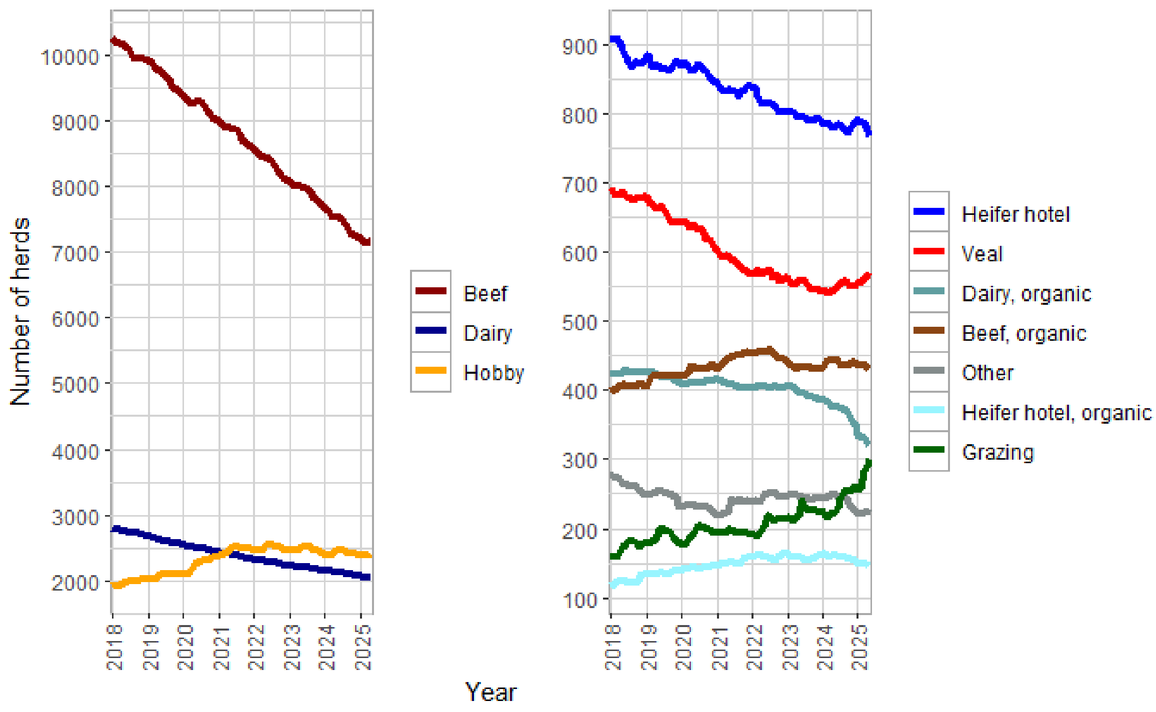

Figure 3.1. Development in number of registered herds from 2018 to 2025 divided by the farmers' registered production types. The left panel shows number of registered beef, dairy and hobby herds. Note the y-axis scale. The right panel shows heifer hotels, veal, organic dairy, organic beef, organic heifer hotels, grazing, and a grouped category "Other" for remaining production types. Note the smaller y-axis scale. There is no overlap between herds within the different categories.

Danish beef herds consist of predominantly cattle of beef breeds such as Limousine, Hereford, Aberdeen Angus, Galloway, or Simmental (SEGES Innovation P/S., n.d.a). The farmers themselves register production type and the distinction between beef and hobby production may not always be clear to the farmer, which is why the allocation into these should be interpreted with care. Small veal productions where hobbyists fatten calves may also be classified under beef or hobby production. In general however, beef or hobby productions houses animals older than one year of age, while veal herds mainly produce calves for veal meat, which means slaughter before year of age.

There is a distinction between conventional and organic production but this, again, is reported by the farmer and not further validated. Dairy production has seen a steady decline in number of herds and animals, but the amount of milk delivered to dairies has increased during the same period (Statistics Denmark, n.d.c). This reflects a

more intensive production with fewer herds housing more animals with a higher milk yield. Heifer hotels refer to herds with heifers intended for later dairy production. These can hold heifers originating from one or more dairy herds. Grazing refers to animals registered in a herd on pasture, typically seasonal grazing, but also conservation grazing. These herds have increased in number, likely reflecting an increased interest in a more natural production. The group “Other” refers to the remaining production types in the Danish Central Husbandry Register (CHR) including, but not limited to, livestock shows, export quarantine units, collection points for carcasses from production, abattoirs, zoos, and herds with bison breeds.
In this thesis the age groups frequently used are defined as follows: Cattle aged less than one year (calves), heifers, bulls and steers between 1 and 2 years of age (youngstock), and cows and cattle aged more than 2 years (adult cattle)

3.3. Veal production in Denmark

The information presented in the following text is based on knowledge obtained during conversations with two Danish veterinarians working extensively with Danish rosé veal production. This is supplemented with observations from the field study described in Manuscript I.
The rosé veal production counts around 550 herds, contrasting with the around 2,000 dairy herds (see Figure 3.1.). In Denmark, most calves are born on dairy farms. Many Danish dairy farmers have breeding programs and use primarily insemination, not a bull. Beef semen and sexed dairy semen have been extensively used for years. Sexed beef semen yielding 90% male offspring has been marketed by the primary cattle breeding company in Denmark, VikingGenetics (VIKINGGENETICS innovative breeding, n.d.). This means that farmers can inseminate with beef semen and even select for crossbred bulls. Calves not intended for dairy production, are sold and moved to veal farms (Arla Foods, n.d.). Typically, this happens around two to four weeks of age, and the calves are moved either directly or via an intermediary. Physical auctions are very rare in a Danish setting, though they do exist (Nordjydsk Landboauktion & Eksportstalde, n.d.). The calves sold for veal production are, primarily, purebred Holstein bulls and large crossbreds such as Holstein x Belgian Blue of both genders. The calves arrive on the veal farms in batches with varying number of origin farms. Farms using an intermediary often receive calves from a considerably larger number of suppliers. Upon arrival, the calves are stabled in pens, huts or sections with a stable setup that facilitates continued milk feeding. The calves are weaned around two months of age. Many Danish veal farmers feed primarily with concentrate supplemented by roughage such as hay or silage after weaning. The veal farms rear the calves from arrival from dairy producers until slaughter at eight to twelve months of age. Most Danish bulls are slaughtered before

one year of age (DAFC, n.d.). Typically, veal farms move the calves internally on the farm between sections intended for different ages and sizes. Many operate with a "starter", "middle" and "finisher" setup. Heifers and bulls are separated at the latest at six months of age. Two major abattoirs receive most of the calves and the meat is sold under concepts with clear requirements outlined for the veal farmers (DAFC, n.d.; Danish Crown, n.d.; Himmerlandskød, n.d.).

Following is a summary of numbers from the annual statistics for beef and veal published by the Danish Agriculture & Food Council (DAFC, n.d.). In 2023, 443,900 animals (118,700t) were slaughtered; of these 126,700 bull calves (27,200t) and 26,900 heifer calves (5,500t). Cows constituted the largest group of slaughtered animals, 166,900 dairy cows (52,000t), followed by bull calves, youngstock heifers, youngstock bulls and bulls, and heifer calves.
In 2023, Denmark exported 60,524t of beef or veal to Europe, 1,191t to Greenland, and 6,939t to other countries. Germany was the primary European recipient and Canada the primary recipient amongst other countries. Denmark imported 70,843t of beef or veal from European countries and 2,997t from other countries; primarily from Germany and the Netherlands in Europe and Brazil and Uruguay amongst other countries. The net import of beef and veal meat is thus larger than the export. Export of live animals in 2023 was primarily bulls (40,884 animals) and to a lesser extent heifers (8,994 animals) younger than two months of age, and youngstock heifers (39,785 animals).

3.4. Danish farmers' "License to treat"

One way of categorising treatments is therapeutic, metaphylactic, and prophylactic. Therapeutic treatments are treatment of clinically sick animals. Metaphylactic treatment has been defined as the treatment of a group of animals in which one or more individuals show clinical signs of infection or treatment of an individual with sub-clinical infection (AVMA, n.d.). In the EU, metaphylactic treatment requires a clinical diagnosis in part of the group of animals and prophylactic treatment is defined as treatment prior to signs of clinical disease; the latter is strictly limited by legislation to exceptional cases in individual animals (Council Regulation (EC) 6/2019). Thus, only therapeutic and metaphylactic treatments are carried out by Danish farmers.

Professional Danish cattle farms of certain sizes, specified based on animals present within each age group (100 cows or 200 calves/youngstock/bulls), must sign mandatory Veterinary Advisory Service Contracts (VASC), which includes review of animal welfare and biosecurity (DVFA, 2021a). Some VASC extensions, which include mandatory extended veterinary advisory services, entitle the farm to initiate and carry out treatments for specific diagnoses. These diagnoses should be based on specific clinical symptoms and expected to occur regularly on-farm; the treatments must be carried out in accordance with detailed treatment protocols outlined by a veterinarian (DVFA, 2021a). The farm must keep records of medicine use, and diseased and dead animals. In farms without VASC extensions, the veterinarian can only prescribe medicine for one treatment course of individual animals diagnosed by the veterinarian, but not for cows, which must be treated by the veterinarian (DVFA, 2023).

3.5. AMU in Danish cattle

In DANMAP, the trends and developments in AMU are summarised per year. The most recent report accessible during the writing of this thesis is DANMAP 2023. In 2023, cattle received only 9.18% of the antimicrobials prescribed for animals in Denmark despite representing almost half of the estimated live animal biomass (DANMAP, 2023). The AMU in adult cattle has been steadily declining since 2014, with beta-lactamase sensitive penicillins being the primary drugs of choice. An opposite development has been observed in calves during the same period, with an increase in the use of amphenicols, macrolides and aminoglycosides. The mentioned antibiotic classes constitute 63.3% of the antimicrobial kg active compound for calves in 2023 (DANMAP, 2023). Since 2020, the use of amphenicols and macrolides measured in Defined Animal Daily Dose per 1,000 animals per day for (DAPD) have increased for calves (DANMAP, 2023).

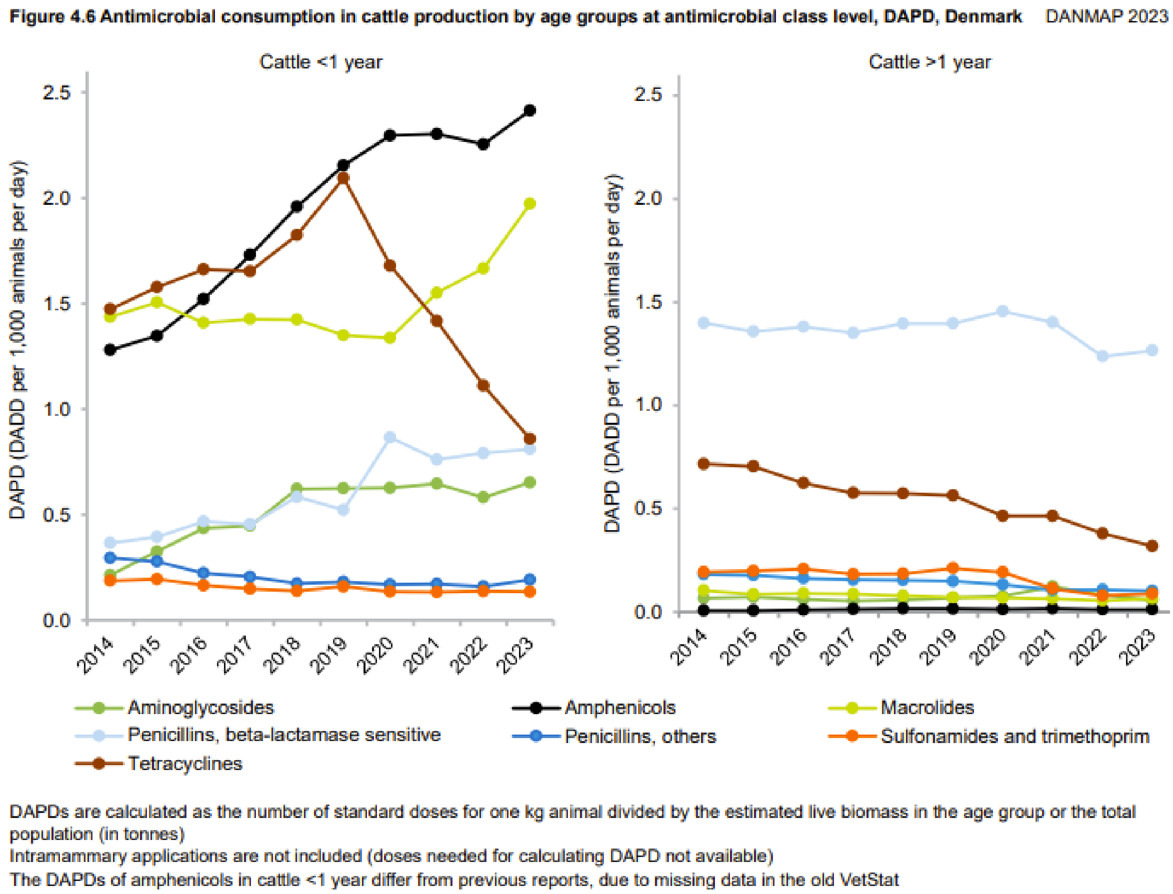

Figure 3.2. Antimicrobial sale for cattle expressed as Defined Animal Daily Dose per 1000 animals per day stratified by antibiotic classes. This figure is extracted from Chapter 4 in DANMAP 2023 on July 15th, 2025.

Summaries on VetStat data from 2020 and forward are available via an online dashboard (https://vetstat.fvst.dk) but require login (DVFA, n.d.a). From the online VetStat dashboard updated sales data are available with more detailed information on antimicrobial classes and route of administration; these data are presented by month or year. In 2024, the total prescribed number of Animal Daily Doses (ADD) were 2,665,623, of these 1,430,783 ADD (53,7%) were prescribed for calves, 1,144,136 ADD (42.9%) were prescribed for adult cattle, and 90,703 ADD (3.4%) were prescribed for youngstock between one and two years of age.

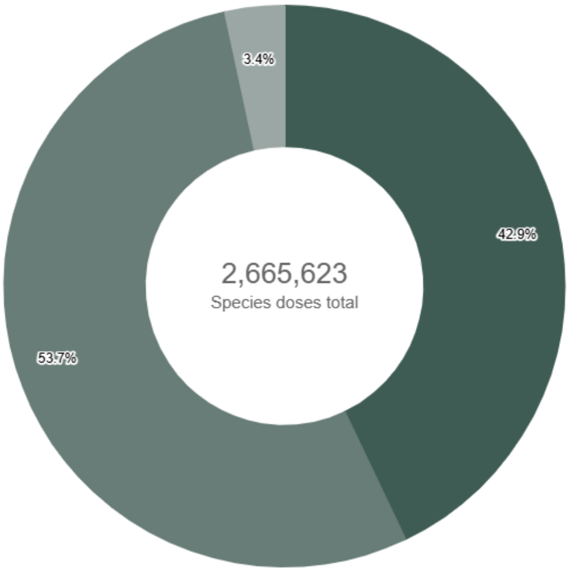

Figure 3.3. Spread of ADD ("Species doses" in Figure) on age group in percent in 2024. This was extracted from https://vetstat.fvst.dk on July 15th 2025. Dark green is adult cattle, green is calves aged less than one year, and light green is youngstock between one and two years of age.

The composition of ADD sold for adult cattle and calves varied with respect to antimicrobial class and route of administration. The majority of ADD sold for adult cattle were beta-lactamase sensitive penicillins administered systemically (54.3%) followed by beta-lactamase sensitive penicillins administered intramammarily (10.5%). Systemic macrolides constituted only 2.1% of the ADD and systemic amphenicols 0.1%. Udder disorders were the most common prescription cause with 65.5% of the total ADD sales. This was followed by the indication "Joints, limbs, hoof, central nervous system, skin" (16%), reproductive disorders (13.5%), and respiratory disorders (7.8%).

For calves amphenicols administered systemically constituted the highest percentage of sale in 2024 with 34%, followed by systemic macrolides (28.4%), systemic beta-lactamase sensitive penicillins (14.3%) and systemic tetracyclines (9.3%). Figure 3.4. outlines the AMU stratified by antimicrobial class for calves by month in 2024. Systemic products dominated sale for calves. Only 7.7% were for oral administration; of these 49.5% were amphenicols, 28.4% tetracyclines, 16.4% macrolides, and the remaining 5.7% were combinations of sulfonamides and trimethoprim. The majority of ADD for calves were prescribed for respiratory disorders (76.1%) followed by the indication ”Joints, limbs, hoof, central nervous system, skin" (14.8%), and gastrointestinal disorders (7.8%).

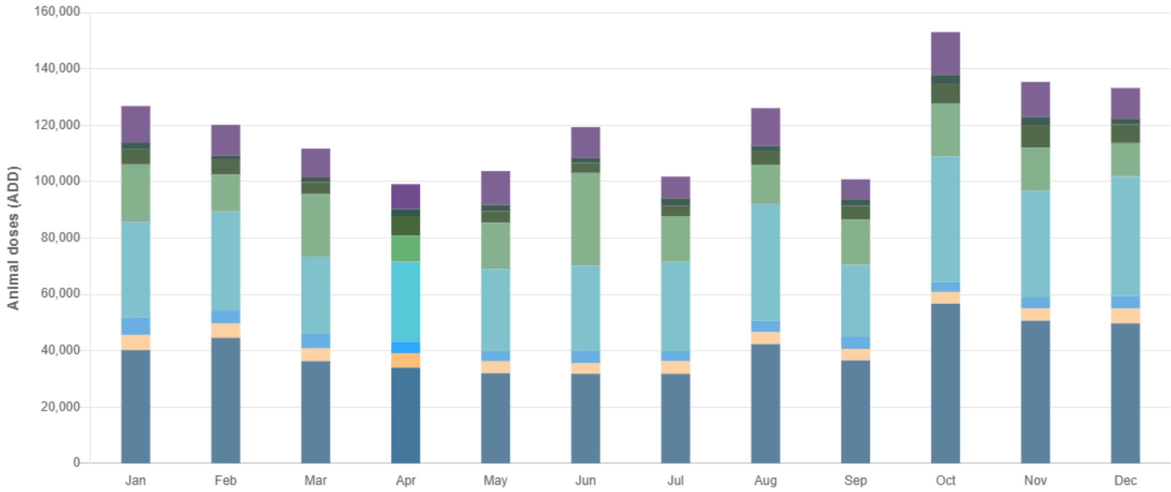

Figure 3.4. Spread of ADD for cattle less than one year by antibiotic class in 2024. This was extracted from https://vetstat.fvst.dk on July 15th 2025. Each color represents a different antimicrobial class.

4. Materials

4.1. The databases

Denmark has a long history of recording data on livestock production. In the following sections, three of the major databases with data relevant to this thesis are presented.

4.1.1. The Danish Central Husbandry Register (CHR)

In Denmark, CHR contains detailed historic data on cattle individuals including: birthday, sex, breed, affiliation with herd, housing site, and ownership information. CHR is owned by the Danish Veterinary and Food Administration (DVFA). The number of animals is expected to be relatively accurate since registrations are mandatory and have been since 1993 (DVFA, 1993). The data flow to and from CHR is illustrated in Figure 4.2.

The CHR has a hierarchical structure. The different levels in the hierarchy are presented in Table 4.1. with the general terms used in the thesis and manuscripts, the Danish term, the ID used for identification of units at each level, and a brief description of the levels.

Table 4.1 Danish terms used in CHR, and their translations used in this thesis including identification keys and descriptions of the terms

Term	Danish term	Identification	Description
Animal	Dyr	CKR-nr.	One unique animal registered with birthday, sex, breed, and herd affiliation.
Herd	Besætning	Besætningsnr.	A group of animals with the same production type (e.g. veal, dairy or beef production) registered at a site with one owner.
Site	Ejendom	CHR-nr.	A defined geographical location housing one or more herds.
Farm	Bedrift/Ejer/ Bruger	CVR-nr.[1] and if not available owner name and address	The whole production under one ownership identified by unique identification of the owner or business responsible for the animals. Businesses are registered in the Danish Central Business Register (CVR)

[1] Unique identification of Danish businesses assigned by the Danish Central Business Register (CVR, n.d.)

In this thesis, farms are defined by ownership status. Each herd has an assigned owner and production type. One owner can own multiple herds located at different sites, which may have different production types. The sites have one owner, but a herd on a given site can have a different owner. Figure 4.1. describes two farms with different ownership structures.

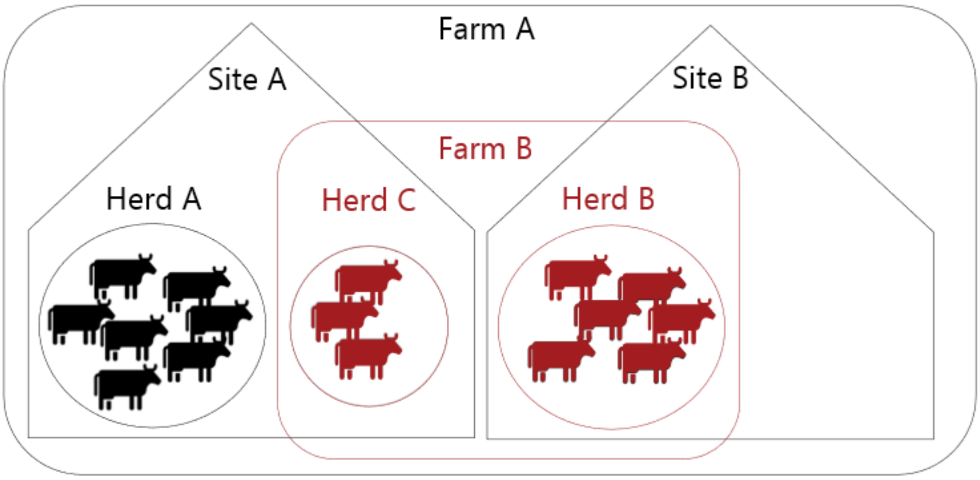

Figure 4.1. Illustrating ownership structures on two farms. Farm A owns Site A and B but no herds on Site B. Farm B owns no sites but owns herds on both Site A and B. CHR differentiates between owner of site and owner of herd, though often the two will be identical, like for Herd A.

From CHR data, "animal-days" are summarised per herd. It is calculated by summarising the number of days an animal within an age group is present on the herd; this is often summarised per month or per year. The animal-days are calculated for the following age groups: Calves, youngstock, and adults. If the animal-days are divided by 365 this converts them to "animal-years". Data on animal-days are transferred to VetStat.

4.1.2. VetStat

VetStat contains data on all prescription medicine sale for animals in Denmark. It is a relational database on an Oracle platform and is owned by DVFA (Stege et al., 2003). VetStat consists of a range of raw, aggregated, supplementary, relational, and historical data sets. The flow of data into VetStat is described in "4.2. Data flow". VetStat contains a large amount of data. Only the data relevant for this thesis work will be presented in the following.

4.1.2.1 Data in VetStat

The raw sales data on medicine for a herd will contain the information presented in Table 4.2. These data are combined with data from data sets containing supplementary information, as described in Table 4.3., either directly with unique identifiers or levels coded with IDs, or via identifiers and IDs linking to relational tables connecting to one or more supplementary tables.

Table 4.2. Content in a raw sales record for a cattle herd in VetStat

Variable	Levels	Description
Date of sale	Date	Day the sale is registered by the pharmacy or the date of use or dispensing by the veterinarian
Herd	VetStat ID	Besætningsnr. from CHR (see Table 4.1) which is pseudonymised as a VetStat ID
Species	ID per level	A list of species is included in VetStat. For this thesis only “Cattle” is relevant
Age group	ID per level	Predefined age groups are listed for each species. Standard weights are assigned from a supplementary table: Calves (200kg), youngstock (200kg), and adults (600kg).
Indication	ID per level	Predefined indications are listed for each species. Those listed here are used for cattle, pigs, small ruminants, fur animals and “other” livestock production animals: “Reproduction and urogenital system”, “Udder”, “Gastrointestinal disorders”, “Respiratory disorders”, “Joints, limbs, hoof, central nervous system, and skin”, “Metabolism, digestion and circulatory system”, “Vaccines and sera”, “Other”, “Replacement code”
Veterinarian	VetStat ID	Prescribing veterinarian is identified with authorisation number which is pseudonymised as a VetStat ID
Pharmacy	VetStat ID	Pharmacy responsible for the sale is identified with a unique code which is pseudonymised as a VetStat ID. This is only recorded for prescriptions, not use or dispensing (see Figure 4.2.)
Product	VetStat ID	Medicine is recorded with Nordic Article Number (Vnr), which is unique for each marketed product in the Nordic countries. This is translated to a VetStat specific ID.
Amount	Numeric	Amount of product. For pharmacies the number of whole packages is recorded and later multiplied with the amount of product in a package from a separate table in VetStat. For veterinarians the specific amount used or dispensed is recorded.

Sources: DMA, 2011; DVFA, 2023; Nordic Article Number*,* n.d.

Data on products are separated into multiple data sets containing different information related to the medicine. In Table 4.3., the supplementary product data used during this thesis work are listed. With this it is possible to summarise, aggregate and stratify sales data in various ways.

Table 4.3. VetStat product data

Supplementary data	Description
Active compound	The strength of each active compound (see ATCvet) in a product. With this information the kg of active compound sold can be calculated.
ADD	Animal Daily Dose defined for each product containing antibiotics with an amount to treat one kg of animal of a given species. It can also be defined as the dose to treat one animal, if the pharmaceutical form is more suited to this, e.g. for intramammary tubes. With this information the number of ADD sold can be calculated.
Antibiotic class	Antibiotic class of the products. The antibiotic classes are defined for specific groups of active compounds with the same route of administration e.g. "Tetracyclines, systemic" or "Penicillins, intramammary".
ATCvet	The active compound of each product is identified with the Anatomical Therapeutic Chemical Classification system for veterinary medicinal products (ATCvet) published by the Norwegian Institute of Public Health WHO Collaborating Centre for Drug Statistics Methodology [1] The fifth level of the ATCvet code is the active compound and provided as both text and ATCvet code.
Pharmaceutical form	The pharmaceutical form refers to the form of the product, e.g. tablets, intramammary suspension, and fluid for injection. The pharmaceutical form is linked to the route of administration.
Product information	Product information includes marketed name of the product and Vnr. (see Table 4.2.). It also includes packaging information with the amount of product per sub-package and number of sub-packages recorded for the specific Vnr. With this, the total amount of a given product in a package can be calculated.
Route of administration	Route of administration registered for each product e.g. systemic, intramammary, or oral.
Units	Units of the amounts recorded for the product, often ml or g, but also doses

[1]NIPH (n.d.)

4.1.2.2 Quantifying AMU in VetStat

ADD200 is defined as the amount of a specific antibiotic product needed to treat one standard calf weighing 200kg. For products recorded with the ADD unit "kg", this is calculated by multiplying the ADD with 200 (see Manuscript III, Equation 1). For products with the ADD unit "doses" the ADD200 will correspond to the ADD. Both reflect an amount of a specific product.

The number of standard doses per 100 calves per day (ADD100) for a month can be calculated by first dividing the sold amounts of a product during this month with the product specific ADD200; with this the number of sold ADD200 are found. Then the number of ADD200 is divided by the number of animal-days summarised for the month and multiplied by 100 to find ADD100 for each product. These ADD100 can then be summarised for all antibiotic products sold to a farm by simple addition. They can also be stratified by factors such as antibiotic class, route of administration and indication.

In Manuscript II, the VetStat data used were existing aggregated tables with ADD100 per month at site-level from the database. Note that aggregation was at site and not herd-level (see “4.1.2.3. Updating VetStat ”). In Manuscript III, the VetStat data used were product data, which could be linked to DCDB data using Vnr. For the descriptive statistics raw sales data were combined with antibiotic product data and aggregated to calculate the number of ADD200 sold.

4.1.2.3. Updating VetStat

During this project VetStat was updated, which resulted in several important structural and content changes in data and the database. The new VetStat holds more options for development and updates (Anonymous, presentation at stakeholder meeting, 2021). The online platform was expanded with a whole range of new automatically generated reports and supplementary material. When the new VetStat was introduced in June 2021, records went from being reported at site-level to being reported at herd-level. In the old VetStat, CHR-nr. was used as an identifier on each record making merging with other data using CHR IDs relatively straightforward. In new VetStat, Besætningsnr. is pseudonymised, making access to a key table necessary for the merging process. In the old VetStat, product data were entered and updated by the DVFA, but in new VetStat, the database receives continuously updated product data from a national medicine database owned by the Danish Health Data Authority (Anonymous, personal communication, 2020). The ADD are still manually entered for each product by the DVFA VetStat administration. During the transition from old to new VetStat the existing ADD were checked for errors and updated (Anonymous, personal communication, 2020). Contrasting old VetStat, new VetStat includes a data validation engine for reported sales data, which should limit the number of errors in the recorded data (Anonymous, presentation at stakeholder meeting, 2021). Errors are assigned to a specific person for correction, depending on the error type and how it entered the database; either veterinarian, pharmacy, feed mill, or DVFA VetStat administration. Veterinarians are notified via the online VetStat platform and must correct errors in a specific error handling module within three months (DVFA, 2023). All changes in the database are now logged (Anonymous, presentation at stakeholder meeting, 2021)

4.1.3. The Danish Cattle Database (DCDB)

The Danish Cattle Database (DCDB) has a more than 50-year history and is the central database containing cattle data in Denmark (Frandsen, 2013). DCDB include mandatory animal data, voluntary farm records on milk, reproduction, health management and feeding, and records from collaborators like hoof trimmers, veterinarians, dairy companies, abattoirs, and artificial insemination technicians (Frandsen, 2013). The database is managed by SEGES Innovation P/S and owned by the industry, the Danish Agriculture & Food Council. The data in the database are primarily owned by the farmers with other stakeholders sharing ownership of relevant data; such as abattoirs owning slaughter data and dairy companies owning milk related data (Frandsen, 2013). While owned by the industry, the DCDB delivers data on cattle to CHR in accordance with agreements established in the 1990s (Frandsen, 2013). DCDB also aggregates data from the veterinarians and transfer it to VetStat (see Figure 4.2.). Data from DCDB have been used in all studies:

Manuscript I: Treatment protocols in DCDB. The treatment protocols could only be extracted as pdfs and were manually entered with the field study questionnaire data after the farm visit. They contain diagnosis, treatment protocol, period of validity, withdrawal period for slaughter, and medicine information. Medicine is listed with name and Vnr. The pdfs also contained Besætningsnr. and CHR-nr.

Manuscript II: An aggregated data set in DCDB with farm data used to categorise sites in the Danish *Salmonella* Dublin monitoring. The data set contains summarised data per month for sites from the previous 12 months with number of animal-years presented by age groups, breed, and sex. Entries and exits are also summarised under categories such as births, live entries, dead, and exported. For each site the CHR-nr. is included along with the status on milk delivery.

Manuscript III: Three data sets from DCDB: “animals”, “treatments”, “medicine”. These data sets were interlinked by unique DCDB IDs. “Animals” contains data on individual animals including animal ID, birthday, sex, breed, and breed of mother. Each animal has a new record for each move between herds with Besætningsnr., entry date and exit date, and reasons for entry and exit. “Treatments” contains data on each performed treatment with a treatment ID, identification of treatment responsible, animal ID, Besætningsnr., date of treatment, diagnosis, and diagnosis ID. Diagnosis IDs are called “LK-koder” (In English: LK-codes) and correspond to a predefined list of diagnoses used in DCDB. “Medicine” contains data on medicine used with treatment ID, origin of medicine (dispensed or used by veterinarian, or used of medicine purchased from pharmacy), product name, Vnr., product amount, and VetStat indication. There is one record for each product used for a unique treatment and they contain identical treatment IDs.

4.2. Data flow

In Figure 4.2. the dataflow between stakeholders and databases is outlined. Details on dataflow are provided in the accompanying figure text.

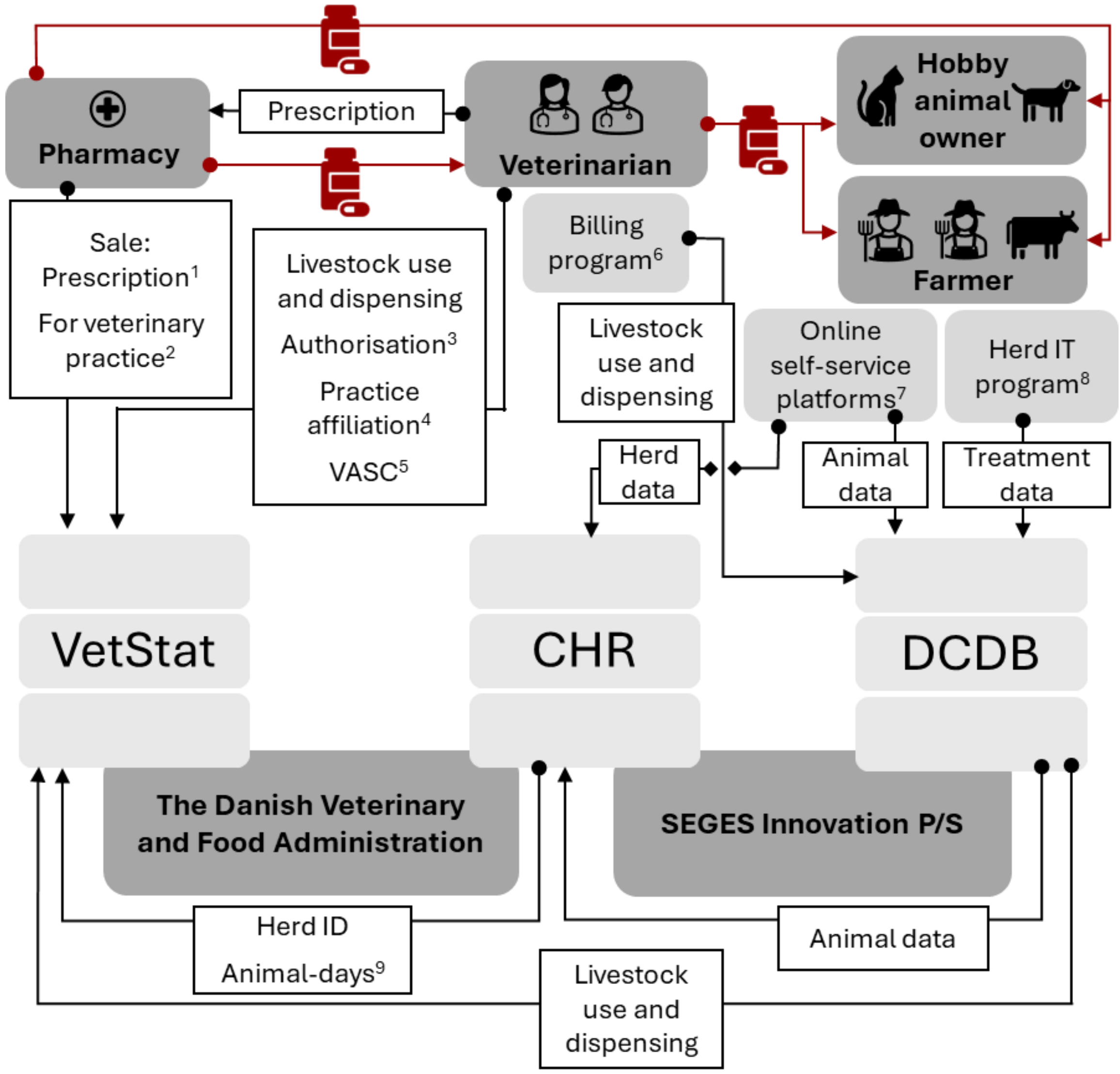

Figure 4.2. Data and medicine flow between stakeholders and databases Stakeholders are illustrated by dark grey squares, databases by triple-layered light grey squares, and online platforms and IT interfaces as grey squares. A stakeholder touching a database indicates a level of responsibility for the database or its content. The flow of medicine is illustrated with red arrows between stakeholders, while the flow of data is illustrated by black arrows with white background textboxes describing the content of the data.

[1]Sale of prescription medicine to all animal species following a veterinary prescription is reported into VetStat by the pharmacy. In rare cases feed mills may also report data but this is a negligible amount of antibiotics for cattle. When a sale is recorded for livestock Besætningsnr. is included the record in addition to species of animal, age group, indication of use, date of sale, prescribing veterinarian, product identification, and amount of product.

[2]Sale of medicine for use and dispensing in veterinary practices is reported into VetStat by the pharmacy and includes identification of veterinary practice, date of sale, product identification, and amount of product. Sale for use in practice is not used in summaries of AMU as use and dispensing data from veterinarians are used instead (see point 6).

[3]People with an approved veterinary education can apply for an authorisation number from the DVFA, which grants the rights to practice as a veterinarian (DVFA, 2024a)

[4]Practicing veterinarians must record affiliation with a practice in VetStat. A veterinary practice is defined as a business from which one or more veterinarians practice their work (DVFA, 2024a)

[5]VASC between a herd and veterinarian are recorded in VetStat (DVFA, 2021a). This is to ensure identification of the veterinarian with the primary responsibility for carrying out advisory services.

[6]Livestock use and dispensing is reported by veterinarians either directly into VetStat or via a billing system sending the data to the DCDB, where it is aggregated at herd-level before the data are transferred to VetStat (Anonymous, personal communication, 2020). These data include Besætningsnr., species of animal, age group, indication of use, date of use/dispensing, using/dispensing veterinarian, product identification, and amount of product. Use and dispensing for non-livestock is not reported. Approximations of this can be found by subtracting veterinary reported livestock use and dispensing from pharmacy reported sale for use in practice; this method is however not ideal (Glavind et al., 2022)

[7] Records on individual animals are entered by the farmer via an online self-service platform (www.webdyr.dk) or an IT program or app into DCDB, while records on housing sites and ownership are entered in CHR by the farmer via an app published by DVFA or an online self-service platform (www.landbrugsindberetning.dk) (DVFA, 2024b).

[8]The farm-personnel can record a multitude of different farm related data, including treatment data, into DCDB via IT programs or apps (SEGES Innovation P/S., n.d.b)

[9]See description of calculating animal-days in “4.1.1. The Danish Central Husbandry Register (CHR)”. These data are transferred from CHR to VetStat for use in ADD100 calculations for cattle (see “4.1.2. VetStat”).

4.3. Interview data

Interview data were recorded on paper and later digitalised.
The full questionnaire can be seen in Danish in “Appendix B”, while the part directly concerning AMU can be found in an English version in “Appendix A”. The data were digitalised with the original recorded answers. In total, 12 separate tables were recorded: Farm basis data, VASC veterinarian, farm advisors, logistics, management of starter calves, medicine management, vaccination strategies, diagnoses, use of diagnoses, qualitative answers, variable description and digitalisation notes, and key for merging with CHR and VetStat data. The key lists herds with their production status and farm association. The tables are interconnected with IDs.

4.4. Tools

Table 4.4. Digital tools used in thesis work

Program/ Package	Use	Reference
Microsoft 365 Excel	Digitalisation	
R-Studio	Interface	Posit team, 2024
R		R Core Team, 2024
broom	Statistical analysis	Robinson et al., 2023
car	Statistical analysis	Fox & Weisberg, 2019
epiDisplay	Statistical analysis	Chongsuvivatwong, 2022
epitools	Statistical analysis	Aragon, 2020
flextable	Data presentation	Gohel & Skintzos, 2024
ggplot2	Data visualisation	Wickham, 2016
goldfinger	Data access	Denwood, 2024
lme4	Statistical analysis	Bates et al., 2015
lmerTest	Statistical analysis	Kuznetsova et al., 2017
patchwork	Data visualisation	Pedersen, 2024
readxl	Data import	Wickham & Bryan, 2023
ResourceSelection	Statistical analysis	Lele et al., 2023
sjPlot	Data presentation	Lüdecke, 2024
tidyverse	Data management	Wickham et al., 2019
vetstat	Data access	Denwood et al., 2024

5. Methods

5.1. Ethical considerations

5.1.1. General approach to responsible conduct of research

The research conducted in the PhD is to the best of my knowledge carried out in accordance with The Danish Code of Conduct for Research Integrity (Ministry of Higher Education and Science, 2014) and The European Code of Conduct for Research Integrity (ALLEA, 2023).

5.1.2. Studies on animals

No approval regarding studies carried out on animals were necessary as the studies in this PhD were solely observational. Participants in the field study were informed orally of my obligation as a veterinarian to act in accordance with Danish animal welfare legislation; this entails contacting the police if I observe gross negligence with regards to the care of animals (DVFA, 2024c). This did not become relevant.

5.1.3. GDPR

Following steps were taken to ensure ethical handling of personal data of individuals:

- The project was registered in the University of Copenhagen's joint record of biobanks and record of research projects containing personal data [Case no.: 514-0718/22-3000, approved 22.04.2022 and valid from 01.03.2020 to 31.12.2029]
- The Research Ethics Committee for the Science and Health Faculties at University of Copenhagen reviewed the project description and found it compliant with relevant Danish and International standards and guidelines for research ethics [CASE: 504-0330/22-5000, approved 24.06.2022]
- A project description was emailed to the Danish Health Research Ethics Committee system, which concluded that the study was not notifiable and could be initiated without approval from them [Journal-nr.: 22023933, decided 21.04.2022].

All approvals were obtained prior to the initiation of the field study.

No GDPR sensitive personal data were collected. However, as opinions on medicine use are the subject of, sometimes heated, public debate in a similar fashion to political orientation, sexuality and religion, the data collected are treated as sensitive in accordance with European GDPR legislation (Council Regulation (EC) 679/2016).

5.1.4. Informed consent

All participants in the field study signed an informed consent form, which was designed in accordance with guidelines published by the Danish Data Protection Agency (DDPA) and the European Union's General Data Protection Regulation (DDPA, 2021; Council Regulation (EC) 679/2016). The Informed consent form is included in "Appendix B". Treatment protocols were accessed in DCDB only after verbal consent from farmers during recruiting.

Consent to obtain digital treatment records, if available, was included as a separate option in the consent form. After the interviews conducted during the field study, treatment data from the DCDB were extracted by SEGES P/S for consenting farms for 2022 and 2023.

5.2. Data management

5.2.1. Access to database data

The work conducted in this thesis is relevant to the veterinary contingency work carried out under the veterinary public service agreement (see "Preface"), which meant that access to data from VetStat and CHR was provided to the University of Copenhagen (UCPH) by DVFA.
From 2020 to 202, access to VetStat data was obtained through data extracts provided as R files directly by DVFA. CHR data were provided as monthly CHR extracts in Excel files. These data were managed and stored by the Department of Veterinary and Animal Sciences at UCPH. From June 1st, 2021, this way of data sharing was abandoned by DVFA and a Danish order required the UCPH to build and maintain a server with a database link, which could receive and store VetStat data (DVFA, 2021b). In March 2022, this requirement was communicated to the UCPH, and the planning process began. A UCHP SQL database was ready for use in April 2023. From here, access to selected copies of data sets from VetStat was possible. Some data sets with frequent or routine input of new information in VetStat are updated with the new information in the UCHP SQL database at intervals. In February 2024 access to CHR data through the UCPH SQL database was facilitated. Due to movement of the server, access to the database was closed between February and April 2024. The first two years of working with the UCPH SQL database were characterised by challenges with access to both the server and critically important data sets necessary for data merging.

Access to data from VetStat and CHR for the studies conducted was obtained in accordance with signed data management agreements approved and stored by the Department of Veterinary and Animal Sciences at UCPH.

Access to data from the DCDB was obtained in accordance with two signed data management agreements approved by SEGES Innovation P/S, one agreement for the study conducted in Manuscript II and one agreement for the study conducted in Manuscript III

5.2.2. Storing and managing data

As previously described some VetStat and CHR data were stored in the UCPH SQL database. Remaining CHR and VetStat data sets were stored on a UCPH server, accessible only to those with valid data management agreements. Other data provided including DCDB extracts, R-scripts, and revised data sets were stored in a private folder in a UCPH server accessible only to me. Data management was carried out locally on a computer connected to the UCPH server via VPN access. Complete anonymisation of data sets used in analyses will be carried out upon acceptance of related manuscripts for publication. These and other data sets acquired during the thesis work will be managed, stored, anonymised, and deleted in accordance with the requirements outlined in the data management agreements. Completed questionnaires in paper format from the field study were stored under lock in my office during data management and disposed as confidential documents afterwards.

5.3. Methods in thesis

The work in this thesis draws on register research and field study to enable a more comprehensive understanding of AMU in Danish cattle. AMU can be viewed as a series of events with several events being of critical importance if the aim is prudent AMU. Figure 5.1. provides a timeline for AMU from prescription to final treatment record with important events grouped by topics. Manuscript II is based on register research and focuses on the utilisation of monitoring data from VetStat sales data recorded by veterinarians and pharmacies prior to on-farm AMU. These are combined with generalised data about farms readily available in other established monitoring programs. Manuscript I is based on a field study and focuses on the events occurring on-farm describing general management of antibiotic products, practices surrounding diagnostics and treatments, and the process of documenting and recording AMU. Manuscript III is primarily register research supplemented with data from the field study. It focuses on digital treatment records from DCDB entered by farm-personnel following on-farm AMU combined with standardisation methods used in VetStat and detailed knowledge about farm structures.

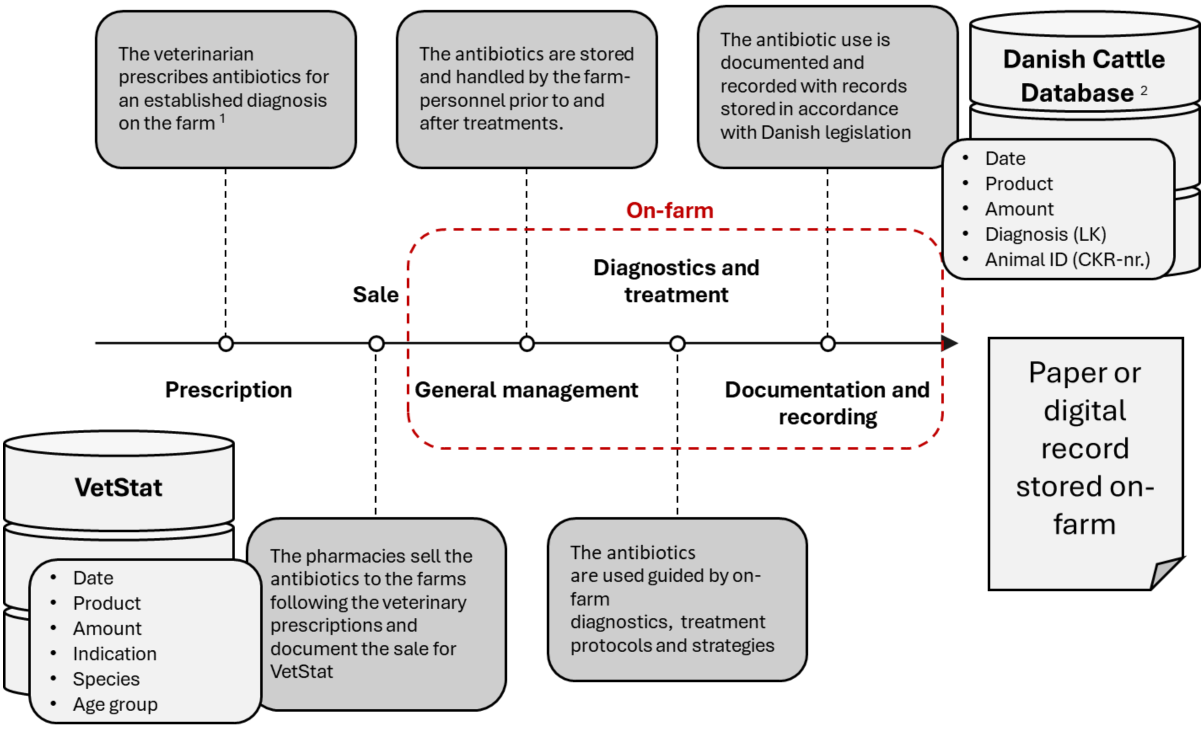

Figure 5.1. Timeline of antimicrobial use from sale to final recording of treatment in Danish cattle farms. Key variables included in the database records in VetStat and DCDB for a given farm are listed with the respective database.
1 Commonly occurring diagnoses identified on a farm can be treated by farmers in accordance with a diagnosis and treatment protocol outlined by the advising veterinarian (DVFA, 2021a).
2 Many farmers register in the Danish Cattle Database through their daily herd health management IT-solution (see “4.2. Data flow”).

Table 5.1. provides a brief overview of study designs, sampling, data and data sources, statistical methods, and specific objectives answered by each manuscript. It also includes a reference guide to presentation of results relevant to each specific objective.

Table 5.1. Overview of manuscript study designs, sampling, data and data sources, statistical methods, specific objectives, and reference guide to presentation of results.

Study design	Data and data source	Method	Results	
Cross-sectional questionnaire interview **Sampling:** Random sampling of 60 eligible farms **Study population:** 36 Danish rosé veal farms	**Data collection:** Field study, spring 2023 **Data source:** Questionnaire, DCDB, and CHR **Data:** Digitalised categorical and qualitative text answers supplemented with printed treatment protocols, satellite images and notes	**Statistical method:** Frequency analysis **Outcome:** Categorical variables and aggregated qualitative answers describing farm AMU management	SO1 SO2 SO3 SO9	Manuscript I All manuscript and "7. Discussion"
Cross-sectional study on register data **Sampling:** All eligible Danish farms included **Study population:** 118 Danish rosé veal farms	**Data collection:** Mandatory monitoring, 2020 **Data source:** VetStat, DCDB, and CHR **Data:** Aggregated monitoring data on AMU from VetStat, aggregated site-level data with farm characteristics from DCDB and aggregated herd-level data on ownership and activity status from CHR	**Statistical method:** Multivariable Linear Regression **Outcome:** Farm-level AMU in standard doses per 100 animals per day (ADD100)	SO5 SO6 SO9	"4.1.2. VetStat" and "6. Results" Manuscript II (See above)
Cross-sectional study on register data supplemented with data from cross-sectional questionnaire interview **Sampling:** Random **Study population:** 27 Danish rosé veal farms with digital treatment records in DCDB	**Data collection:** Active farm data recording, mandatory monitoring and field study, 2022-2023 **Data source:** VetStat, DCDB, and CHR **Data:** Product information from VetStat in raw format, treatment records and individual animal data from DCDB in customised data sets and aggregated herd-level data on ownership and activity status from CHR	**Statistical method:** Linear Mixed-Effects Model **Outcome:** Proportion of a standard dose used per treatment	SO4 SO5 SO7 SO8 SO9	"4.1.3. The Danish Cattle Database (DCDB)" and "6. Results" (See above) Manuscript III (See above)

The reasons for the chosen approaches and methods used in the conducted studies are presented in greater detail in Manuscript I-III. Here, a few of the core considerations regarding methods are listed for each study.
To improve the understanding of on-farm antibiotic management, use, and recording practices a questionnaire interview field study was conducted. The argument for an on-site approach was that it aided the aim of a comprehensive understanding of farm-level AMU in Danish rosé veal farms by allowing for observations of physical settings and other relevant context. A quantitative approach was chosen to allow frequency analyses of practices within the study population, which could be used to identify common practices. The initial sample size of 60 farms was chosen based on previous experiences within the research groups with achieving statistically significant results while being limited by time and resource constraints in field studies with only one interviewer.
To investigate how farm characteristics are associated with the level of AMU in VetStat, a register study was performed. The farm characteristics investigated were farm size, proportion of crossbred bulls on-farm, number of suppliers, proportion of heifers on-farm, mortality, and number of sites per farm. The argument for using existing monitoring data was that it represented the current national monitoring of farms and AMU-level, limited the amount of data management, and made the study easily reproducible. A Multivariable Linear Regression was chosen because it made quantifying the effect of the continuous variables, farm size and number of suppliers, on the outcome ADD100 relatively simple and intuitive and it allowed for simple graphic illustrations of the effects.
To evaluate the accuracy of the Danish metric ADD200 in describing the doses used for daily on-farm treatments a register study was performed on digital treatment records from DCDB. The argument for a register study on DCDB data was that it allowed accurate merging with VetStat product information, which made conversion of used doses to ADD200 straightforward. A Linear Mixed-Effects Model was chosen to investigate effect of calf age at treatment, antibiotic class, location of disorder, and route of administration on the proportion of ADD200 used per recorded treatment (UDDprop) in DCDB. This model allowed inclusion of farm as a random effect, while having the same benefits as the Multivariable Linear Regression Model previously described. Correcting for farm was considered important as previous studies had shown significant variations between farms.

6. Results

6.1. Findings reported in Manuscripts

The central findings from the manuscripts and thesis are presented addressing the objectives outlined in Table 2.1 chronologically. For a more detailed account of results consult the individual manuscripts. A key to the main text describing results can be found in Table 5.1

SO1: Description of on-farm general management related to medicine storage and handling

Results from the field study are presented in Manuscript I. The study population consisted of 36 Danish rosé veal farms, who all received a visit with a farm walk-through during which they completed the questionnaire interview. Central answers regarding general management of antibiotics on-farm are presented with a frequency analysis in “Manuscript I, Table 1” and a full frequency analysis can be found in Table M1S1T1 in “Appendix A”. One of the main finds were that 92% of the farms had treatment protocols using procaine benzylpenicillin (recommended storage temperature 5°C) and 58% of farms used refrigerators for unopened antibiotic packages and 44% used refrigerators for antibiotics with a broken seal. A second important find was that the required skill set of personnel treating calves varied prior to hiring. And while the training of new personnel in treatment procedures was uniformly reported as peer-to-peer training the duration of the training period varied from one day to six months.

SO2: On-farm treatment strategies and the conditions for initiating treatments including diagnostics performed

The full range of results are presented in Manuscript I. One of the main finds was that while pneumonia was a concern in all farms, only 50% of the farms had done laboratory diagnostics on samples related to the respiratory system (see Manuscript I, Table 2). A second main find was that described clinical signs used to determine need for treatment for a given diagnosis varied between farms. A full list of the clinical signs described by interviewees for the diagnoses identified on the farms is given in Table M1S2T1 in “Appendix A”. A third main find was that 47% of the farms reported strategies with systematic group treatments at pen-level upon arrival. A fourth main find was that 64% of farms reported challenges with complying with the treatment protocols outlined by their advising veterinarian. The reported non-compliance areas encompassed indication of use, dosage, duration of treatment, and route of administration. Regarding dosage, three strategies were identified:

dosage based on estimated animal weight (39% of farms), fixed dosages for pens (17% of farms), and a mix of the two previous approaches (44% of farms).

SO3: On-farm documentation and recording practices for AMU including storage and digitalisation of treatment records

The full range of results regarding documentation and recording practices are presented in Manuscript I and in Table M1S1T1 in "Appendix A". Table 3 in Manuscript I provides an overview of the key documentation and recording practices in the study farms and the associated frequencies of answers. One of the main finds was that 81% of farms had multiple steps in their treatment documentation; 61% of farms used physical writing in the first documentation, while 19% of farms used either physical writing or digital logs. A second find was that the locations of first treatment logs and final treatment records varied (see Table M1S1T1 in "Appendix A"); the locations mentioned were stable, milk room, office, anteroom, lunch room, and "other" locations. Typically, the first treatment documentation was carried out in the stable (81%). A third find was that in 36% of the farms, the person responsible for recording treatment was a fixed person, and not necessarily the person carrying out the treatment. A fourth find was that the time interval from treatment to final recording reported by the interviewees for farms varied: "Immediately" (22%), "Within 24 hours" (36%), "48 hours to 72 hours" (28%), and "More than 5 days" (14%). Final treatment records were digitalised in 81% of the farms and stored in paper format in the remaining farms. In Manuscript III, only 27 farms equalling 75% of the farms in the field study had digital treatment records in DCDB.

SO4: Structure and content of antibiotic treatment records available in the Danish Cattle Database, including potentials for merging with data from other sources

Structure and content of the DCDB data is described in "4.1.3. The Danish Cattle Database (DCDB)". In the following, key findings on potential for merging are included. Vnr. used in DCDB data, pdf treatment protocols and "medicine" data, can be used to merge with VetStat product information data. Besætningsnr. or CHR-nr. are available in the DCDB data, which allows merging with CHR and VetStat data. A VetStat key data set translating a VetStat ID to Besætningsnr. is necessary for merging with new VetStat data. This key data set was not initially made available but provided at a later stage. At the time of data acquisition for Manuscript II (aggregated farm characterisation data), the old VetStat was still in use, which made merging with this data set straightforward as CHR-nr. is a common ID between the data sets. The merging process for Manuscript II is outlined in Figure 6.1.

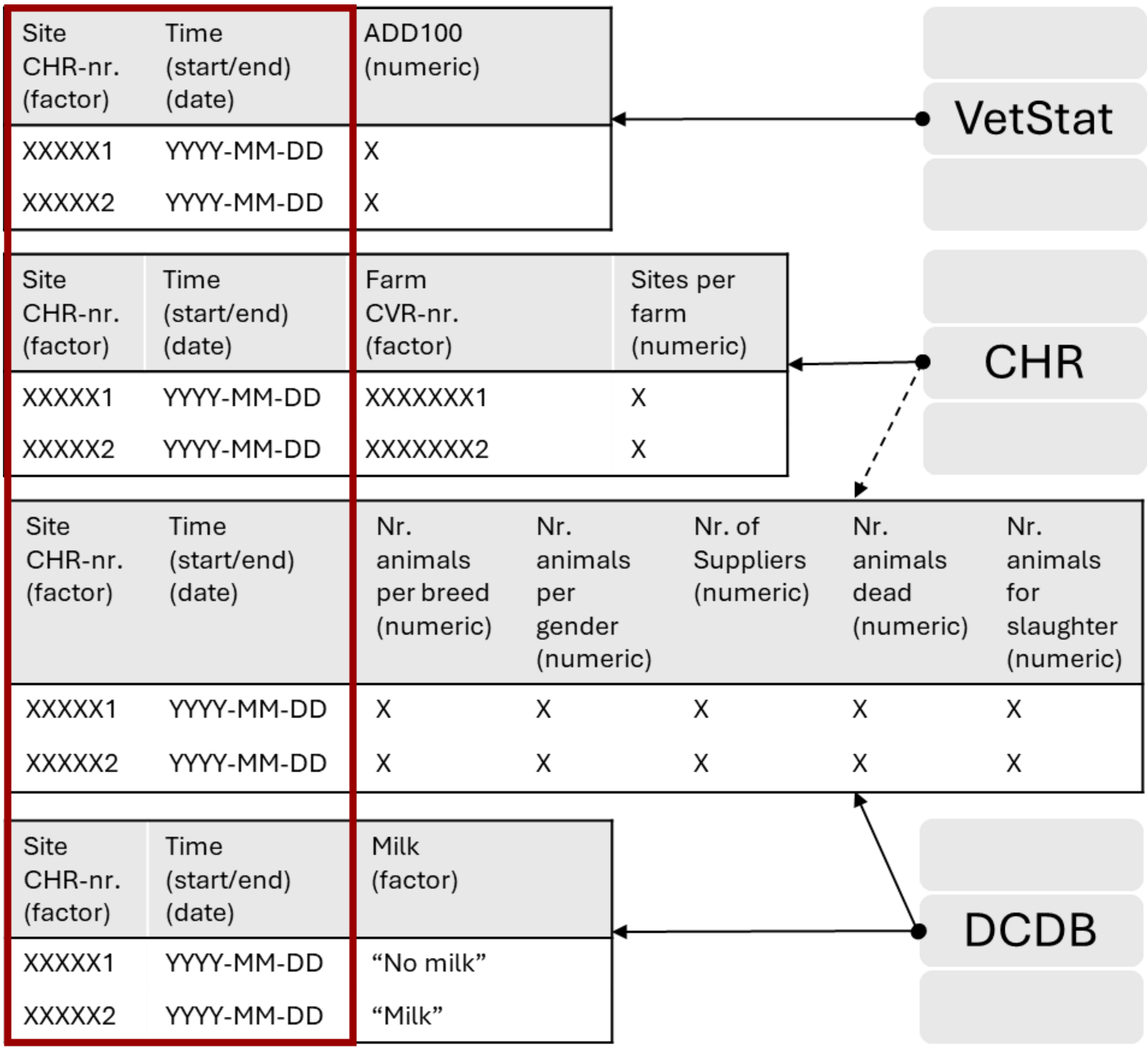

Figure 6.1. Merging of data from VetStat, CHR, and DCDB for the register study in Manuscript II. Each table represents a separate data set with an arrow from the database providing access. One data set was extracted from DCDB, but data were also stored in CHR symbolised by an arrow with a dotted line. The common variables used for merging are marked by the red box. Prior to merging data were aggregated separately in all data sets for a one-year period (2020).

SO5: Structure and content of VetStat including structure of records, and calculations and variables used for AMU quantification

Structure and content of VetStat data is described in “4.1.2. VetStat” and the dataflow into VetStat is described in Figure 4.2. In the following, key comments on VetStat and VetStat data relevant to the thesis work are summarised. VetStat data allow for stratification and aggregation of data in multiple ways. Sales data can be aggregated into relevant time intervals and stratified by recording responsible, herd, species, age group, indication, prescribing veterinarian, and product. By adding product data, it is possible to stratify further by factors such as antibiotic class, ATCvet, and route of administration. Quantification can be done by calculating number of standard doses, ADD, by species age groups. The ADD are defined per product and calves are assigned a standard weight of 200 kg. This can be combined with animal-days to calculate ADD100. One key development during the thesis work was the update of VetStat, which was associated with significant changes to the database. The principles for recording and quantification of AMU in VetStat remained the same, but records went from site- to herd-level and a data validation engine was introduced.

SO6: Farm-level characteristics affecting level of AMU in VetStat monitoring identified in existing national monitoring data

Results from the first register study are presented in Manuscript I. The study population consisted of 119 Danish rosé veal farms and was conducted on aggregated monitoring data from 2020. The farms included 154 sites with a median of 1 site per farm, a mean of 1.4 sites per farm, and a maximum of 4 sites per farm. The study population encompassed all eligible farms from the target population after application of the inclusion criteria listed in “Manuscript II, Figure 1”. The farm-characteristics are summarised for the study population in “Manuscript II, Table 1”. For the factors included in the final model following distributions of data were found: Farm-size varied between 203 animal-years and 4,750 animal-years (median 483 animal-years, mean 734 animal-years), crossbred percent of bulls varied between 6% and 83% (median 25%, mean 29%), number of suppliers varied between 1 supplier and 280 suppliers (median 19 suppliers, mean 35 suppliers). All farm-level characteristic factors were log-transformed in the model. Farm-level AMU expressed as square root transformed ADD100 was found to significantly increase with farm size ($p < 0.001$) and number of suppliers ($p = 0.01$). A significant decrease ($p = 0.02$) in level of AMU was found for the crossbred percentage of bulls, though this effect could not be separated from the effect of percentage of heifers on-farm. The model is illustrated in “Manuscript II, Figure 2” with associated model output listed in “Manuscript II, Table III”.

SO7: Comparisons of the doses used and recorded in DCDB for on-farm treatments and the standard doses ADD200 defined for cattle and youngstock in VetStat

Results from the second register study are presented in Manuscript III. The study population included 27 Danish rosé veal farms, selected from the study population in the field study based on them having digital treatment records routinely entered into DCDB. The farms included 46 herds with a median of 1 herd per farm, a mean of 1.4 herds per farm, and a maximum of 4 herds per farm. The farm size ranged from 206 animal-years to 3,191 animal-years (median 620 animal-years, mean 983 animal-years). The antibiotics sold to the study farms based on prescriptions (i.e.

from pharmacies) included 15% of all ADD200 sold for calves in Denmark during 2023. The number of sold ADD200 was 4% higher than the number of used ADD200 based on converted used doses. The difference between sold and used ADD200 varied between farms from 27% lower sale than use to 37% higher sale than use with a median and mean difference of 2% and 5% higher sale than use, respectively. In “Manuscript III, Table 3” differences between use and sale are stratified by antibiotic classes. After including treatment records in the model data in accordance with the criteria presented in “Manuscript III, Figure 1”, UDDprop varied from 0.1UDDprop to 12UDDprop with a median of 1.1UDDprop and a mean of 1.27UDDprop.

SO8: Factors affecting the accuracy of the Danish metric ADD200 from VetStat in describing the doses used for daily on-farm treatments in Danish rosé veal farms

Results regarding factors affecting the UDDprop in the second register study are presented in Manuscript III. Violin plots of UDDprop or calf age at treatment stratified by the investigated categorical factors can be seen in “Manuscript III, Figure 2” and “Manuscript III, Figure 3”. In univariable analyses, UDDprop was found to vary significantly with different levels or categories of the investigated factor. The only continuous variable was calf age at treatment, which ranged from 3 days to 364 days with a median of 66 days and a mean of 86 days. For the VetStat indication group “Joints, limbs, hoof, central nervous system, skin”, several locations of disorder were defined (see “Manuscript III, Table 1); significant variations in mean UDDprop between locations of disorder within this indication group were found. Due to correlation between all factors, location of disorder and route of administration were excluded from further analyses. The data set was reduced to include only records of systemic treatments on lung disorders. The final model is outlined in “Manuscript III, Equation 3”. In the model, UDDprop was found to increase with age with different predicted slopes for the antibiotic classes (see “Manuscript III, Figure 4” and “Manuscript III, Table 5”). The predicted slope for macrolides represented the highest UDDprop, with UDDprop exceeding 1 when the calves are approximately 6 days old. Farm included as a random effect explained 61% of the variation observed in the model data. In “Manuscript III, Figure 5”, farms are shown to have different predicted slopes when UDDprop is plotted against calf age at treatment for systemic treatments of lung disorders with amphenicols.

SO9: Current challenges interpretation when VetStat monitoring of AMU is used to make inference about on-farm AMU and evaluate their potential implications

This is addressed in detail in “7. Discussion” in the context of the three studies carried out and presented in Manuscript I-III and the experiences gained working with data during this thesis.

6.2. Additional findings

6.2.1. Treatment failure

Qualitative data related to treatment failure were collected during the field study. One question concerning the use of diagnoses and treatment protocols covered actions in cases of insufficient treatment effect. The question asked was: *“What would you (red. personnel on the farm) do if this treatment protocol did not work?”*. Following medicine-based treatment approaches were identified for at least one treatment protocol per farm: Repeat of first treatment protocol (75%), switch to a second-choice treatment protocol (72%), follow-up treatment with pain medication alone (6%) or in combination with antibiotics (8%). In the group having a second-choice protocol, they either switched directly or repeated the first protocol before switching; in some cases the second-choice protocol was for a different location of disorder.

For two farms (6%) no data on medicine treatment follow-up were recorded. For the remaining 34 farms (94%) they had antibiotic treatment follow-up for at least one treatment protocol. Seven farms (19%) reported euthanasia as procedure directly after TF for specific diagnoses and seven farms (19%) reported euthanasia following one or more follow-up treatments; in total 12 farms (33%) reported using euthanasia. Only 6 farms (17%) reported using a sick pen for calves following TF.

6.2.2. Identifying farm in CHR data

To find CHR data on farms, herd- or site-level data had to be aggregated to farm-level data. Before a farm could be identified and defined, information on ownership, size, production type, and activity status, including changes over time, had to be determined and summarised within a given period for each herd or site. In all manuscripts, the period was set to one year. The criteria used in defining and including farms in Manuscripts I and III are presented in ”Manuscript I, Figure 1”. The criteria used in defining and including farms in Manuscript II are presented in ”Manuscript II, Figure 1”. In the latter, production type and ownership could not be used directly as this is given on herd-level. The issue with production type was solved by applying a set of criteria to farm characteristics, which were expected to reflect professional veal farms: No milk deliveries, housing 200 or more animals expressed in animal-years, and number of slaughtered animals equal to or larger than housed animals. The issue with determining ownership was solved by including only sites, where at least 95% of the animals registered at the affiliated herds had one owner; this owner was set as owner of all animals on the site.

7. Discussion

In this chapter, four main themes are discussed and the findings from the studies are placed in a broader context based on the approach “from cattle to computer – and back again”. The specific results of each separate study are discussed in detail in the respective manuscripts. The first two themes addressed are central for the work across all manuscripts: Interpretive challenges to AMU monitoring at farm-level, and heterogeneous farms and their motivations for changing AMU. Under these themes, I address the most important findings identified during my thesis work and their potential implications for monitoring and quantification. Concurrently, I address the relevance and significance for, and agreement with previous work done on AMU quantification in a broader context. In the third discussion theme, I summarise concrete recommendations for improving AMU monitoring and quantification in a Danish context. In the fourth discussion theme, I elaborate on the limitations and strengths of the thesis approach, utilized materials and choice of methods.

7.1. Interpretive challenges to AMU monitoring at farm-level

Ideally, when monitoring AMU at farm-level, one should be able to make inference about the actual on-farm AMU. Monitoring accurately reflecting on-farm AMU could aid in identifying farms with injudicious AMU or highlight inappropriate farm practices. Therefore, an important goal in this thesis work was to gain a comprehensive understanding of the AMU on-farm and the corresponding AMU reported, using Danish rosé veal farms as an example of a relevant population for such work. This was done by investigating topics chronologically along the entire AMU event series (see Figure 5.1.). The aim was to identify events and practices resulting in flawed or skewed assumptions about on-farm AMU. In this thesis, a farm is defined as a whole production under one ownership including one or more herds or sites.

7.1.1. On the farm

In AMU monitoring, the focus is often on what is measured. During interpretations, it might be beneficial to keep in mind and communicate what is not measured or corrected for. During the investigation of the on-farm practices prior to treatment, several conditions potentially affecting how the measured AMU is interpreted by different stakeholders, were identified. Two of these are discussed here: Amount, but not effect, is measured under “7.1.1.1. Efficacy of treatment” and used or sold doses, but not needed doses, are reported under “7.1.1.2. Necessity of treatment”. In this part of the discussion, I focus on respiratory disease, which is a major concern in veal production worldwide. In the last part about on-farm challenges, the process of documenting treatments and the associated challenges for interpretation are briefly discussed under “7.1.1.3. Treatment recording”.

7.1.1.1. Efficacy of treatment

In Manuscript I, concerns are raised about a sub-optimal effect of treatments. Two major concerns are the lack of on-farm compliance with veterinarian or pharmaceutical company recommendations, and the lack of diagnostics leading to the use of antibiotics with limited or no effect against the disease-causing pathogens. This could result in misinterpretations of the prudency of the on-farm AMU as two farms with similar AMU expressed in monitoring could have a different efficacy of their used antibiotics. One farm may comply with the recommendations and have efficient treatment protocols in place based on laboratory diagnostics and susceptibility testing resulting in good cure rates indicating good efficacy of the antibiotics used. The other farm could have severe challenges with compliance and ineffective treatment protocols resulting in frequent TF and thus poor efficacy of the antibiotics used. Unfortunately, sub-optimal effects of treatments are difficult to quantify in general and hard to identify through monitoring.

The array of factors influencing treatment efficacy and their mutual relationship is complex and characterized by many knowledge gaps. Veterinary antibiotics losing efficacy due to faulty storage conditions are discussed in Manuscript I, and have, to my knowledge, not been indisputably documented (Ondrak et al., 2015). For many humane medicinal products, including antibiotics, shelf-life extending beyond the listed expiration date has been documented indicating high stability beyond pharmaceutical company recommendations (Lyon et al., 2006; Zilker et al., 2019). However, use of expired antibiotics has also been reported to cause TF and, in worst cases, toxic reactions in humans (Davido et al., 2024). Thus, the use of expired products could pose a threat to animal welfare through longer convalescence, complete TF, or adverse health effects. TF is a highly relevant topic in the discussion of antibiotic efficacy, amongst others, due to the potential association with higher AMU and increased risk of AMR (Booker & Lubbers, 2020). Booker (2020) defined TF as cases in which an animal became chronically ill, required follow-up treatments, or was culled from the herd through salvage slaughter or euthanasia. Apley (2015) remarked that the classification as TF could depend on timing of the evaluation and defined posttreatment interval, and on whether a full or only partial recovery was required. TF is not directly addressed in the manuscripts of this thesis, but some results from the field study are included in “6.2.1. Treatment failure". The question asked during the field study lacked proper clinical definitions of a TF: “*the treatment protocol did not work*” is, at best, loosely worded. Apley (2015) suggested that specific clinical parameters should be used to identify TF. Including these considerations could have improved the quality of the data collected but also increased the complexity of the questionnaire and the required time for the farm visits. While lacking proper definitions of TF, the study did identify farm procedures for cases where the efficacy of initial treatment was deemed insufficient: 94% of the farms described potential follow-up treatment with antibiotics for at least one diagnosis. This indicates the occurrence of TF in the study population, though the data do not allow for estimation of frequency or severity of TF.

TF has been reported to be a general concern in European veal production (Carmo et al., 2018a). Several factors and their interactions may cause TF making investigation of causal relationships complex; suggested causes of TF include the following: Compliance with treatment protocols, farm-personnel treating the animals, diagnostics performed, timing of treatment, disease-causing pathogen, presence of AMR, host, and environment (Abi Younes et al., 2024; Apley, 2015; Booker & Lubbers, 2020; Carmo et al., 2018a). Challenges associated with the first three factors were identified under Danish conditions during the field study and are discussed in Manuscript I, however, the effect of TF on AMU cannot be satisfactorily evaluated and quantified with the current knowledge. Nonetheless, it is important to consider when discussing on-farm AMU and corresponding monitoring.

7.1.1.2. Necessity of treatment

In monitoring, used or sold doses are reported. But one central question is whether this reflects the doses needed. There is a tendency to categorize health status as dichotomous, either sick or healthy. In reality, calves are often treated at different stages ranging from healthy, infected, sub-clinically, mildly or severely clinically ill, to chronically ill. Identification and classification of disease stages have been mentioned as important steps towards ensuring prudent AMU (Hoffelner et al., 2023). Haines et al. (2001) defined chronically ill calves as calves unresponsive to therapy. In these cases, treatment with antibiotics will constitute overuse. Similarly, the treatment of healthy calves will also contribute to overuse of antibiotics. The practice of metaphylactic treatments introduces the risk of treating healthy calves and often results in higher AMU (Credille et al., 2024; Horton et al., 2023). As previously mentioned in “3.4. Danish farmers’ “License to Treat””, only metaphylaxis is allowed under Danish conditions. In this thesis work, treatment protocols which were routinely administered at pen-level were identified in 47% of the study farms in the field study described in Manuscript I providing evidence that metaphylaxis is a common practice in Danish rosé veal production. Distinguishing between metaphylaxis and prophylaxis in literature, which does not clearly define metaphylaxis, or which uses the terms “routine” or “group” treatment, poses a challenge when attempting to compare practices across studies. The benefits and drawbacks of metaphylaxis are discussed in greater detail in Manuscript I. The key take-home messages are that metaphylactic treatments are widely used against bovine respiratory disease in veal production worldwide, has been proven in some studies to have beneficial effects on a range of production parameters, and can result in overuse of antibiotics with the associated risk of AMR development. One recent study suggested that metaphylactic treatments could be applied randomly to 66% of the calves in a pen without reducing the growth performance and increasing the occurrence of respiratory disease compared to treatment of all calves in a pen (Dornbach et al., 2025). This could decrease overuse, but the problem with potential treatment of healthy calves remains an issue.

Antibiotic treatments should be targeting animals with acute clinical disease, where the therapy is expected to efficiently combat disease and result in restoration of health. The timing of treatment is crucial, particularly for respiratory disease. Lung lesions have been shown by ultrasound to occur five days before peak in clinical illness score and prompt treatment resulted in a high success rate for treatment (Lisuzzo et al., 2024). Identifying and treating sick calves early could help improve treatment efficacy and animal welfare. In Manuscript I, the results showed that there were some disease detection efforts in many of the study farms, but not efforts reliable enough for consistently initiating early treatment in many cases. In Table M1S1T1 in “Appendix A”, the on-farm procedures for finding sick animals are listed; these findings show that calves were observed daily for the presence of disease, mainly during rounds dedicated to finding sick calves (72% of farms). In Table M1S2T1 in “Appendix A”, the clinical symptoms mentioned by the interviewees are included. Many of the symptoms for pneumonia overlap with symptoms described in internationally used clinical scoring systems for detection of bovine respiratory disease (Ferraro et al., 2021; Love et al., 2014). An observation from the field study, which was not recorded or reported in the collected data, was that the interviewees generally expressed the opinion that sick calves should be treated, but their thresholds for initiating treatment varied, sometimes even within farm. Unfortunately, diagnostics relying solely on clinical signs for identifying diseased animals have challenges with sensitivity and specificity (Lowie et al., 2022; White & Renter, 2009). This introduces the risk of both treating animals not requiring treatment and neglecting treatment of animals in need of treatment. Alternative diagnostic methods, with promising potential for early disease detection, such as thoracic ultrasound, sensor-based movement data, and data from automatic feeding stations, are currently being investigated (e.g. Bushby et al., 2024; Kamel et al., 2024; Schupbach et al., 2025; Sun et al., 2021). Still, accurate on-farm diagnostic approaches prove illusive, and a multifaceted approach may be necessary (Kamel et al., 2024). With an optimised search process for the animals requiring treatment and timely and relevant treatment applied AMU may be reduced.

The presented considerations regarding the treatments carried out versus the treatments that were actually necessary for welfare reasons should be considered when using monitoring data. Care should be taken, especially if AMU monitoring data are used to make inference about the health status or disease occurrence on a farm; not all treatments will correspond to a disease occurrence and some diseased animals may not have received treatment.

7.1.1.3. Treatment recording

In AMU monitoring, accuracy and completeness of data should be considered (Agunos et al., 2019). In the study by Henningsen et al. (2024), we raised concerns about these issues for treatment data from the DCDB. To address the accuracy of treatment records, the field study questionnaire included questions about procedures for documenting and recording treatment data on-farm. The focus was on the responsibility for recording, timing of recording, the type (digital or paper) of documentation, and the storage of records. While the stated objective was to describe the practices, the purpose behind it was to understand if these practices could impact the accuracy of the recorded data. Several practices described in Manuscript III can be problematic and lead to errors in data: Multiple steps in recording (e.g. first on paper and then digitalisation), different treatment documentation stored at different locations, the person performing the treatment not always entering the final treatment record, and the final recording of treatment taking place long after the treatment (> 5 days in 14% of the farms). Each time data are transferred by a person, e.g. from a paper log to a computer program, there is a risk of transcription errors. One farmer mentioned issues with number blindness, which could severely increase this risk. If person responsible for recording is handling paper logs written by others, this may also cause errors if e.g. handwriting is misinterpreted. If the time interval from treatment to recording is long, recall bias may also become a more systematic issue affecting the total number of errors (Dohoo et al., 2014; Houe et al., 2004). Another cause for systematic errors could be due to lack of compliance. If one treatment protocol is systematically used for a different indication, which was also reported by some farms during the field study, this could lead to misclassification bias (Dohoo et al., 2014; Houe et al., 2004). Based on these findings, it is deemed highly likely that errors and to some extent bias in treatment recording can occur, but the prevalence and frequency cannot be determined. Generally, a systematic approach to documentation and recording was observed on the farms, with each farm having a well-established procedure. This should minimise the errors and bias-proneness of the treatment records and make them reliable sources of information on on-farm AMU. Still, it is important to be aware that treatment records in DCDB may be subject to errors and bias. Incomplete treatment records have previously been found for calves in American dairy productions in a study, which also investigated potential factors contributing to improved recording practices; digital recording and storage of records near the animals were found to improve completeness of records, and questionnaire respondents suggested mobile recording and an easy-to-use recording system as potential initiatives to increase likelihood of recording a treatment event (Edwards et al., 2024). The same study also highlighted how analysis of records and feedback motivate farmers to improve their recording practices. Analysis of treatment data can easily be carried out under Danish conditions, especially if the user has access to the interface connected to DCDB. Here farmers can access pre-defined analyses themselves. As reported in Manuscript III, not all farms from the field study had digital records. DCDB contained treatment registrations from 31 farms (86%) of the 36 study farms, but only 28 farms (78%) reported performing systematic treatment recording in the database using the interface. One farm (4%) out of the 28 farms, which reported digital treatment registrations, had no registrations in the data extract from DCDB provided by SEGES. Therefore, the final study population in Manuscript III became 27 farms. Farms with combined production agreements ("Samdrift") are required to use DCDB for treatment records but for others it is voluntary (DVFA, 2021a). From this, a conclusion is that some farms will lack records in DCDB potentially resulting in incomplete data for a given study population. This should be considered in future studies using this data.

7.1.2. In the database

Once AMU data are entered into the respective databases, new interpretive challenges become relevant. Three main topics are included in this part of the discussion: Differences in sales and recorded use, challenges with herd age groups as a unit in benchmarking, and impact of standardisation metrics and methods.

7.1.2.1. Differences in sales and recorded use

A key observation in Manuscript III is that the sale monitored in VetStat does not equal the use reported by the farms; the use was 4% lower than the sale. This is not surprising, and this overall difference can be considered low. Becker & Meylan (2021) suggested factors such as expired medicine or broken bottles as a reason for the discrepancy between amounts used and sold. Though not specifically reported for antibiotics, these issues were mentioned by farmers during the field study. However, large differences between sold and used were found for some of the individual farms, which is more concerning. As already discussed in Manuscript III, large differences can be attributed to the time difference between sale and use. If a farm receives medicine with large intervals between prescriptions, a prescription just prior to or after the study period, could have a large effect on the relationship between used and sold amount. A more serious concern is when the discrepancy is caused by on-farm challenges with correct recording of the used medicine such as systematically over- or under-reporting of doses used or frequently missed recording of treatments carried out. This could severely impact the interpretation of overall level of AMU in farms when monitoring is based on reported amounts used in DCDB. One benefit of using VetStat sales data is that it represents all medicine entering the farm, provided the sales data are correct. With the error handling module incorporated into new VetStat the risk of errors in sales data has decreased markedly. If a bottle is dropped and broken the medicine will still enter the stable environment and while its potential impact cannot be quantified, the amount will still be accounted for. A challenge with VetStat data on the other hand is a lower granularity of data compared to DCDB data. With accurate and complete use data from the DCDB, a farmer or veterinarian may extract the full treatment history for a calf and assess the treatments carried out on-farm in greater detail and with the accurate timing of the AMU. This could be useful for things such as identifying chronically ill calves or early detection of disease outbreaks.

7.1.2.2. Challenges with herd age groups as a unit in benchmarking

Farm-level benchmarking has been widely implemented and is recognised as an important tool in farm-level AMU monitoring systems in livestock sectors (AACTING, n.d.a.; Murphy et al., 2017). One issue with benchmarking is the structure of data – data need to be aggregated and presented in a way that allows meaningful comparisons (Murphy et al., 2017).

The decision to work with farms and the hierarchic structure of CHR data proved to be a challenge across all studies conducted as VetStat and DCDB data operate at either herd or site level. Restructuring data from CHR to correctly identify farms based on herd or site ownership information requires a considerable amount of data management. The argument for choosing farm, despite the challenges, was that logically herds or sites from the same farm will be subject to similar conditions regarding factors such as production practices, treatment strategies and general attitude towards AMU. All visited farms during the field study, were full-line rosé veal productions, but many were separated into multiple sites or herds. The mean number of herds reported in Manuscript III was 1.4 herds per farm, and 1.4 was also the number of sites per farm observed in Manuscript II. Monitoring AMU on multiple-herd farms should consider the full-line production, especially if benchmarking against single-herd farms is carried out.

Production type is not included in the Yellow Card Scheme, which may be problematic. Analyses of level of AMU in different herd types based on the animal composition show clear tendencies to differences between herd types (Stege et al., 2021; Stege et al., 2022). The herds with a high proportion of calves and youngstock compared to adult animals showed a larger median level of AMU than farms with more than 25% adult cattle present. This tendency increased with herd size. This indicates potentially significant differences between production types within the same benchmarking group. Increasing level of AMU with increasing farm size was proven specifically for veal in the study in Manuscript II. Accounting for farm structure, production type, and size will increase the comparability within groups. Benchmarking with the current system used in the Yellow Card Scheme, will likely target large rosé veal productions. This will make the target of the benchmarking narrow, resulting in a reduced relevance of the benchmarking for the population as a whole, and it will likely be perceived as unfair by veal farmers. The issue with lack of production type and farm size was also pointed out by practicing Danish cattle and pig veterinarians in a recent questionnaire pilot study (Kruuse et al., 2024). Production type has been implemented in the national monitoring and benchmarking in the Netherlands, where veal is even separated into white veal, rosé veal starter, rosé veal fattening, and rosé veal full-line (AACTING, n.d.b; SDa, n.d.)

7.1.2.3. Impact of standardisation metrics and methods

When standardising in AMU monitoring, a goal is to find a measure which reflects the on-farm situation. A standard daily dose should therefore preferably reflect the dose used to treat one animal for one day on the farm. This can be investigated in multiple ways.

One approach to investigate this is to compare the number of on-farm treatments with the number of standard doses. In Henningsen et al. (2024), we did not compare the amounts of products in the respective databases but looked solely at the number of VetStat standard doses for adult cattle with a standard weight of 600kg in VetStat (1,316,758) and the number of treatments of one adult animal for one diagnosis on one day in DCDB (1,079,588). The number of daily treatments estimated in DCDB by Henningsen et al. (2024) was 20% lower than the number of standard doses reported in VetStat. This was similar to the findings reported for calves in Manuscript III, where the number of days of treatment in DCDB (148,591 DOT) was 25% lower than the number of reported VetStat standard doses (191,764 ADD200). This indicates that the standard doses in VetStat in general overestimate the number of treatments carried out for both adult cattle and calves. For adult cattle, one concern was the use of combination treatments, in particular for udder disorders (Henningsen et al., 2024). This was less of a concern for calves in Manuscript III, where the number of days of treatment was only 1% lower than the number of treatment records, which means treatments typically consisted of one antibiotic product per treatment day. This approach does not take into account the differences in the amounts of antibiotics sold and used, which may skew the results.

Another approach to evaluating standardisation, which is not affected by differences in amounts sold and used, was used in Manuscript III. Here, the amount used for a treatment was divided by the amount in a standard dose to find proportion of standard doses (or number of standard doses) per on-farm treatment. The amounts for each treatment carried out and their relationship with standard doses were thus investigated. The main finding was that an ADD200 did not correspond to a used daily dose on-farm. The relationship between the two was found to be affected by antibiotic class, calf age at treatment, location of disorder and route of administration, though only the first two were included in the final model. In the following impact of antibiotic class, calf age at treatment, and location of disorder on interpretation of AMU monitoring at farm-level is discussed.

7.1.2.3.1. Antibiotic classes

In Manuscript III, antibiotic classes were found to impact the relationship between used and standard doses. This issue has been documented by others before (Becker & Meylan; 2021; Jarrige et al., 2017; Merle et al., 2014). One factor potentially explaining some of this impact is the differing duration of effect for antibiotic products and classes. Macrolides exhibited the highest UDDprop in the model and the most frequently used macrolide in the study, tulathromycin, is a long-acting active compound. The potential impact of long-acting is well-described, but a consensus on a solution has not been reached, though many studies suggest correcting for the effect by dividing a standard daily dose with the expected duration of effect in days (Apley et al., 2023; Lardé et al., 2020; Lava et al., 2016; Merle & Meyer-Kühling, 2020; Postma et al., 2015; Taverne et al., 2015; Werner et al., 2018). Multiplying or dividing by a factor and listing the used factors for each product will improve transparency of AMU reporting and monitoring. Documenting the steps taken in choosing the factor would further improve transparency. Becker & Meylan (2021) detailed a method of accounting for long-acting effect based on the duration of effect listed in the SPC, which could be modified to calculate duration of effect of a given product. If the durations were given, these were used directly; if they were given as ranges the average was chosen; and if effect was absent from the SPC, the duration was determined based on evidence from existing literature. Data on ADD per product are already available to farmers and veterinarians through the online VetStat platform so adding this additional information should be possible. It would require an effort to document the factors, but the cost and time required are difficult to determine without knowing the extent of work which has already been completed. As discussed in Manuscript III, some products with prolonged effect have already been corrected with a factor in VetStat as the ADD is markedly lower than the recommended dose in the SPC. Still, especially for macrolides, the standard doses systematically overestimate the number of daily treatments, which is an important information when interpreting AMU monitoring.

7.1.2.3.2. Weight at treatment

VetStat previously used a standard weight of 100kg for calves and 300kg for youngstock but currently both groups have a standard weight of 200kg in VetStat calculations (Dupont & Stege, 2012). As discussed in Manuscript III, the standard weight of 200kg used in VetStat poorly represents the average weight at treatment, which was estimated to be around 142kg based on an average age at treatment of 86 days. The 100kg used previously is thus markedly lower and the current weight of 200kg higher making neither an accurate representation of the average calf treated. Age may not be the best proxy for body weight in the model as it assumes equal weight and growth curves for the calves. It has previously been demonstrated in Danish calves that weight and weight gain at given ages vary between breeds and sexes (Vestergaard et al., 2019). Kasabova et al. (2019) estimated animal weight at slaughter for pigs and broilers based on the assumption that the used dose corresponded to the recommended dose per day in the SPC. With additional information on total amount of active compound, the number of animals treated, and treatment days the individual body weight could be calculated for the animals. This approach was not chosen in Manuscript III as we assumed that the relationship between used and recommended doses could differ between farms, in part, due to the differing dosage strategies described in Manuscript I. Kasabova et al. (2019) found that treatment frequencies for administered daily doses and calculated standard doses differed markedly. They highlighted the large change in weight as one of the major contributors to this difference; change by a factor 40-60 for broilers during lifespan, a factor 5-6 for suckling pigs, and a factor 4 for fattening pigs. For a fictive rosé veal calf, the change in weight from birth to slaughter (8-10 months of age) would be around a factor 6-8 ((243days to 304days$_{\text{slaughter age}}$ * 1.074kg/day$_{\text{Standard daily weight gain from Sandelin et al. (2021)}}$ + 50kg$_{\text{birthweight}}$)/ 50kg$_{\text{birthweight}}$). One way to address the issue of large change in weight during livestock production is to introduce more age groups. This could be applied in VetStat with few alterations as animal-years are already based on individual animal records making an inclusion of one or more new groupings straightforward. For each group a standard weight should be assigned based on estimated mean weight at treatment. For these calculations, age could be used as a proxy for weight. For population AMU monitoring, basing the median weight on calculations similar to the ones carried out by Kasabova et al. (2019) could also be used. Currently, all cattle, regardless of production type, are monitored in the same age groups, which means these calculations should be carried out for the population as a whole. Alternatively, if production type is introduced as a category in monitoring the calculations should be carried out separately for the individual major production types, in a Danish context this could be dairy, rosé veal, and a category containing “other” production types. In Denmark, animals under one year of age are already categorised into two groups by Statistics Denmark for overall population monitoring (Statistics Denmark, n.d.b). This could be easily applied in VetStat.

The effect of weight is mainly relevant for livestock production with large factor changes in weight, but it should also be considered in other cases. In Henningsen et al. (2024), we discussed the challenge for adult cattle where some farms base their dairy production on the lighter breed Jersey compared to the most predominant Danish Holstein. In Denmark, Danish Holstein had 763,818 animals registered per January 1st, 2025, and Jersey had 160,109 animals registered corresponding to a 1:5 relationship between the two breeds (SEGES Innovation P/S., n.d.a). A similar ADD100 in VetStat reported for a Jersey and a Danish Holstein dairy production will likely mask a higher AMU in the Jersey farm. The weight issue is therefore also important to be aware of when addressing AMU.

7.1.2.3.3. Location of disorder

In Manuscript III, the location of disorder was found to be significantly associated with the number of standard doses per treatment, which indicates differences in AMU patterns between locations. A potential consequence is that large variations in disease occurrence patterns between farms could affect the results of AMU monitoring. If one farm struggles mainly with ear disorders and another farm struggles mainly with lung disorders, the median proportion of standard doses used per treatment could be lower for the first farm (see “Manuscript III, Figure 2”). Location of disorder was found to be correlated with age at treatment and antibiotic class, which means that a difference between farms could also be contributed to a slightly lower age at treatment on the first farm or a difference in used antibiotic classes. Nevertheless, the potential influence of location on the relationship between used and standardised doses cannot be dismissed.

In Henningsen et al. (2024), treatment frequencies reported in VetStat and DCDB using the same denominator were compared using Bland-Altman plots; separate plots were created for indication groups and antibiotic compounds. The two calculated treatment frequencies were found to exhibit significant differences for the indication “Udder” and the active compound “procaine benzylpenicillin”. This could indicate that standardisation can also vary with indication and antibiotic class for adult cattle.

In line with the findings in Manuscript III, respiratory disorders are reported as the most common treatment indication in veal production internationally (Carmo et al., 2018b; Lava et al., 2016; Mallioris et al., 2024; Pardon et al., 2012; Schnyder et al., 2019). This highly skewed distribution of treatments on treatment locations could affect the results and their relevance for the remaining cattle population. Krogh et al. (2020) found respiratory disorders to be the primary indication in Danish dairy herds (51% of treatment incidence in conventional herds), which is lower than the 80% of treatment records reported for rosé veal in Manuscript III. They also found gastrointestinal disorders to be the second largest indication (36% of treatment incidence in conventional herds), whereas gastrointestinal disorders only accounted for 1% of treatment records in Manuscript III. Characteristics of the study populations likely contribute to this observed difference, where the dairy calves in the study by Krogh et al. (2020) are included from birth, the calves in Manuscript III are only included after arrival to the rosé veal farm. In an international context, gastrointestinal disorders have been reported as the most common indication for dairy calves (Zhang et al., 2022). Location of disorder may therefore be a relevant consideration, when evaluating AMU and AMU monitoring in dairy calves with a model similar to the one presented in Manuscript III. Here, gastrointestinal disorders should be included or addressed in an additional model due to the higher proportion of treatments.

Location of disorder is a valuable tool for stratifying monitoring data as it can help identify where and how antibiotics are used. No common consensus on how to stratify indications exists, and classification into indications vary between studies (Apley et al., 2023; Merle et al., 2014; Redding et al., 2019). In Manuscript III, an identified challenge was that the VetStat indication group “Joints, limbs, hoof, central nervous system, skin” included treatments at multiple locations which differed markedly with regards to choice of antibiotics and timing of treatment. This broad indication reduces the granularity of monitoring. For cattle, separating at least joint, limb, and hoof disorders into a separate indication could increase the usefulness of stratification significantly.

One common theme relevant to the factors influencing the relationship between standardised AMU and on-farm AMU is the need for transparency in how standardisation is carried out. Discussed here are the issues of effect duration for long-acting products, choice of standard weight, and choice of stratification methods, which can all affect AMU monitoring and its interpretation. Hence, a general transparency in and need for documentation of data collection, standardisation methods, and analytical procedures is highly relevant (Collineau et al., 2017; Moura et al., 2023)

7.2. Heterogeneous farms and farmers’ motivations for changing AMU

The on-line Merriam-Webster defines heterogeneity as “the quality or state of consisting of dissimilar or diverse elements” (Merriam-Webster., n.d.). In this thesis, heterogeneity is used about the study farms as units. In all manuscripts, farm heterogeneity was evident. The studies conducted have focused mainly on the practical and quantitatively measurable factors contributing to differences between farms. During the field study, the farms were found to vary with regards to many aspects such as AMU practices, structure, and logistics as described in Manuscript

I. In Manuscript II, the results from a register study found the level of AMU to be influenced by farm characteristics. Increasing farm size and increasing number of suppliers were associated with higher levels of AMU in VetStat. The effect of the on-farm composition of animals with regards to breed was confounded by sex and the association could therefore not be fully elucidated, but differing AMU-levels for breeds and sexes have been described previously (Bokma et al., 2019; Diana et al., 2021). The 119 included rosé veal farms varied greatly for all examined factors underscoring the heterogeneity of the study population. Based on experiences from the study in Manuscript I and II, an effect of farm as a variable on AMU was expected, thus farm was included as a random effect in the model. The resulting model showed that farm explained 61% of the variation observed in the model data. This truly highlights the importance of considering individual farm-related conditions and practices when working towards prudent AMU. This issue is addressed by many studies, but the mechanisms driving on-farm AMU are complex and several angles for potential interventions should be considered, as one-size does not fit all (Guenin et al., 2023).

Farmer mindset, explained as a combination of management and opinion, has been described as important when distinguishing between dairy farms with high and low AMU in young calves (Holstege et al., 2018). Holstege et al. (2018) suggested that a change in both aspects was important for achieving lower AMU. While human factors such as attitudes and motivations driving on-farm practices have not been a focus of this thesis, several other studies have addressed this in livestock (Borelli et al., 2023; Coleman & Hemsworth, 2014; Shrestha et al., 2025; Skjølstrup et al., 2021). McKernan et al. (2021) identified knowledge and awareness of antibiotics and attitudes towards antibiotics as important factors influencing AMU behaviour. Coleman & Hemsworth (2014) summarised how attitudes affect behaviour, work motivation, and motivation to learn, which in turn affected the acquired technical skills and knowledge and the final work performance. Therefore, understanding how to best educate farmers on AMU and change attitudes are important topics.

In Denmark, peer-to-peer initiatives amongst cattle farmers, such as “Stable Schools”, has long been used with the aim of reducing AMU (Vaarst et al., 2007). The Stable School concept is based on meetings amongst groups of farmers and a facilitator (veterinarian or another advisor with agricultural background); each farmer receives visits and participates in visits to other farms, where farm-specific issues are discussed in a structured way by the group allowing all peers to provide their input on where changes could be made (DVFA, 2021a; Vaarst et al, 2007). A reduction effect on AMU has been documented through the Stable School concept making it a relevant tool for changing farmer behaviour and attitude (Bennedsgaard et al., 2010), although not all farmers feel motivated to enter such initiatives. Benchmarking has already been discussed as an initiative in monitoring AMU, but it can also be used to motivate AMU reduction (Murphy et al., 2017). As already discussed under "*7.1.2.2.* Challenges with herd age groups as a unit in benchmarking", the structure and level of aggregation of data used in benchmarking is a challenge. In the field study, one farmer expressed frustration with VetStat benchmarking, i.e. the Yellow Card Scheme. His starter-herd had a high level of AMU, and his finisher-herd had a low level of AMU, which, in his opinion, made the benchmarking carried out useless to him. This is an important consideration. The farmers' perceived relevance of benchmarking efforts are likely crucial for inspiring change in AMU behaviour. Benchmarking on colostrum management has been shown to affect dairy farmers interest in adopting other practices, but the effect of benchmarking was influenced by available farm resources, the farmers' perception of the problem, management strategies, and the farmers' values (Wilson et al., 2023). This further underscores the complexity of drivers behind AMU and the importance of addressing both practical and human factors.

While farmers are the main users of antibiotics, the role of the veterinarian should not be overlooked. In a review by Guenin et al. (2023), positive outcomes on herd AMU or AMR were attributed to the farmer-veterinarian relationship for several studies. The importance of this relationship is widely recognised and veterinarians play an important role in advising and educating farmers (McKernan et al., 2021). Implementing benchmarking amongst veterinarians on antibiotic prescriptions could be a tool to increase awareness of this role amongst veterinarians and encourage conversation and exchange of experience amongst peers. The Netherlands already have a national benchmarking of veterinarians implemented, and the Danish authorities have explored options for implementing a system in Denmark (AACTING, n.d.b.; Stege et al., 2021; Stege et al., 2022). In a Danish pilot study, half of the pig and cattle veterinarians responding saw benchmarking as a good tool for increasing experience exchange, though more than half were not motivated to change their antibiotic prescription patterns (Kruuse et al., 2024). Veterinarians are typically the farmers' closest advisors with regular contact and (in Denmark) mandatory advisory services focused on health management and AMU practices (DVFA, 2021a). Speksnijder et al. (2015) highlighted different barriers for promoting prudent AMU for different groups of Dutch veterinarians. Fostering communication between veterinarians about potentials for AMU reduction or change towards prudent AMU practices based on knowledge and experiences is an important step first.

To conclude, farms vary greatly, and the success of different approaches in achieving prudent AMU and implementing relevant practices likely depends heavily on the individual farm context, farmer, and advising veterinarian. Recognizing the importance of local, evidence-based strategies grounded in a holistic approach is a crucial first step toward prudent AMU.

7.3. Recommendations for improved AMU monitoring and quantification in Danish cattle

The overall aim of this thesis is to promote prudent AMU in livestock. It is insufficient to merely describe on-farm AMU, its associated monitoring practices, and the interrelationship between the two. It is equally important to translate this understanding into actionable initiatives that effectively support and advance prudent AMU.
The choice and contextual relevance of initiatives is highly dependent on the stakeholders implementing them and their respective agenda, incentives, and motivation. Stakeholders can be defined and described in many ways, but here I have chosen to group them together into international, national, and local stakeholders. International stakeholders are mainly concerned with global issues, in this context, the threat of AMR and associated consequences for the present and future health and welfare of humans, animals, and the environment. For this group, efforts to promote prudent AMU will primarily take the form of broad international recommendations and agreements that are applicable across countries and regions with differing capacities to meet requirements and implement guidelines (WHO, 2022; WOAH,2022). National stakeholders' concerns mirror the international stakeholders with an additional layer focused on concrete national challenges with AMU and AMR but also the image of the country and implications for trading animals or animal products. These stakeholders can be the representatives of the industry, but here, I choose to focus the discussion of initiatives on the authorities. The last group are the local stakeholders. This group is comprised of those physically close to the AMU such as farmers, farm personnel, veterinarians, and advisors. I chose to focus on the initiatives relevant to farmers.

The authorities have the capacity to implement initiatives and impose restrictions on AMU as already outlined in “1. Introduction”. The Yellow Card Scheme contain thresholds for both pigs and cattle, but currently they are only enforced in pigs and have not been updated for cattle since implementation (DVFA, n.d.b; DVFA, 2014). Enforcement of the Yellow Card Scheme from 2010 was found to cause a decrease of 25% in total AMU per pig produced in Danish pig herds between 2009 and 2011; with 76% of the reduction being attributed to reduced prescription of oral medication for gastrointestinal disorders in weaners and finishers (Jensen et al., 2014). Dupont et al. (2017b) studied implemented measures in Danish pig herds aimed at reducing AMU and found farmers and veterinarians attributing reduction to implementation of vaccines, less group medication (primarily oral), and staff education. They indicated that these measures may have been implemented due to the enforcement of the Yellow Card Scheme. Thus, enforcement of the Yellow Card Scheme may hold potential for reduction of AMU in cattle, too. However, as described in Manuscript I, many rosé veal farms already vaccinate (72%), and while group treatments are described, oral treatments constituted less than 4% of the treatments on the farms included in the study presented in Manuscript III. Therefore, enforcing AMU may be less effective than what was seen for pigs. In addition, as shown in this thesis, there are challenges with the accuracy of monitoring, and the structure of the current Yellow Card Scheme when used for cattle.

Several initiatives can be proposed to improve the alignment between on-farm antibiotic usage and the antibiotic use data reported in VetStat. The recommendations are directed at two main aims: 1) Improving overall accuracy of monitoring in VetStat, 2) Improving relevance of benchmarking to the farmer. This includes following recommendations:

Improving overall accuracy of monitoring in Vetstat

- Implement a factor for duration of effect for all products with an ADD in VetStat
- Increase the number of age groups used for calves in VetStat
- Update standard weights based on average weight at treatment within relevant age groups
- Split the current indication group ”Joints, limbs, hoof, central nervous system, skin" into two groups: “Sensory” (central nervous system, eyes, ear, skin) and “Extremities” (joints, limbs, hoof).

Improving relevance of benchmarking to the farmer

- Include ownership information from CHR in VetStat and benchmark by farm
- Include production type from CHR in VetStat and benchmark by production type
- Include size categories in VetStat and benchmark by farm size

In addition to these proposed changes, suggested topics which should be communicated to farmers and veterinarians are:

What quantification can and cannot do

- The level of AMU in VetStat may be affected by on-farm antibiotic management and treatment strategies. Concerns about low efficacy of treatments or sub-optimal treatment strategies may prime and motivate farmers to critically evaluate their on-farm practices and seek advice on how to improve them with the aim of reaching a lower overall AMU without compromising on animal welfare.

The importance and usefulness of good quality data

- Detailed on-farm AMU recordings may help farmers and veterinarians identify issues with AMU and apply relevant timely interventions. This requires accurate and complete data, which again requires reliable systematic on-farm documentation and recording practices.

These are concrete recommendations for improving quantification and understanding of patterns in AMU in Danish cattle. The recommendations for concrete changes to VetStat are dependent on action by DVFA. Sharing insights and facilitating dialogue about AMU between multiple stakeholders in the livestock sector can help identify barriers for achieving prudent AMU (Vaarst et al, 2025). Even if the changes proposed here are not implemented, the identification of key challenges may still be valuable knowledge for stakeholders, as it enables a more critical and evidence-informed perspective on the current Danish monitoring system and AMU quantification.

7.4. Study designs - strengths and limitations

7.4.1. Study designs

Developments and changes in AMU over time are highly relevant when discussing monitoring. This is not addressed in this study due to the cross-sectional study designs chosen in all studies in this thesis, which is an important limiting factor. If the results presented in Manuscript II and III were based on multiple consecutive years, they could have identified developments and increased the reliability of the results if findings were similar between years. With access to VetStat, CHR and DCDB data cohort studies should be easy to conduct, as data are continuously collected and historical data are available. Unfortunately, several factors not directly related to the studies had to be considered in the choice of study design. Originally the field study was planned for the spring of 2021, but the COVID-19 pandemic and three periods of leave of absence postponed the study for two years. Conducting the field study on-site was deemed important due to the improved understanding of rosé veal production and improved rapport with interviewees as described in Manuscript I. The delay impacted the possible study designs rendering a cohort study infeasible due to time and resource constraints.

The transition from old to new VetStat introduced time constraints due to the increased time allocated to data acquisition and management. More importantly it limited the possibilities for conducting retrospective studies spanning across the implementation date. For the study in Manuscript II, the use of the most recent available data was deemed important to ensure relevance to the current rosé veal production. This resulted in a cross-sectional study based on data from a full year (2020), which should limit the potential confounding effect of season. The DCDB data acquired for Manuscript III spanned two years from 2022 to 2023 and used data from new VetStat. Several factors contributed to only 2023 being used for the study, amongst other the potential for including more farms, as some farms started recording after January 1st, 2022. While cohort studies could have provided perspectives on changes over time, the expectation is that the effect on the overall conclusions and recommendations for AMU and AMU quantifications presented is limited.

7.4.2. Sample size

The sample size in the studies in Manuscript I and III is relatively small. The sampling was subject to time and resource constraints, which limited the number sampled farms. A Dutch cross-sectional digital survey study conducted in starter rosé veal farms included the same number of farms (36 farms) as the study in Manuscript I (Mallioris et al., 2024). Their study sample included 14.5% of the eligible study farms in the population and was found to have significant statistical power for their model. In Manuscript I, 118 rosé veal farms were identified as professional without ownership changes, which translates to the study farms in Manuscript I comprising 31% of the eligible population and 23% of the eligible population in Manuscript III. If the criterium of changes in production size less than 25% is applied, this increases to 34% for Manuscript I and 25% for Manuscript III. The study population resembled the target population with regards to size and geographical distribution in study in Manuscript I and the study farms were larger in study in Manuscript III, the latter probably reflecting a more widespread use of digital treatment recording amongst larger farms. Based on these considerations about the study and target population, the sample size is considered sufficient for drawing generalised conclusions about the Danish veal production.

7.4.3. Study population

The study population could be considered a niche production in a Danish context. The 550 herds mentioned in “3.3. Veal production in Denmark” is a significantly larger number of farms than the estimated 118 farms in Manuscript I and 119 farms in Manuscript II. This can be due to the combination of herds into farms conducted in both manuscripts, but as seen in “Manuscript I, Figure 1” it is also due to many herds being relatively small housing fewer than 200 animals. This thesis focuses on rosé veal production, but Danish monitoring encompasses all cattle productions. As seen in Figure 3.1. veal herds represent a small proportion of the total number of herds with the predominant production types being beef, hobby, and dairy with the dairy associated heifer hotels. The AMU management and practices observed in rosé veal farms vary from these, which may cause some findings to be relevant only in a narrow context, especially the findings presented in Manuscript I. As already described in “3.5. AMU in Danish cattle”, the AMU in Danish calves and adult cattle vary markedly, and it was discussed previously, how AMU vary between in Danish dairy and veal calves. This again underscores the challenge with the lack of production type used in AMU monitoring. The specific numbers and proportions reported across the studies are mainly relevant to the Danish rosé veal production. The identified issues discussed, which support the recommendations presented, should remain relevant in a broader context of cattle and even livestock production in general, as most of the findings agree with other studies on AMU monitoring and quantification.

7.4.4. Quantitative or qualitative

Investigating the practical and human angles mentioned in “7.2. Heterogeneous farms and farmers’ motivations for changing AMU” requires different approaches. Practical on-farm conditions are often addressed through a quantitative approach. But understanding knowledge and motivations behind choices and actions requires qualitative research. The studies in this thesis are primarily of a quantitative character focused on the practical factors influencing farm-level AMU. This is a limiting factor for achieving the comprehensive understanding of on-farm AMU, as the human aspect is very important. The argument for choosing a quantitative approach was that the focus of the thesis is on the implications for monitoring and quantification. A quantitative approach yielded results on farm-level AMU, which were easier to relate directly to monitoring efforts and quantification methods. In the manuscripts, we point to systematic challenges with AMU quantification and monitoring, which may also be relevant in a broader context in livestock production. It should be considered whether attitudes and motivations driving AMU could have a potentially confounding effect on the presented results. One example could be that the farmers' attitude will be an important deciding factor in choosing the use of metaphylactic treatments or the use of a slightly higher dose than needed for a given treatment; both of which would result in a higher AMU. The farmer may also choose a product with prolonged effect for practical reasons as it limits the number of times a calf needs to be treated; it saves time and resources for the farmer but may impact the antibiotic classes used on-farm.

Due to the complexity, we do not and may never understand the full extent of factors influencing on-farm AMU and their confounding effects and interactions on and with each other. The recommendations presented in this thesis can improve the accuracy of AMU monitoring and quantification, providing a stronger foundation for national and industry initiatives aimed at promoting prudent use. However, meaningful change must begin where antibiotics are actually used — on the farms — with a recognition that this is a complex issue influenced by multiple, interrelated factors and opportunities.

8. Conclusion

The aim of this thesis is to promote prudent AMU by improving quantification and understanding of patterns in antimicrobial use in Danish cattle. To address this aim, the approach “from cattle to computer – and back again” was adopted. The goal with this approach was to ensure a comprehensive understanding of AMU in Danish rosé veal productions. Rosé veal was chosen as a study population due to the high proportion of the total Danish antibiotic prescriptions for calves being used there, despite the production representing few farms compared to the Danish dairy industry. The studies carried out are a combination of field study (Manuscript I) and register studies (Manuscript II and Manuscript III) utilizing data from a questionnaire and the databases VetStat, DCDB, and CHR. The studies expand on existing knowledge about the relationship between the AMU on-farm and the corresponding quantified AMU in VetStat, while highlighting several challenges, which can affect our interpretation of the observed patterns in monitored AMU. A list of specific recommendations is provided, aimed at improving overall accuracy of monitoring in VetStat and improving relevance of VetStat benchmarking to the farmer.
In the following four important findings and their implications are included: 1) There was a notable discrepancy between on-farm AMU and quantified AMU in VetStat. This stemmed from both differences in overall amounts used and sold, and from the quantification method and the factors affecting it. These issues pose significant barriers for accurate AMU quantification and monitoring at both national and farm-level. 2) Interpreting AMU data at the herd-level presents challenges, as many farmers operate at the farm-level, where multiple herds may be part of a single production system. Failure to account for farm-level structures likely reduces the relevance and effectiveness of AMU benchmarking. 3) Quantification methods in VetStat currently have challenges with accuracy but some of these can be mitigated through targeted initiatives. These initiatives include refining stratification methods by adjusting to more cattle-relevant strata, and refining quantification methods by adjusting standard animal weights and enhancing transparency in the correction for long-acting antibiotic effects. 4) The study population showed a marked heterogeneity across all studies, underscoring the complexity of farm-level AMU. This highlights the need for local evidence-based strategies grounded in a holistic approach i.e. understanding farm-level practices, perceptions, motivations, and challenges, and then using this knowledge to promote prudent AMU.
The limitations in VetStat quantification and monitoring accuracy identified in this thesis may affect future risk assessments and undermine the validity of their conclusions—both locally and nationally. Addressing these limitations, and raising

awareness of them, is essential for improving the accuracy of AMU monitoring and supporting efforts to ensure prudent AMU.

Ultimately, sustained communication among stakeholders and coordinated actions across multiple levels remain critical to advancing a shared commitment to prudent AMU and safeguarding animal and public health.

9. Perspectives and future studies

I could probably include 1001 ideas for future studies and perspectives on AMU and AMU monitoring in Danish cattle, but I have limited myself to three topics. The first is a concrete suggestion for a study on treatment failure, the second is a suggestion for further studies on vaccination as an alternative to AMU, and the third is a few perspectives on our way of producing veal with reflections on potentials during a green transition.

9.1. Treatment failure

Investigating the prevalence and frequency of TF could aid in understanding the extent. This could provide valuable information to stakeholders and help guide towards relevant application of diagnostics, including sensitivity testing. TF is often not systematically recorded, which makes identification of it difficult. In VetStat data, identification of TF is not possible due to the data being aggregated at herd-level. In DCDB treatment data, TF could be identified by examining time-series of treatments on individual animals. A challenge with this approach is differentiating between TF and new disease occurrence; treatment after 7 days from previous treatment days was suggested by Sandelin et al. (2021) and Apley (2015) described a 10 day interval. The presence of chronically ill calves should be considered in such an analysis, potentially while including on-farm clinical data on calves. Other relevant considerations include testing the on-farm antibiotics' clinical efficacy and potential toxicity. Such studies could provide valuable insights, which could be used in developing guidelines and educating farmers on general management of antibiotics.

9.2. Antibiotics are not the only medicine

This thesis focuses on antibiotics, but antibiotics are not the only types of medicine used. Vaccines and analgesics are extensively used and are proposed as tools to reduce or remove AMU. With data collection on all prescription medicines in VetStat, we can explore these alternatives. The aim with vaccination is generally to avoid or decrease infectious disease occurrence. In Figure 9.1. the development in administered doses of vaccines against respiratory diseases is shown. A marked increase in number of doses can be observed indicating a growing interest in and use of vaccination as part of the health management on-farm. During the field study interviewees were asked about their vaccination protocols. The 26 different vaccination protocols identified are presented in Figure 9.2. The variation in vaccination protocols is interesting, as this could indicate that the protocols are tailored to the individual farm. The efficacy of these protocols in a Danish setting have not been clearly established. Further studies should aim at determining the effect of the different protocols on health outcomes such as the prevalence of pneumonia and production parameters of interest to the farmer. Compared to antibiotics vaccines are relatively costly per dose, which should increase the farmers' interest in achieving optimal efficacy of their vaccination protocols.

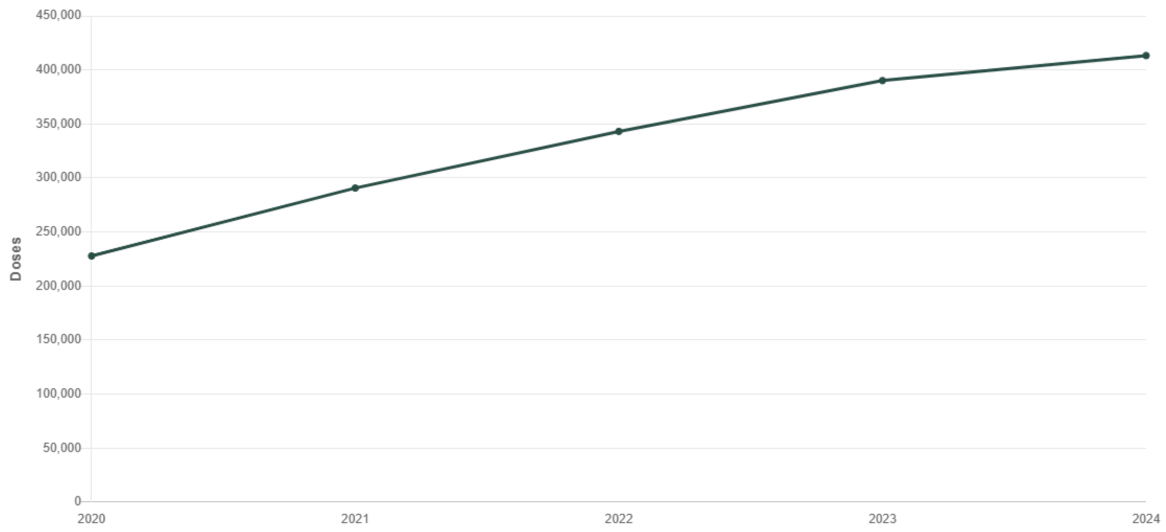

Figure 9.1. Doses of vaccines against infectious agents associated with respiratory disorders sold for use in cattle from 2020 to 2024. Number of vaccine doses sold increased by 81% during this period. This plot was extracted from https://vetstat.fvst.dk on July 15th, 2025. Only vaccines against one or more of these infectious agents are included in the plot: Bovine Respiratory Syncytial Virus, Bovine Parainfluenza 3, Pasteurella Multocida, Mannheimia Haemolytica, Histophilus Somni, Infectious Bovine Rhinotracheitis.

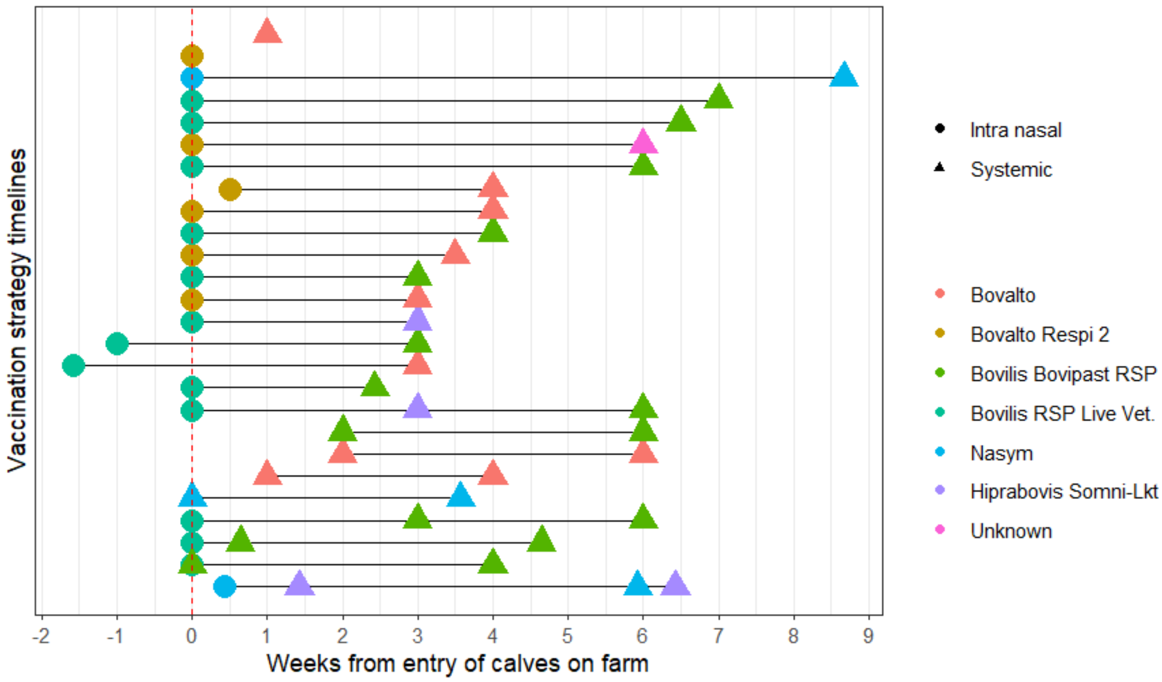

Figure 9.2. Vaccination strategies for 26 Danish rosé veal farms. The x-axis show the number of weeks from calf entry to the farm. Each horisontal line (point or triangle for the observations from the top) represents one farm strategy. The line shows the interval between vaccination doses and the points (intra-nasal administration) and triangles (systemic administration) represent a vaccination dose.

9.3. Intensive or extensive farming in the future

With the agreement on a green transition of the agricultural sector, Denmark has taken a giant step which will indisputably affect Danish livestock production. In this process, the existing systems can be questioned and challenged, and alternative productions and solutions may be considered. Traditionally, Denmark has practiced intensive farming with high productivity. This type of farming is often accompanied by production related challenges, including higher disease prevalence and AMU, driven by factors such as stocking density and a production system that is partially incompatible with the behavioral and physiological needs of the animals. With the increase in land taken out of arable production in the green transition, grazing may become a relevant option for rearing youngstock intended for slaughter in a Danish context. In this extensive production, the stocking density will be reduced, and the feed will be suited to the natural use of the ruminant digestive system. This may result in desirable outcomes such as lower disease prevalence, AMU, and potentially improved overall animal welfare. Further investigations are needed on the implications for the animals. Concerns such as the economic viability and practical feasibility of extensive production for the farmer should also be addressed, because without this few farmers will be motivated to change their production. Without proper motivation, change is rarely chosen.

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11. Manuscripts

Manuscript I

Kristensen, J., Skarbye, A. P., Kruse, A. B., Nielsen, L. R. (n.d.). On-farm Antibiotic Management, Use and Recording Practices: Questionnaire-based interviews in 36 Danish Rosé Veal Farms (Unpublished, planned submission for peer-review in *Acta Veterinaria Scandinavica*)

Manuscript II

Kristensen, J., Kruse, A. B., Kjeldsen, A. M. H., & Nielsen, L. R. (2025). Key farm characteristics associated with the level of antimicrobial use in rosé veal production – A Danish database study. *Preventive Veterinary Medicine*, *235*. https://doi.org/10.1016/j.prevetmed.2024.106406

Manuscript III

Kristensen, J, Kruse, A. B., Skarbye, A. P., Nielsen, L. R. (n.d.). Evaluation of the accuracy of a standard metric (ADD200) to monitor on-farm use of antibiotics for Danish rosé veal calves less than one year old (Unpublished, planned submission for peer-review in *Preventive Veterinary Medicine*)

12.1. Manuscript I

On-farm Antibiotic Management, Use and Recording Practices: Questionnaire-based interviews in 36 Danish Rosé Veal Farms

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Note: Supplementary material for this manuscript is included in Appendix A

Abstract

Background: Antimicrobial resistance (AMR) poses a global threat to human and animal health and welfare. Antimicrobial use (AMU) is an important driver of AMR, necessitating discussion and implementation of strategies for ensuring prudent AMU worldwide. Danish veal production has previously been identified as an area with significant potential for reduction in AMU. Identifying the best approach to achieve reduced AMU and identifying injudicious AMU requires knowledge of the on-farm practical approach to antibiotic management, use and recording practices, which we currently lack. Therefore, we conducted an on-site questionnaire-based interview study involving 36 Danish rosé veal farms visited during the spring of 2023.

Results: Three main topics central to on-farm AMU practices were covered: General management, diagnostics and treatment, and documentation and recording practices. These were presented as frequency tables and aggregated information from qualitative text answers. This provided a structured initial overview of antibiotic management, use and recording practices from product arrival on farm to treatment application and waste management. Based on this we identified three themes, which we find important for ensuring prudent AMU: 1) Calves requiring or receiving treatment: all farms used single-animal treatment with injections, 83% of these used pen-level treatments, 47% of the study farms used routine metaphylactic antibiotic treatments; 2) Efficacy of the antibiotics: We identified a lack of on-farm compliance with recommended (by pharmaceutical companies or veterinarians) indication, dosage, duration of treatment, route of administration and recommended storage conditions; and 3) Choosing the correct antibiotics: use of routine diagnostics were not a general practice in the study population. All farms had treatment protocols for pneumonia, but only 50% had done diagnostics on lungs, nose swabs and/or lung fluid, and 19% of the farms reported never having laboratory diagnostics done.

Conclusions: We improved the general understanding of on-farm antibiotic management, use and recording practices in Danish rosé veal farms and identified practices linked to potentially injudicious AMU. Based on our findings, we recommend exploring alternatives to metaphylactic treatment, implementing antimicrobial stewardship training programmes and providing guidelines, conducting awareness campaigns and considering incentives for improving AMU, and exploring options for diagnostics tailored to the individual farm.

Keywords

veal, farm, field study, questionnaire, management, practices, antibiotic, treatment, recording, Denmark

List of abbreviations

AMU: Antimicrobial use

AMR: Antimicrobial resistance

CHR: The Danish Central Husbandry Register

DCDB: The Danish Cattle Database

DVFA: Danish Veterinary and Food Administration

VASC: Veterinary Advisory Service Contracts

Background

Prudent antimicrobial use (AMU) is an important goal worldwide due to the link with antimicrobial resistance (AMR), which is a long-recognised threat to global health (Redman-White et al., 2023; World Health Organization, 2015). Several initiatives and combat strategies aimed at ensuring prudent AMU have been discussed and implemented locally and globally across multiple sectors since then with the livestock sector being an important contributor (Jacobsen et al., 2023; World Health Organization, 2015).

In Denmark, the cattle sector banned the use of 3rd and 4th generation cephalosporins in 2019 and later targeted a 10% annual reduction in AMU for cattle less than one year of age from 2021 to 2023 (DANMAP, 2022; DANMAP, 2023). Unfortunately, the last goal has not been met yet and high AMU for calves remain a concern.

Danish veal production together with Portuguese and Swiss hold significant potential for AMU reduction according to expert opinion in a publication from 2018, but the antibiotic treatments carried out in the countries differ with regards to indications and route of administration (Carmo et al., 2018a; Carmo et al., 2018b). So, while a consensus may be reached regarding potential for AMU reduction, the best method likely differs between the countries. Large variations in definitions of veal and the associated production practices including AMU are seen world-wide (Bokma et al., 2019; Cheng et al., 2023; Fertner et al., 2016; Jarrige et al., 2017; Lava et al, 2016; Mallioris et al., 2024; Meat and Livestock Australia, 2020; Sandelin et al., 2021). Carmo et al. (2018a) hypothesized that views on potential for reduction were influenced by local disease epidemiology, animal husbandry, and socio-economic factors. This highlights the importance of defining and describing the within country or even local production conditions and practices and the practices and protocols for AMU.

In the European Union regulations dictate the allowed use of antibiotics with the aim of ensuring prudent AMU and combating AMR (Simjee & Ippolito, 2022). Additional legislation within each country can further specify allowed practised and requirements. Under Danish conditions the farm can only purchase antibiotics following a prescription from a veterinarian, must comply with treatment protocols outlined by a licensed veterinarian affiliated with the farm, and must carry out detailed record-keeping of diseased animals, use of prescription medicine and dead animals (DVFA, 2021).

While the rules and regulations surrounding AMU in Danish farms is well described, we lack knowledge of the on-farm practical approach to antibiotic management, use and recording practices.

Concerns have been raised about the storage conditions of antibiotics; exposure to extreme temperatures, humidity or light may affect drug stability (Fagunwa et al., 2024; Ondrak et al., 2015). Generally, drug stability testing prior to approval is well regulated which should ensure stability if correctly stored; differences in definition of general storage exist around the world (Naicker et al 2024). Farmer's adherence to labelled storage conditions in Danish cattle farms is currently poorly described.

Antimicrobial stewardship training of farm-personnel carrying out treatments in veal farms has previously been found effective in changing behaviour and reducing AMU (Pempek et al., 2022). Challenging behaviours include farm-personnel deviating from treatment protocols, which has been demonstrated previously (Aghamohammadi et al., 2018; Campler et al., 2021, Pardon et al., 2012). Skjølstrup et al. (2021) documented deviations from veterinary prescriptions in Danish dairy. This finding is supported by field experience from veterinarians in Danish cattle practise. The extent and type of deviations in veal production is currently unknown.

Diagnostics and treatment strategies have a major influence on AMU. Lack of proper and relevant diagnostics may lead to misdiagnosis, potentially affecting the efficacy of the treatment, for instance due to incorrect choice of antibiotic class used. Regarding treatment strategies, pen-level treatments have been documented in veal production (Cheng et al., 2023; Jarrige et al., 2017; Lava et al., 2016). A major concern with pen-level antimicrobial treatment is the treatment of healthy animals, leading to an overuse of antibiotics. Understanding and describing treatment strategies and the associated diagnostics could provide valuable insights in AMU.

In this on-site questionnaire-based interview study, we investigate what happens with the antibiotic drugs from arrival on the veal farm until the use and it's recording followed by the discarding of empty containers. In addition, we address the diagnostics performed and the strategies for using the treatment protocols. The objective is to improve the understanding of on-farm antibiotic management, use and recording practices in Danish rosé veal farms, and to discuss how this may affect AMU and the implications for prudent use.

Methods

Study design

The study was carried out as an observational cross-sectional on-site field study in Danish rosé veal farms. One interviewer (first author) collected and recorded all data in a questionnaire-based on-farm interview using a semi-quantitative questionnaire, covering three topics in the on-farm AMU: general antibiotic management, diagnostics and treatment, and documentation and recording.

Study population

The population of interest in this study was professional Danish rosé veal productions. We used data from the Danish Central Husbandry Register (CHR) to identify the target population. CHR owned by the Danish Veterinary and Food Administration (DVFA) contain records of all farms in Denmark including geographical location, ownership, species and number of animals present. For ruminant all animals are individually identifiable by unique ID (CKR-nr.) and their movements between locations are tracked and recorded continuously in accordance with Danish legislation (DVFA, 2024).

A set of inclusion and exclusion criteria were applied to CHR data from 2022: 1) Registered with production type “veal production”, 2) No changes in production type, owner and affiliated veterinary practice, 3) Changes in the number of animals not exceeding 25% from January to December, 4) Housed 200 or more bulls, bull calves or heifers on average.

The size criterium, which we used to differentiate between hobby and professional farms, is the legal threshold for mandatory Veterinary Advisory Service Contracts (VASC) (DVFA, 2021). Farms with certain types of VASC can treat animals if they follow treatment protocols defined by their affiliated veterinarian for specific disorders with a predefined set of clinical symptoms (DVFA, 2021). No limitations were put on geographical location within the Danish borders. We randomly selected 60 farms for contact from the identified target population; unique random numbers were assigned using the statistical software R (4.4.2) and the 60 lowest numbers were extracted (R Core Team, 2024).

Recruiting

Recruiting was carried out by phone using contact information obtained from the Danish Central Business Register (CVR), a Danish webpage listing addresses (https://www.118.dk/), and Google searches. If no contact was established after several phone contact attempts, an email and a follow-up email were sent to the address provided in CVR. The recruiting process and the reasons for declining to participate were recorded using Microsoft 365 Excel.

Data collection

On arrival at the farm, the interviewee was informed of the purpose of the study and the plan for the visit. The interview was conducted during a walk-through in the farm, which followed the path from entry of calves to exit for slaughter. The interview process was aided by printed Google Maps satellite images of farm sites and, if available, treatment protocols extracted from the Danish Cattle Database (DCDB).

We chose an on-farm dialogue-based approach to ensure the best conditions for interactive data collection in the physical setting of production. The aim was to ensure a good rapport with the interviewee, avoid miscommunication, and aid the interviewer's understanding of the farm setting.

Questionnaire

Questionnaire development

A standardized questionnaire was developed using the author's knowledge about the current antibiotic management practices in Danish cattle farms and adjusted after input from a veterinarian working with Danish veal production. The questionnaire primarily contained questions with categorical answers with optional addition of free text for context.

The initial questionnaire was pre-tested in three Danish rosé veal farms in January 2023 on three separate dates. After each pre-test, the questionnaire was adapted based on the interviewer's experience and relevant feedback from the interviewees.

Questionnaire content

The questions were grouped by subject for overview (Dohoo et al., 2014). They were listed in the order they were expected to be relevant during the physical walk-through. Basic information about the farm was included in the beginning of the questionnaire; title of interviewee, owner, number of herds, buildings, sections and employees, used advisors, advising veterinarian, farm structure and internal logistics, purchase of calves, milk-feeding, and used abattoirs.

Three sections focusing on medicine, including both antibiotics and vaccines, were included in the questionnaire.

The first section was designed to provide an overview of how the antibiotic moved through the farm from entry and initial storage to handling and use during treatments to disposal of antibiotic contaminated waste (See Supplementary 1, M1S1F1). In this section, five areas were covered: storage and disposal (29 questions: 16 categorical, 3 numeric, 2 free text, 8 interviewer categorical observations), antibiotic in the stable (16 categorical questions: 8 categorical, 8 interviewer categorical observations), personnel handling antibiotic (12 questions: 5 categorical, 6 numeric, 1 free text), handling and documenting treatment (28 questions: 17 categorical, 11 numeric), and approach to dosage (8 questions: 4 categorical, 2 numeric, 2 free text).

The second section contained records of the treatment protocols on the farm including the diagnosis, drug prescribed, route of administration, dose and unit, number of doses in a treatment course, interval between doses, and length of the treatment course (See Supplementary 1, M1S1F2).

The third section focused on how the farm used the treatment protocols in practice; including diagnosis listed in the treatment protocol, type of diagnostics performed, observed clinical signs, perceived frequency of use of the diagnosis, treatment strategy (single-animal or pen-level), compliance with the treatment protocol from section two, and actions in cases of treatment failure (See Supplementary 1, M1S1F3).

Data management

Informed consent and GDPR considerations

The data collected did not classify as sensitive personal data according to European GDPR legislation but was treated as GDPR sensitive personal data as a precautionary measure (Council Regulation (EC) 679/2016).

Prior to the visits interviewees were informed of the interviewer's legal obligation as a veterinarian to report cases of gross neglect to the local police, which did not become relevant during the study. After the interview the interviewees signed an informed consent and were informed orally and in writing of the process for retraction of consent, the pseudonymization during data management and full anonymization after the project finished in addition to the planned use, management and storing of data.

Data availability

Access to historical CHR data was obtained as part of the project "VetStat-Cattle: Improving quantification and understanding of patterns in antimicrobial use in Danish cattle herds" (Kristensen, n.d.). Current CHR data is available in Danish through an online web platform (www.chr.fvst.dk). DMS is the most frequently used digital management tool in Danish cattle farms and exchanges data with DCDB (Frandsen, 2013; Henningsen et al., 2024). Some veterinarians have access to DMS and can set up treatment protocols after which the farmer can record treatments directly in the tool. During collaboration with SEGES P/S access to DMS was provided to the interviewer allowing for extraction of treatment protocols during the field study. All contact and ownership information used during recruiting were publicly available online.

Digitalisation and management

Questionnaire recordings on paper were digitalized by the interviewer during September and October 2023 using Microsoft 365 Excel. Each questionnaire section was entered, using recorded answers directly, in a separate sheet and interrelated by assigned pseudonymized IDs.

All data management and analyses were carried out using R (4.4.2) and RStudio (2024.12.0.467) (R Core Team, 2024; Posit team, 2024). The primary R packages used were “tidyverse” (Wickham et al., 2019) and “flextable” (Gohel & Skintzos, 2024). Any corrections in data records after digitalization were done in R to avoid changes in the original data.

Data analysis

The data was summarised as described in the following sections:

1) General management related to medicine storage, handling and waste management.
2) Performed diagnostics and use of medicine related to treatment of animals including the farm specific treatment strategies.
3) Documentation and recording practices including where, how and when medicine use was documented and how recordings of medicine use were performed and stored.

For each categorical question, the provided answers were assessed, and relevant regrouping was carried out. For each numeric or frequency question appropriate categorical levels were chosen based on the observed answers. If relevant, percentages were calculated from numerical answers for better comparability across farms.

General management

For general management, which was addressed in the first section of the questionnaire. A frequency analysis was performed for the assigned levels of the variables.

Diagnostics and treatment

Laboratory diagnostics

From the first section of the questionnaire information on the overall frequency of laboratory diagnostics and the types of diagnostics mentioned on each farm were extracted and presented as a frequency analysis.

On-farm diagnostics

From the second and third questionnaire section the treatment protocols were extracted. The treatment protocols were grouped into eight overall groups depending on the location: ears, eyes, gastrointestinal, hoofs, limbs, lungs, skin, other. The interviewees were asked to describe the clinical symptoms observed for each diagnosis, which would lead to treatment of calves. These clinical symptoms were aggregated and grouped by location. The most frequently mentioned clinical sign was identified. The treatment protocols were assessed for clinical signs not occurring at the assigned locations according to existing literature.

Treatment strategies

From section one different approaches to dosage were summarised as frequencies. From section two and three information on the antimicrobial use at animal- or pen-level, including use of metaphylactic and systematic treatments was extracted and summarised as simple frequencies. In addition, reported challenges with compliance with treatment protocols were extracted.

Documentation and recording

From section one, the answers related to documenting and recording treatments were extracted and presented as a frequency analysis.

Results

Study population

The process for target population identification and study farm recruitment is outlined in Figure 1. Recruitment of participants and data collection were carried out between March 1st and July 1st, 2023. We were able to contact 52 of the 60 farms within the study period, and 38 of those agreed to participate. Two farms had to cancel the visits due to schedule changes at the farm. For the 36 farms in the final sample, the visits and interviews were completed. Questions with missing answers in the questionnaire are documented in "Supplementary 1, M1S1T1". Sixteen of the 36 farms had multiple herds with different geographic locations: ranging from 2 to 5 herds with a median of 2 and a mean of 2.6 herds per farm. For the 36 study farms, 74 herds were identified based on ownership data in CHR. During the interviews, 62 of the 74 herds were confirmed as part of the veal production. Some farms had a small hobby herd with beef cows on a site, but these were excluded. All veal herds were included regardless of the number of animals. The first author visited 48 (77.4%) herds during the field study. The remaining herds were discussed, with the help of pre-printed satellite images, during the interviews. Number of buildings per farm ranged from 2-84 (median = 8.5, mean = 14.2) when huts were counted as separate buildings, and number of sections ranged from 3-285 (median = 12.5, mean = 29); when section was defined as stable areas where no nose-to-nose contact was possible.

Visit time per farm ranged from 90 minutes to six hours. The interviewees were primarily the farm owner (23 farms, 64%), while at five farms (14%) the manager was interviewed. At the remaining eight farms more than one person participated in part of the interview, because the main interviewee suggested additional personnel to supplement his/her answers.

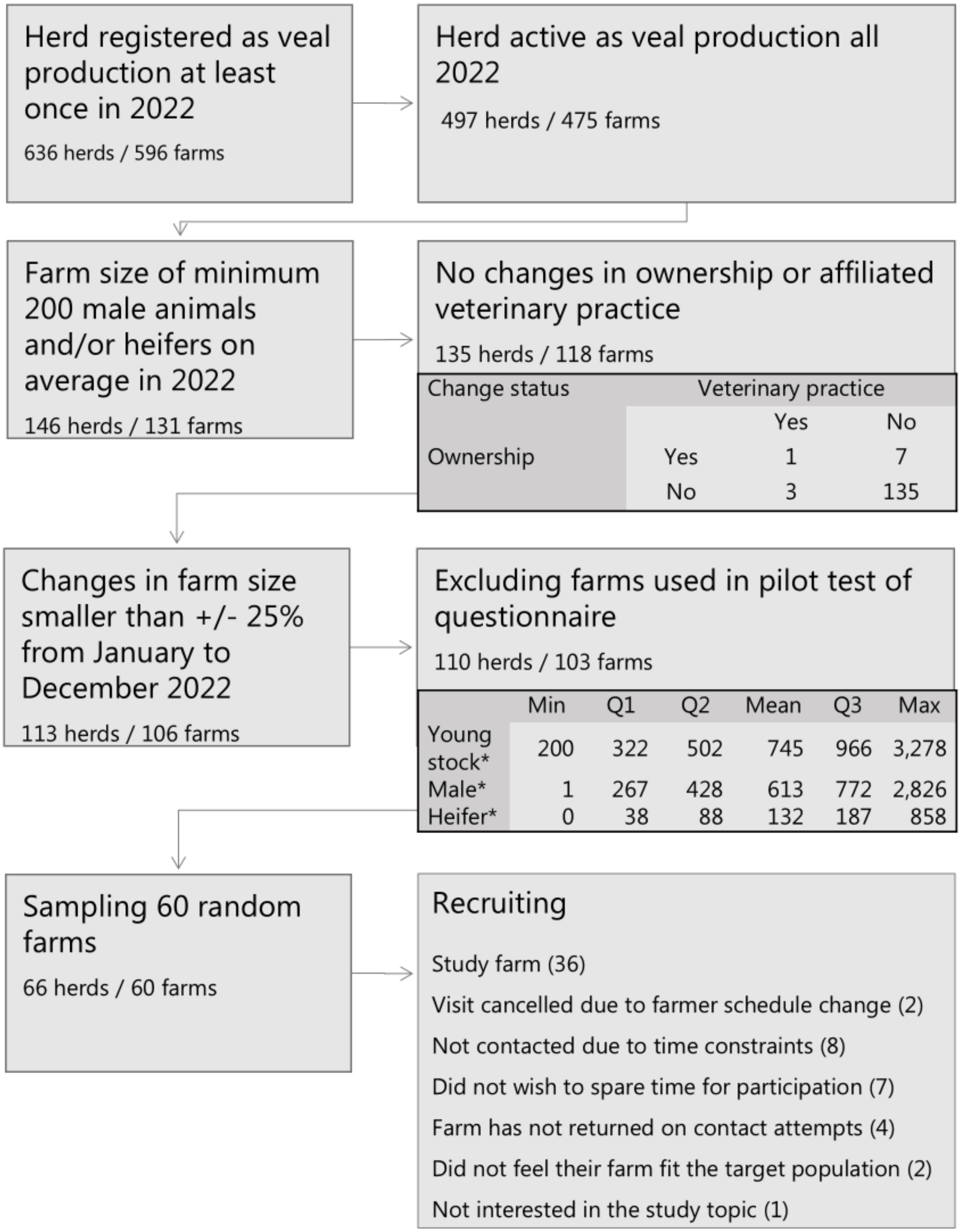

Figure 1: Overview of study population recruitment and inclusion criteria. One farm can consist of multiple herds explaining the difference between the two numbers.

** Animal-years: number of days an animal is present in the herd during a year summarised for all animals in the herd and divided by 365 days.*

The study farms resembled the target population with respect to number of animals per location. If all study farm locations were summarised: Min=19, Q1=254, median=449, mean=706, Q3=875, max=2750. If only study farm locations with 200 young stock animals or more were summarised: Min=202, Q1=358, median=535, mean=799, Q3=1073, max=2750. The geographical distribution of the study farms on regions in Denmark also corresponded well to the distribution of the target population.

All farms purchased calves either directly from the primary producer or via an intermediary, typically a transporter or a livestock dealer, and housed them until slaughter. Most farms (89%) had a fixed list of suppliers. Of the 32 farms with fixed suppliers 15 farms (47%) reported supplementing with calves from a livestock dealer or another source. Only four farms relied solely on a livestock dealer. Farms either collected calves themselves (36%), had them delivered (25%), or a combination of the two (39%). Batch arrival frequencies ranged from one to 13 weeks with 50% of farm reporting fixed biweekly arrivals. Only one farm reported varying intervals, and five farms reported different intervals for different suppliers. Vaccination against respiratory disease was conducted in 26 of the farms (72%), typically upon arrival.

The minimum weight and age of the calves at arrival required by the veal farm ranged from 45-70 kg and 7-21 days of age, with some interviewees reporting no requirements beyond legal in a Danish context. Calves were reported weaned on the veal farms (92% of farms responded to this question) at 64 days of age on average with a median of 65 days. Thirteen farms (36%) used two types of milk powder on farm while the remaining farms used one type of milk powder. Nineteen farms (53%) used solely milk powder, six farms (17%) used whey powder, eight farms (22%) used a combination of milk and whey powder, and for the remaining three farms (8%) the type of powder was not identified. Different concentrations for mixing were reported between farms and nine farms (25%) reported varying concentration depending on season. Feeding methods reported were trough (17%), milk bar (14%), automatic calf feeder (8%), teat bucket (3%), bucket and trough (17%), and the remaining farms used various combinations of the mentioned methods. Half of the farms had one milk feeding strategy, while 15 farms (42%) had 2 strategies and 3 farms (8%) had 3 strategies dependent on primarily weight of the calves but also age, health status and appetite. The maximum amount of milk per calf per day varied from 3-8l. Length of weaning varied from 4-28 days with a differing number of reduction steps (1-14) with each step corresponding to between 0.4l and 4l milk. No identical feeding strategies were identified. After weaning the calves were fed on a diet of grain and roughage until slaughter at eight to ten months of age.

Production was structured around a starter, middle and finisher stable in 26 farms (72%), while the remaining eight farms operated with a starter and finisher stable. The farms had vastly different logistics. Total number of within-farm movements of an individual calf between sections ranged from 1-10. Reported number of calves per starter pen ranged from 1-60. And weeks from arrival to first movement ranged from two weeks to slaughter age.

All farms reported selling to either of the two major abattoirs in Denmark, either Danish Crown (72%) or Himmerlandskød A/S (28%). All farms had an associated advising veterinarian, and 25 different veterinarians were mentioned. Most farms (92%) also reported using some kind of other productions specific advisory service and 28 farms (78%) participated in some kind of peer-to-peer experience exchange group. Two thirds of the farms (67%) delivered manure to a local biogas plant.

General management

Table 1 shows the frequencies of answers to selected questions regarding general management of medicine; the full frequency analysis including original answers for the questionnaire data is available in "Supplementary 1, M1S1T1".

The primary use of antibiotics on the study farms was for treatment protocols, where treatment was initiated and completed by the farm-personnel. Medicine was received at regular intervals with an interval of one month or less between deliveries at approximately half of the farms (19 farms, 53%).

Table 1: General management questions and answers summarised with number of observations (n) and percentages (%).

Question	Answers	n	%
	Medicine entering the farm		
Person(s) responsible for receiving medicine on-farm	Fixed	19	52.8
	Primarily fixed	2	5.6
	Varying	15	41.7
Medicine use on-farm	Treatment protocols	23	63.9
	Treatment protocols and veterinary treatments	13	36.1
Interval between medicine receival	Varies	1	2.8
	2 weeks	2	5.6
	4 weeks/1 month	16	44.4
	6 weeks-2 months	12	33.3
	10-13 weeks	5	13.9
	Medicine storage		
Storage of unopened antibiotics, location	Refrigerator	17	47.2
	Refrigerator and other	4	11.1
	Other	15	41.7

Question	Answers	n	%
Storage of opened antibiotics	Refrigerator	12	33.3
	Refrigerator and other	4	11.1
	Other	20	55.6
Thermometer in medicine refrigerator	Yes	16	44.4
	No	17	47.2
	NA's	3	8.3
Alarm on medicine refrigerator	Yes	4	11.1
	No	29	80.6
	NA's	3	8.3
Procedure for temperature control of medicine refrigerator	Control procedure	2	5.6
	Cooling determined upon access	20	55.6
	No	12	33.3
	NA's	2	5.6
Medicine disposal			
Discarding of medicine occurring on-farm	Yes	8	22.2
	No	26	72.2
	NA's	2	5.6
Waste management, empty medicine containers	Sorted as 'Hazardous waste'	16	44.4
	Other	5	13.9
	Discarded with regular waste	15	41.7
Medicine in the stable			
Number of animal adjacent medicine storage locations	0	3	8.3
	1	23	63.9
	2	4	11.1
	3-5	6	16.7
Medicine in 'starter' stable, presence	During treatment	19	52.8
	During feeding and treatment	7	19.4
	Always	10	27.8
Medicine in 'starter' stable, storage	Stored in stable	9	25.0
	On person	12	33.3
	In container	13	36.1
	On person and in container	2	5.6
Medicine in 'finisher' stable, presence	During treatment	28	77.8
	During feeding and treatment	3	8.3
	Always	4	11.1
	NA's	1	2.8
Medicine in 'finisher' stable, storage	Stored in stable	3	8.3
	On person	17	47.2
	In container	12	33.3
	On person and in container	3	8.3

Question	Answers	n	%
	NA's	1	2.8
	Medicine handling		
Number of employees treating with medicine	1-2	19	52.8
	3-4	13	36.1
	5-9	4	11.1
Employees with medicine access who treats (%)	0%-25%	1	2.8
	26%-50%	7	19.4
	51%-75%	6	16.7
	76%-100%	22	61.1
Treaters with medicine handling course (%)	0%-25%	12	33.3
	26%-50%	8	22.2
	51%-75%	6	16.7
	76%-100%	10	27.8
Treaters exempt from medicine handling course (%)	0%-25%	15	41.7
	26%-50%	6	16.7
	51%-75%	5	13.9
	76%-100%	9	25.0
	NA's	1	2.8
Treatment responsibility strategy	Fixed	26	72.2
	Work-rotation	6	16.7
	Varying	4	11.1
Days until new treaters are independent	1-2 days	7	19.4
	7-14 days	8	22.2
	>14-180 days	4	11.1
	Only one with treatment responsibility	10	27.8
	Irrelevant	6	16.7
	NA's	1	2.8
Treaters minimum level of influence on production	Economic	14	38.9
	Procedure	21	58.3
	None	1	2.8

Storage

Of the 36 farms, 33 farms (92%) had treatment protocols with drugs containing procaine benzylpenicillin (ATCvet: QJ01CE09). For unopened antibiotics 21 farms (58%) used a refrigerator, but for opened i.e. partially used medication packages this number had decreased to 16 farms (44%). During the farm visits, food or drink for human consumption in refrigerators for storing medicine (not limited to antibiotics) was observed, but the frequency of this observation was not recorded.

Handling

On 9 farms (25%) all personnel treating calves had taken a medicine handling course and on 10 farms no personnel had taken a medicine handling course. Generally, in cases where personnel did not have the course, exemption due to experience was cited as the reason.

Interviewees were asked about their requirements when hiring new employees with treatment responsibility and this question was perceived differently; some focused on criteria for hiring and some on criteria for allowing personnel to treat. Two repeatedly mentioned that criteria for hiring were that the employees had interest in performing treatments and the absence of language or communication barriers. A challenge reported for the hiring process was difficulties in finding qualified personnel. One interviewee mentioned agricultural students with literacy challenges and another mentioned number blindness as an issue. Some interviewees said they required new employees to have experience working with cattle or pigs, or an agricultural education. In contrast to this, one interviewee said: "*The less the employees know when they start the better*", followed by an explanation of how it was then easier to get the employees to follow the desired protocols.

Training of new employees in treatment procedures was reported as peer-to-peer training on all farms where this was relevant. The length of training varied from one day to six months before a person was considered fully independent in performing treatments. Some farms had fixed procedures for introducing new employees to treatments, while others had a more fluid approach dependent on the employee and their qualifications. One interviewee explained how new employees gradually went from administering vitamins to administering pain medication, to finally administering antibiotics during training.

The role of the employees on the farms and their involvement in the daily management varied to some degree. In all cases but one, the personnel treating had some level of influence on the production. Many interviewees mentioned being open to new suggestions from employees regarding changes in management procedures. Of the 14 farms that reported economic influence on the production by the personnel with treatment responsibility, 10 farms had only one person responsible for treatments, typically the owner. One farm included all employees in biweekly meetings where production numbers were presented. On this farm the interviewee explained how the idea "*Not everyone thinks like you*" was incorporated into their planning, which meant standardising procedures, including criteria for initiating treatment. On another farm, the interviewee described how they focused on ensuring a common understanding where all employees understood why the things should be done in a certain way.

Waste management

When asked if they discarded any medicine (including vaccines and analgesics) on the farm, 26 interviewees responded “No” while eight responded “Yes”; no answer was collected from the remaining two farms. The reasons for discarding medicine and types of medicine discarded were not systematically recorded during the interview but two interviewees mentioned expiration as a reason. One interviewee reported delivering discarded medicine at the pharmacy, one reported giving it to the farm veterinarian, and one reported disposing it with the emptied medicine containers on-farm.

Four farms (11%) delivered empty medicine containers to their farm veterinarian for disposal, 16 farms (44%) sorted empty containers as “Hazardous waste”, one farm (3%) sorted containers according to their material, while the remaining 15 farms (42%) disposed of medicine with their regular waste.

Diagnostics and treatment strategies

Seven farms (19%) reported never doing laboratory diagnostics on calves or samples from calves, while 11 farms (31%) did laboratory diagnostics once per year, and three farms (8%) did diagnostics rarer. Of the eight farms doing diagnostics four times per year or more, six farms did laboratory diagnostics on blood samples.

Generally, the indication of main concern on the study farms was pneumonia. Out of the 36 study farms, 18 farms (50%) reported having done diagnostics on lungs, nose swabs and/or lung fluid. The types of diagnostics performed can be seen in Table 2.

Table 2: Laboratory diagnostic type performed and number of observations (n) and percentages (%).

Question	Answers	n	%
Frequency of laboratory diagnostics	Once per year or rarer	14	38.9
	2-7 times per year	13	36.1
	Never	7	19.4
	NA's	2	5.6
Diagnostics on blood	Yes	10	27.8
	No	26	72.2
Diagnostics on feces	Yes	7	19.4
	No	29	80.6
Diagnostics on lungs	Yes	12	33.3
	No	24	66.7
Diagnostics on lung fluid	Yes	8	22.2
	No	28	77.8
Diagnostics on nose swab	Yes	3	8.3
	No	33	91.7
Necropsies performed	Yes	9	25.0
	No	27	75.0

On-farm diagnostics – clinical signs

During assessment of the location of clinical signs and expected location of clinical signs based on the diagnoses, the following was observed. For the group “Ears” the clinical signs “Joint swelling” and “Acute onset of panting and high fever” were described. For the group “Lungs” many described unspecific symptoms such as “Depressed” or “Weak” calves or calves with a “Poor performance” without a simultaneous check for fever using a thermometer. A table of clinical signs in layman’s terms by group and diagnosis can be seen in “Supplementary 2, M1S2T1”.

Treatment strategies

All 36 farms (100%) used single animal treatments with injectable antibiotics. Six farms (17%) used no pen-level treatments, while the remaining 30 farms (83%) used pen-level treatments. In total, 17 farms (47%) specifically reported using routine metaphylactic antibiotic treatments of calves at pen-level upon arrival, and one farm (3%) reported using pain medication routinely upon arrival. Of the 261 farm treatment protocols with antibiotics identified on the 36 farms; 240 (92%) were with antibiotics administered by injection, 15 (6%) were with oral administration, five (2%) with spray administration, and one (0.4%) with pour-on administration. Treatment protocols with oral administration of antibiotics were reported on 13 farms (36%). Information on coccidiosis treatments were not systematically collected, but 25 farms (69%) reported oral treatment for coccidiosis.

Approach to dosage

The farms had three general strategies for dosage; 14 farms (39%) had an adaptive approach based on individual animal weight, six farms (17%) had a fixed approach based on general weight of calves in specific pens, and 16 farms (44%) had a mixed approach. For the farms with mixed approach, they reported having fixed doses for specific diagnoses or groups of animals or they dosed by fixed weight intervals e.g. 40 kg weight increments. One farm reported having fixed doses, which they adjusted for outliers. For the six farms using fixed doses no dosage calculations were carried out. For the remaining farms, the preferred method by 23 farms (64%) for determining dosage was mental arithmetic, while four farms (11%) reported using aid from digital tools. No response to this question was obtained in the remaining three farms (8%). The dosage increments used when calculating a dose for a given treatment were less than 0.5ml for seven farms, 1 ml for 23 farms (64%), 1.5ml-2ml for four farms (11%), and no answers were obtained from the remaining 2 farms (6%). All farmers cited experience with animal weighing as basis for dosage choice. The frequency of calibrating weight estimation by weighing or weight measurement using measuring tape ranged from weekly (five farms) to never (14 farms). Administration of antibiotics with manual syringes was carried out on 23 farms (64%), while five farms (14%) used automatic syringes, seven farms (19%) used both manual and automatic syringes, and no answers were obtained from one farm (3%).

Compliance with treatment protocols

In total, 23 farms (64%) reported experiencing challenges with complying with the outlined treatment protocols. The challenges mentioned were length of the treatment course, number of treatments in the treatment course, dosage, indication, animal age group described in the diagnosis, and in one case, route of administration.

Documentation and recording

The interviewees were asked about the documentation process for treatments. An overview of answers is provided in Table 3. At 28 farms (78%) the personnel kept a physical or digital log of calves, which were intended for treatment. For calves in a treatment course, 34 farms (94%) reported keeping a log of calves; for the remaining two farms (6%) the farms performed only treatments with one single dosage of antibiotics. The log was kept in different formats: paper, digital on phone, on whiteboards or similar structures. One farm marked calves in treatment with spray paint approved for this use. All interviewees replied that they checked daily to see if initiated treatment courses were completed, if relevant, for the calves. All Danish calves wear ear tag with their CKR-nr. A digital solution is available, which allows scanning of an ear tag and succinct recording of treatment with a mobile phone. However, all study farms reported manual read of ear tags.

On 22 farms (61%) the person performing the treatment was responsible for the final registration of the treatment, on 13 farms (36%) a fixed person was responsible for treatment registrations; the remaining farm (3%) reported registration by the treatment responsible with some inconsistency. The time from treatment until the final treatment registration varied from immediately to 2 months (Q1 = 1 hour, median = 10 hours, mean = 76 hours, Q3 = 54 hours).

Table 3: Documentation and recording answers and number of observations (n) and percentages (%).

Question	Answers	n	%
Documentation around time of treatment			
Log with calves intended for treatment	Digital log (phone)	6	16.7
	Physical log (paper or whiteboard)	18	50.0
	No log (oral or from memory)	3	8.3
	Not relevant	9	25.0
Log with calves in treatment course	Digital log (phone)	6	16.7
	Physical log (paper or whiteboard)	21	58.3
	Physical and digital log	7	19.4
	No log	2	5.6
First record after treatment	Paper or digital	7	19.4
	Paper	22	61.1
	Irrelevant	7	19.4
First record of treatment, registry location	Stable	29	80.6
	Irrelevant	7	19.4
Final treatment records			
Responsible for entering final treatment record	Treater	22	61.1
	Fixed person(s)	13	33.3
	NA's	1	5.6
Maximum hours from treatment to final registry of treatment	Immediately	8	22.2
	<24 hours	13	36.1
	48-72 hours	10	27.8
	>120 hours (5 days)	5	13.9
Final treatment record	Computer	16	44.4
	Telephone	13	36.1
	Paper	7	19.4
Final treatment record, registry location	Stable	16	44.4
	Other location	20	55.6
Treatment records format	Digital	16	44.4
	Paper	7	19.4
	Digital and paper	13	36.1
IT solutions	Computer program	10	27.8
	Computer program and phone app	19	52.8
	None	7	19.4

Discussion

The main finding of this study was that antibiotic management, use and recording practices varied between the 36 farms visited indicating a rather heterogeneous study population. Despite this, we were able to identify some questions with categories, which could be used for frequency analyses for each question regarding general management and documentation and recording. We were also able to describe the laboratory diagnostics carried out on the farms and the clinical signs used for decision-making regarding initiation of treatments for different diagnoses at each location of disorders. The recorded answers regarding dosage procedures, and treatment protocols and their use further allowed us to identify overall antibiotic treatment strategies on the farms.

Our study reports on many factors related to AMU. We have decided to highlight three themes in the discussion, which we find important for ensuring prudent AMU: Calves requiring or receiving treatment, efficacy of the antibiotics and choosing the correct antibiotics. In addition, we discuss the performance of our questionnaire during the field study.

Calves requiring or receiving treatment

One of the cornerstones in prudent AMU is ensuring that treatments are only carried out when it is expected to efficiently combat a disease adversely affecting the animal. We found treatment protocols labelled by the interviewee as routine, i.e. metaphylactic in 47% of the study farms. Use of metaphylaxis against bovine respiratory disease is well documented in veal production around the world (Cheng et al.,2023, Jarrige et al., 2017; Lava et al., 2016). The main concern regarding metaphylaxis is that farm-personnel risk treating clinically healthy calves leading to an overuse of AMU potentially promoting AMR.

Arguments supported by scientific studies for using metaphylactic treatments include lower morbidity and mortality indicating better animal health, higher carcass weights and average daily weight gains, and higher and less variable economic returns per calf (Credille et al., 2024; Dennis et al., 2020; Horton et al., 2023; Word et al., 2021). Horton et al. (2023) compared selective (pull-and-treat) treatment of sick calves to metaphylactic treatment at pen-level in a randomized complete block design and while they documented lower morbidity and mortality and greater carcass weights with metaphylaxis, they did not find significant differences in economic net returns per animals between the two groups and the AMU was higher. The samples size was significantly smaller than the study documenting economic effect by Dennis et al. (2020), which may explain the lack of documented economic effect. The lack of differences in economic net returns could also be explained by differences in the pen-composition with regards to sex, entry weights, number of animals and growth curves (Kopp et al., 2024). Higher AMU with metaphylaxis was also reported by Credille et al. (2024) and they did not find a corresponding increase in AMR in bacterial isolates from the nasopharynx in a blinded, cluster-randomized, complete block trial study on 155 calves. These findings contrast the findings by Crosby et al, (2023), who documented significantly increased odds of isolating multidrug resistant *Mannheimia haemolytica* in the group receiving metaphylaxis. The studies were conducted on similar study populations and the latter study had a larger study population of 331 calves, which should result in a higher statistical power, but it was not blinded. The findings regarding effect of metaphylaxis on AMR prevalence appear inconclusive.

The documented benefits of metaphylactic treatments are of high priority in the veal production, which makes finding alternatives resulting in the same benefits highly relevant and desired. In a questionnaire addressed to European veterinarians working with livestock, three main alternatives to metaphylaxis were identified as relevant: vaccination, improved biosecurity and improved health management on the farms (Jerab et al., 2022). We chose to focus on use of antibiotics in the presentation of our study, but an additional finding worth mentioning was the extensive use of vaccination upon arrival (75% of the farms). This is a marked increase from the 9% reported for Danish veal farms in 2014 and 2015 (Fertner et al., 2016). This indicates a will in the study population to explore alternatives to antibiotic use, which should be further investigated and encouraged while working towards prudent AMU.

Efficacy of the antibiotics

Veterinary drugs containing antibiotics are marketed with an indication, dosage, duration of treatment, route of administration and recommended storage conditions. This is based on well-regulated testing done by the pharmaceutical compagnies prior to receiving marketing authorization by the relevant regulatory authorities. In the European Union this is the European Medicines Agency (EMA) (Council Regulation (EC) 6/2019; EMA, n.d.). Adherence to these guidelines, should ensure optimal efficacy of the drug. In our study, we identified challenges related to compliance with these guidelines.

Stability of some drugs may be compromised due to incorrect storage. According to their Summary of Product Characteristics (SPC) drugs containing procaine benzylpenicillin should be stored in a refrigerator at a temperature between 2°C and 8°C (Ethacilin Vet., Penovet Vet., Streptocillin Vet.). Drugs containing this active compound were used on most farms but less than half of the farms in the study used the refrigerator for storage once the seal on the packaging was broken and the majority of farms using cooling did not have an alarm or specific control procedure in place to control if the refrigerator temperature matched the SPC guidelines. Ondrak et al. (2015) conducted a brief review of reported stability of active compounds, many of which are also frequently used in Danish large animal practice, when stored outside of the recommended storage. None of the active compounds were demonstrated to be unstable and many were found to be stable outside of recommendation, but benzylpenicillin and doxycycline were found to have equivocal data, meaning a reduced efficacy could not be disproved. Testing efficacy of improperly stored drugs is therefore relevant. One study remarked that high storage temperature may have contributed to a loss of efficacy of antibiotics (amoxicillin, chloramphenicol , ciprofloxacin and tetracycline) when used in vitro against selected bacterial strains (Gnarmey et al., 2019). Loss of efficacy can lead to treatment failures often resulting in repeated treatment leading to higher AMU and increased risk of AMR. These results suggest a need for improved compliance with guidelines regarding storage of antibiotics. Most farms in a Danish setting have inlaid electricity and purchase and use of a refrigerator is a cheap and easily implementable intervention.

The majority of farms (64%) reported challenges with complying with the treatment protocols outlined by their VASC veterinarian related to either indication, dosage, duration of treatment or route of administration. Assuming the VASC veterinarians have created the treatment protocols in accordance with the pharmaceutical compagnie’s guidelines and their own and their colleague's professional knowledge, the treatment protocols should represent the best practise to ensure optimal antibiotic efficacy. Lack of compliance is therefore a serious concern. The issue of deviations from treatment protocols is not a novel discovery. Widespread deviations from labelled drug use with either a shorter or longer duration of treatment, or a different frequency of administration than recommended has previously been described (Aghamohammadi et al., 2018). In a Danish setting, use of medicine originally prescribed to an adult animal for a calf with a different diagnosis has been described (Skjølstrup et al., 2021). Use of different drugs and deviations from dosage recommendations have also been described (Campler et al., 2021). Concerns about differing weight estimations and used dosage causing a discrepancy between prescription (treatment protocol) and dispensation (use) have also been raised (Jarrige et al., 2017). We did not address under- and overdosing in our study, but we did identify different strategies for dosage. Fixed doses based on e.g. mean weight poses a risk of over- and underdosing of the individual animal if animals in a pen vary greatly in weight. For adaptive dosing correct weight estimation by the treatment responsible is crucial, and level of this skill may vary. A study found no association between risk of culling or death and lack of compliance with, amongst other, recommended dosage (Campler et al., 2021). But further investigations of how and when lack of compliance affect treatment outcome and the risk of AMR are warranted.

In the study by Campler et al. (2021), the authors remarked on the risk for animal welfare with lack of compliance and emphasised the potentially beneficial effect of proper training of farm owners. The importance of well-educated and skilled farm-personnel in the livestock sector is well described (Coleman and Hemsworth, 2014; Daigle and Ridge, 2018). In our study, we found the requirements regarding skill sets in the farm-personnel and the training related to AMU differed between farms. All farms, where training of new personnel in identification and treatment of diseased calves were relevant reported peer-to-peer training. This is in line with findings from Cheng et al. (2023). The percentage of farm-personnel with a medicine handling course differed, but less than a third of the farms reported most (>75%) of their personnel having completed it. A medicine handling course is mandatory, but if the personnel have more than six months of experience with administration of medicine to livestock animals prior to February 2007 they can be exempted (DVFA, 2023). This exemption may be justified by the findings by Borelli et al. (2023), which documented older farmers as being more likely to be classified as low antimicrobial users. However, a higher level of educations and trusting the information provided by the veterinarian on responsible AMU was also found to be associated with better knowledge of antibiotics and AMR in the same study (Borelli et al., 2023). Antimicrobial stewardship training on calf producers has been shown to promote prudent AMU through change in producers' behaviours (Pempek et al., 2022). Applying local targeted education by veterinarians, advisors and peers, providing guidelines and conducting awareness campaigns on AMU and AMR has been suggested as important for prudent AMU (Bokma et al., 2018; Borelli et al., 2023; Cheng et al., 2023, McKernan et al., 2021; Pempek et al., 2022). Based on our findings, we find these initiatives to also be relevant in Danish veal production and recommend implementing them. This may also aid in reducing farm-personnels' deviations from treatment protocols.

Choosing the correct antibiotics

We found the level of diagnostics performed in our study population to be limited, despite all study farms having treatment protocols for pneumonia only half of the farms had done diagnostics on airways within the last year on either lungs from dead calves, lung fluid from bronchoalveolar lavage or nose swabs. This finding may be subject to some level of recall bias or interviewees may not always have been fully aware of diagnostics initiated by their veterinarian. Better quality data may have been obtained from VASC veterinarians. Regardless, based on the interviews we are relatively confident that laboratory diagnostics does not seem to be a routine in most of our study population. Reasons for not doing diagnostics previously cited are cost, waiting period for results, delay in treatment initiation, and uncertainty regarding the credibility and effectiveness of provided results (McKernan et al., 2021).

Ideally, laboratory diagnostics should provide knowledge of the pathogens, which will aid in deciding on the best choice of therapy. Unfortunately, choice and use of diagnostics may not always be straightforward. Firstly, pneumonia in calves, or as it is frequently referred to bovine respiratory disease (BRD), is often a multifactorial disease caused by more than one pathogen, where many of the pathogens are also present as commensals in healthy calves (Fulton, 2009, Murray et al., 2016). Secondly, identification of the pathogens causing disease may be influenced by choice of diagnostics. A multitude of diagnostic tests exists with different strengths and limitations regarding performance and succinct interpretation (Fulton and Confer, 2012). In comparisons of real-time PCR on paired nasal swabs and brocho alveolar lavage samples from Danish calves the challenges with detecting pathogens were highlighted as nasal swabs were found to be poor to moderate predictors of pathogens in the lower respiratory tract; additionally, many positive samples were collected from calves deemed clinically healthy and negative samples were collected from clinically sick calves (Otten et al., 2024). Further complications to diagnostic testing can be differing cut-offs for different pathogens (Klompmaker et al., 2021).

To summarise, choice and use of diagnostics is a complicated area, and it is entirely understandable if farmers sometimes find the use of diagnostics redundant due to the uncertainty of the results. Despite the challenges diagnostics are still relevant, but care should be taken in tailoring the approach to the concrete case (Otten et al 2024). Relevant initiatives discussed by Klompmaker et al. (2021) such as group testing or repeated testing could aid the farmers and veterinarians in understanding the on-farm development in disease with regards to pathogen profiles. This could aid in planning the timing and choice of treatment protocols, including preventive initiatives such as vaccination. Previously it has been described, how prior sensitivity testing is used for less than 10% of the antibiotic treatments (Carmo et al., 2018a). In cases of AMR, knowing the disease-causing pathogens' antibiotic sensitivity profile should be considered essential. Thus, we also recommend exploring options for diagnostics tailored to the needs of the individual farm.

Strengths and limitations of a questionnaire-based approach

A questionnaire-based interview on-site as our method of collecting data proved to have both strengths and limitations during our field study. In choosing the study method, our main goal was to ensure a data collection, where we gained an insight into Danish rosé veal production and its' antibiotic management, use and recording practices while limiting interviewer bias, miscommunications and misconceptions.

The questionnaire design collected primarily categorical data ensuring a uniform and structured data collection, where the possibility for interpretation by the interviewer was minimised to mitigate interviewer bias potentially caused by face-to-face communication

(Houe et al., 2004). Digitalisation was done using the recorded answers directly, which increased the risk of recording error; a benefit was easier interpretable data with values meaningful to the data manager. To limit misunderstandings and doubts on the text content and relevant recording all steps in data collection and management were carried out by the interviewer.

One aim of the walk-through approach was to equip the interviewer with a basic understanding of the specific farm's daily routines, production procedures, and strategies. The on-site interview data collection was expected to improve rapport between interviewee and interviewer; the use of body language and a common understanding of the physical settings in which the veal production was placed aided communication (Dohoo et al., 2014). The dialogue-based use of the questionnaire allowed both interviewees and interviewer to ask for clarifications or add context, thereby reducing misconceptions and miscommunication. An on-site interview increased the likelihood of interviewees completing the questionnaire (Dohoo et al., 2014). In-person interviews may have impacted how interviewees responded to questions where their actions could be perceived unfavorably (Midanik et al, 2001). To counteract this effect, the interviewer underscored that all data would be treated anonymously at the beginning of the interview and adopted a curious, open, and nonjudgmental attitude. Generally, our assessment is that interviewees responded honestly to the questions and felt comfortable expressing their opinions to and correcting the interviewer.

The heterogeneous study population proved to be a challenge and sometimes, the categorical levels included in the questionnaire (Supplementary 1, M1S1F1) did not cover the answers given by the interviewees or were found to be irrelevant. This was partially solved by recording answers in text and later regrouping provided answers into relevant categories. It did complicate the recording process and following digitalisation. The diverse physical settings on the study farms with differing number of locations and internal logistics and the attitudes and expectations of the interviewees required a changed order of the topics covered in the interview, which could complicate the interview process and may be a cause in cases where questions were skipped. No strict timekeeping was implemented by the interviewer and the duration of the interview varied from 1.5-6h; depending mainly on the talkativeness of the farmer. The varying time likely reflect the level of interest by the interviewees. It was our experience that some interviewees used the visit to conduct an evaluation of their own practices, while others just wanted to finish the interview quickly.

To our knowledge, this study is the first conducted in Danish rosé veal farms with the aim of gaining an overview of antibiotic management, use and recording practices. An interview without an expectation of clearly categorizable answers might have been better suited to the explorative character of the study. This could also provide a basis for the development of a consecutive shorter, more manageable, and less time- and resource-consuming questionnaire aimed at either determining frequencies of relevant practices or identify challenges for prudent AMU.

Despite the challenges with the questionnaire and its use, we have improved upon the understanding of on-farm antibiotic management, use and recording practices in Danish rosé veal farms and provided the insights into Danish veal production. We have identified themes in on-farm practices, which may result in injudicious AMU and suggested interventions for mitigation. Many of the questions and categories from our questionnaire, though applied and identified in Danish veal farms, could be relevant in a broader context for farms with other species and/or production types across borders. Reporting on these could give a structured initial overview of antibiotic management, use and recording practices from arrival to treatment application and waste management. With this knowledge the interpreter may identify areas requiring further investigation or, if used in an advisory context, interventions.

Conclusions

In this questionnaire-based field study, we have improved the understanding of on-farm antibiotic management, use and recording practices in Danish rosé veal farms by exploring three main topics: General management, diagnostics and treatment, and documentation and recording practices.

Several practices potentially associated with injudicious AMU were identified and three themes were highlighted: Calves requiring or receiving treatment, efficacy of the antibiotics and choosing the correct antibiotics. Routine metaphylactic treatments were used by almost half of the study farms. This adds to previous concerns about overuse of antibiotics and treatment of clinically health calves leading to AMR development. Regarding efficacy of antibiotics the major concern was lack of compliance with the guidelines in the SPCs. We found compliance challenges, and thereby risks of injudicious AMU, with all aspects in the guidelines: indication, dosage, duration of treatment, route of administration, and recommended storage conditions. Routine diagnostics were not reported as a general practice in our study population leading to concerns on whether the disease-causing pathogens were intrinsically resistant or had acquired resistance to the antibiotics used.

Based on our findings, we recommend exploring alternatives to metaphylactic treatment, implementing antimicrobial stewardship training programmes and providing guidelines, and conducting awareness campaigns promoting and encouraging prudent AMU, and exploring options for diagnostics tailored to the needs of the individual farm.

Declarations

Ethics approval and consent to participate

The study was approved by the University of Copenhagen; Health Science Faculty secretariat [Journal nr.: 514-0718/22-3000], and the Faculty of Science and Faculty of Health Science Research Ethics Committee [Journal nr.: 504-0330/22-5000].

Written informed consent was obtained from all participants and in accordance with guidelines published by the Danish Data Protection Agency.

Consent for publication

Not applicable

Availability of data and materials

Interview data cannot be made available. The informed consent from the participants does not permit data sharing.

Used CHR data cannot be shared. Separate permission to use data should be requested from The Danish Veterinary and Food Administration.

Exempt from the questionnaire and summaries of raw questionnaire data are provided in Supplementary 1 and Supplementary 2.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

JK: Conceptualization, methodology, data curation, formal analysis and investigation, software, visualisation, writing-original draft preparation, funding acquisition

ABK: Supervision, methodology, review and editing

APS: Supervision, methodology, review and editing

LRN: Methodology, review and editing, funding acquisition and project administration

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Authors' information

JK has two years of experience working as a veterinary practitioner with Danish dairy and hobby beef farms. Additionally, JK has experience with work as an official veterinarian employed by the Danish Veterinary and Food Administration. Thus, a prior knowledge of the legislation, and mechanisms for enforcement and practical implementation in Danish farms was utilized during the planning and execution of the field study.

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12.2. Manuscript II

Key farm characteristics associated with the level of antimicrobial use in rosé veal production - a Danish database study

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Key farm characteristics associated with the level of antimicrobial use in rosé veal production – A Danish database study

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ABSTRACT

Antimicrobial use (AMU) in veal production is high compared to other bovine production types and has been suggested as an area with potential for AMU reduction. High AMU is a public health concern due to its association with antimicrobial resistance (AMR). Identifying farm characteristics associated with AMU could provide valuable insights for stakeholders seeking to monitor and implement initiatives to reduce AMU. This study aimed at investigating farm characteristics associated with AMU in Danish rosé veal farms, which is the main veal production type in Denmark. The AMU and characteristics included were extracted from two Danish national databases; The Danish Central Husbandry Register (CHR) and the Danish Veterinary Medicines Statistics Program (VetStat). Characteristics included were farm size, mortality, number of suppliers, sites per farm, and farm-level composition of animals with regards to sex and breed. The 118 farms included in the study received 41 % of the total amount of antimicrobials prescribed for Danish calves and young stock in 2020 measured in Animal Daily Doses (ADD). A multivariable linear regression model with the annual average farm-level AMU as outcome was created. AMU was measured as ADD per 100 animals per day (ADD100) and square root-transformed in the model. Increasing farm size and number of suppliers and decreasing proportion of crossbred bulls were found to be significantly associated with higher AMU. However, proportion of crossbred bulls was correlated with proportion of females. Separating the effects of breed and sex was not possible, partly due to the highly summarised data structure. Mortality and number of sites were not significantly associated with AMU. Farms with the type "starter-farms" has previously been shown to have a higher AMU compared to other rosé veal farm types. An important finding in this study was that grouping multiple sites into farms by using ownership data made it possible to summarise AMU for the full line of production from arrival at the veal farm to exit for slaughter. The results and approaches from this paper present an opportunity for repeated evaluation of farm characteristics associated with AMU, which could be used to continuously adapt and target AMU monitoring and control. In addition, it is done on existing surveillance data which keeps the cost of the study low in terms of data collection and data management.

1. Introduction

Antimicrobial resistance (AMR) is a critical global challenge affecting both human and animal health. The association between antimicrobial use (AMU) and AMR in the food chain has been repeatedly documented (Bennani et al., 2020), and recently Ardakani et al. (2023) has documented a positive correlation between AMU in livestock and AMR in humans. Reduction in AMU in livestock has been associated with a reduction of prevalence of AMR in livestock production (Tang et al., 2017). This offers an opportunity to prevent AMR by optimising and reducing AMU in livestock, especially in farms that use AMU extensively, routinely, or incorrectly.

Abbreviations: AMU, antimicrobial use; AMR, antimicrobial resistance; CHR, the Danish Central Husbandry Register; VetStat, the Danish Veterinary Medicines Statistics Program; DVFA, the Danish Veterinary and Food Administration, DCDB, the Danish Cattle Database; ADD, Animal Daily Dose; ADD100, Animal Daily Doses per 100 animals per day.

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The Danish animal-based food production sectors describe prudent AMU as using “as little as possible but as much as necessary” (Danish Agriculture and Food Council, 2016). This principle is a central part of the Danish national action plans and industry initiatives to combat AMR (Anon, 2013; Danish Agriculture and Food Council, 2016).

Historically, Denmark, has been proactive in surveillance of AMR and AMU. The Danish programme for surveillance of antimicrobial consumption and resistance in bacteria from food animals, food, and humans (DANMAP) was established in 1995 and annual reports have been published since 1996 (DTU National Food Institute and Statens Serum Institute, 2022).

Denmark has been proactive and among the first to implement AMU reduction initiatives driven by both the authorities and livestock sectors. Antimicrobial growth promoters were phased out by the sectors across the entire Danish food animal production system already by the end of 1999 (Jensen and Hayes, 2014) Another example is the phasing out of 3rd and 4th generation cephalosporins initiated in 2014 and encouraged by the cattle sector, which was followed by a voluntary ban in 2019 (DANMAP, 2022).

This objective has been achieved as from 2012 to 2018, the cattle sector targeted a 20 % reduction in AMU (Danish Agriculture and Food Council, 2016). The overall AMU for Danish cattle decreased more than 20 % from 2012 to 2022 (DANMAP, 2022). However, from 2018 to 2019, the AMU for cattle under one year of age increased (DANMAP, 2020) showing that there is still a need to decrease AMU within the sector.

A study on 2010 data from Denmark and the Netherlands found the relative AMU for veal calves and young beef to be higher than the AMU for dairy and other cattle. It was especially pronounced in the Dutch production (Bondt et al., 2013). This pattern was supported by Bos et al. (2013). In an international study based on expert opinion published in 2018, veal production was suggested as an area with a large potential for AMU reductions in Denmark, Portugal, and Switzerland (Carmo et al., 2018).

In the European Union, meat from cattle under one year of age is divided into two categories dependant on age at slaughter; 1. Under eight months of age, and 2. Between eight and twelve months of age (Council Regulation (EC) 1308/2013). The cattle label varies depending on the country. Rosé veal is the only veal production type in Denmark. Typically, the Danish veal farmers buy calves directly from dairy farms or through livestock traders and rear the calves in a full-line production until slaughter.

When planning AMU reduction initiatives, it is important to identify factors associated with AMU. This allows for targeted surveillance and more effective interventions. A review by Redman-White et al. (2023) summarised research on predictors of AMU in, amongst others, the beef production cycle. They listed fewer than 10 studies conducted on beef and veal production highlighting the need for further studies.

Diana et al. (2021) found the AMU higher in bull calves than in heifer calves in Italian beef production and suggested a potential effect of breed. An association between breed and AMU was also found in a study of Belgian veal productions, where the Belgian Blue breed had a higher AMU compared to Holstein Friesians and Holstein Friesian Belgian Blue crossbreds (Bokma et al., 2019). Other factors potentially associated with AMU at farm-level are mortality (Jarrige et al., 2017) and shared air space for several groups of calves (Lava et al., 2016a).

Fertner et al. (2016) found that in full-line single-site veal farms an increasing number of purchased calves was associated with an increased AMU. They hypothesised that increased number of suppliers and increased number of introduced calves, which were strongly correlated in their analyses, could be considered a proxy for increased risk of introducing pathogens, which could in turn impact the AMU. Following up on the study by Fertner et al. (2016) and including multi-site veal farms could add valuable information to help achieve the goal of AMU reduction in veal farms.

Denmark has a large amount of compulsory routinely collected cattle data. The Danish Central Husbandry Register (CHR) gathers and stores animal-specific data on cattle, including date of birth, sex, breed, and location. Additionally, information is available about the number of animals, specific geographical location, and unique ownership identification at site-level. Data on prescribed antimicrobials at site-level can be extracted from the Danish Veterinary Medicines Statistics Program (VetStat). Both the CHR and VetStat databases are owned and managed by the Danish Veterinary and Food Administration (DVFA). Some of the data enters these databases via the Danish Cattle Database (DCDB), which is owned by Danish Agriculture & Food Council and managed by SEGES Innovation P/S, e.g. animal-specific data in CHR and records of veterinary use and dispensing of antibiotics in VetStat. In addition, the DCDB also contains milk delivery and slaughter data.

The objective of this study was to utilise routinely gathered and summarised data from databases to investigate how farm characteristics are associated with AMU in calves and young stock on Danish rosé veal farms. Using this data reduces the cost of performing a study by eliminating the data gathering step. It also makes repeating analyses easy and reproducible with minimal additional data management needed. Thus, the analyses could potentially be implemented in future surveillance.

2. Materials and methods

The farm characteristics investigated were; farm size, number of suppliers, number of sites, the composition of animals expressed by distribution across breeds and sexes, and mortality.

2.1. Data acquisition

Data from the year 2020 from three sources; VetStat, CHR, and the DCDB were used.

The Danish Yellow card AMU surveillance is a national benchmarking system implemented for pigs and cattle in 2010 (DANMAP, 2022), which reports AMU for cattle monthly as number of purchased animal daily doses (ADD) per 100 year-animals per day (ADD100) at farm-level.

Records of farm characteristics are based on summaries of DCDB data conducted by SEGES Innovation P/S and stored in the DCDB. These summaries are currently used for farm classification in the Danish *Salmonella* Dublin eradication programme (Conrady et al., 2024).

Data from the CHR is updated continuously by farmers and can be used to establish a farm’s activity status and to identify farms with multiple locations based on ownership data.

2.2. Study population

In this study, a farm-business (from here on called ‘farm’) is defined as having one unique owner. A farm can encompass multiple sites. On a site multiple herds, i.e. registered groups of animals, can be present. The term ‘year-animal’ is defined as the average number of animals on the farm in the period from 1/1 2020–31/12 2020. Rosé veal farms available for inclusion in the study fulfilled the following criteria:

Assumed professional, specialised rosé veal production:

I. No farms with parallel dairy and veal production (no milk deliveries)
II. At least 200 year-animals registered in the full line of production of the farm
III. Number of slaughtered animals should be equal to or larger than number of housed year-animals

The application of these criteria should ensure inclusion of primarily farms driven as rosé veal farms in a professional capacity i.e. no hobby farms. In addition, Danish legislation mandates Veterinary Advisory Service Contracts (VASC) for farms exceeding 200 bulls or heifers making this a relevant threshold in a Danish setting (Danish Veterinary and Food Administration, 2021).

The inclusion process was as follows (illustrated in Fig. 1). From a full 2020 dataset containing herds, sites, and farm data from the CHR, only herds with records of animal presence and one unique herd owner registered all year 2020 were extracted. If multiple herds were registered on a site, the site was included if animals with same registered ownership accounted for at least 95 % of the animals. Herds were grouped by sites, and the sites were aggregated into unique farms using ownership data. Only farms with positive AMU records in VetStat on at least one site were included. Then the criteria for assumed professional, specialised veal production was applied. Farms were only included in the final dataset, if a minimum 95 % of the year-animals registered with the farm owner were registered on sites available for inclusion to ensure the inclusion of the complete production.

2.3. Response variable

The response variable was AMU expressed as ADD100. The ADDs are calculated in VetStat using a standard technical dose per kg bodyweight defined for each prescribed product and a standard bodyweight per age group. For the calculation of ADD100, VetStat uses a standard weight of 200 kg bodyweight for all prescriptions for the age group calves and young stock. Only antibiotics prescribed for this age group were included in the calculations of AMU. The ADDs were extracted from the "Yellow Card" statements that are made available in VetStat for each site per month. ADDs were summarised for each farm to the total annual number of ADDs.

The number of year-animals per farm was extracted from CHR data and converted to 'days-at-risk' by multiplying year-animals by number of days in a year. ADD100 was then calculated by dividing the total farm ADD with farm "days-at-risk" and multiplying by 100.

2.4. Explanatory variables

The following potential explanatory variables were tested in the statistical models: *Farm size*: Number of year-animals summarised per farm; *Sex*: Proportion of heifer year-animals calculated for each farm; *Breed*: Proportion of crossbred bull calves (due to significant differences in proportion of crossbreds between sexes this approach was chosen), calculated for each farm based on the number of purebred (dairy breed) or crossbred (dairy X beef breed) bull year-animals; *Number of sites*: The number of sites registered with the farm; *Suppliers*: The maximum number of suppliers registered on a single site in the farm; *Mortality*: Proportion of dead animals out of the total number of calves leaving the farm as either dead or for slaughter during the study period. The mortality could not be calculated using the number of calves entering a farm per year as this could not be extracted from the summarised data. Thus, number of animals exiting the farm was used as a proxy for number animals entering the farm in the analyses.

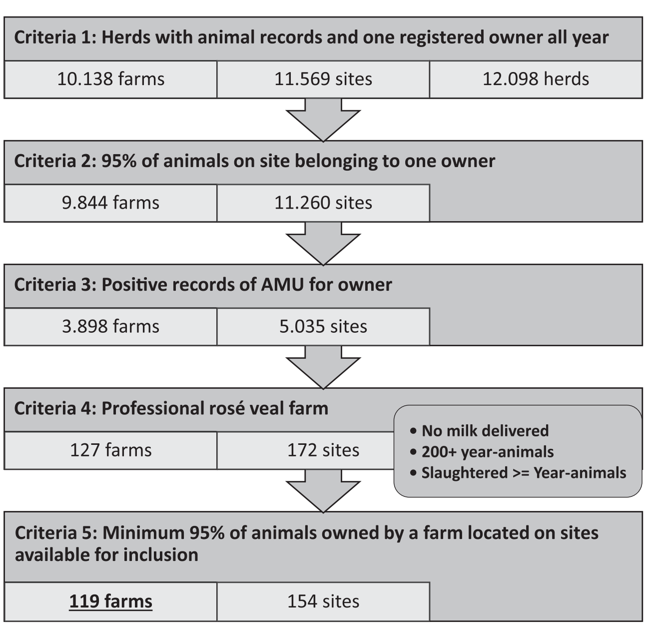

Fig. 1. The inclusion process with applied criteria and count of farms, sites, and herds included for each step in the process. After 'Criteria 2' herds were grouped by sites and excluded from further counts.

2.5. Statistical analyses

2.5.1. Descriptive statistics

The response variable was visually assessed for normal distribution and transformed with transformation from the Box Cox family (Box and Cox, 1964) if this obtained a better normal distribution of data. The final dataset was assessed for extreme values in the outcome variable through visual data plots.

The data distribution was also examined for the explanatory variables. Each explanatory variable was plotted against the response variable to visually assess correlation. If the correlation was linear no further adjustments were made. If a non-linear relationship was apparent, relevant transformations from the Box Cox family were assessed and performed. If no linear relationship could be obtained through transformation, the potentially explanatory variable was grouped into a maximum of three categories by sorting each variable from highest to lowest and grouping using the 33 % and 66 % quantile. The adjusted explanatory variables were then entered into univariable analyses.

2.5.2. Univariable analyses

All potential explanatory variables were tested against the response variable in univariable analyses. Linear regression analyses were used for quantitative variables and ANOVAs were used for categorical variables. Variables with a significance level $p < 0.20$ were considered eligible for inclusion in the final univariate multivariable linear regression analysis.

2.5.3. Independence

All explanatory variables were tested pairwise for independence. Quantitative variables were tested pairwise with Pearsons's correlation coefficient. In cases with a coefficient < 0.6, both variables were included in the multivariable model. For comparison with a qualitative and quantitative variable, the quantitative variables were converted into categorical variables using the 33 % and 66 % quantiles as break points. A test for independence was then done using a X^2-test, $p > 0.05$ used as indicator of independence. In cases of correlation, the significant variable with the lowest p-value was kept.

2.5.4. Multivariable analysis

The explanatory variables eligible for inclusion in the study model were included in a multivariable regression analysis. Square root transformation of the response variable was selected as a fitting compromise between expected response in ADD100 with a change in the respective explanatory variables and an optimisation of model fit.

Equation 1: Multivariable linear regression model

$$\sqrt{y_i} = \beta_0 + \beta_1 \log(x_{i1}) + \beta_2 \log(x_{i2}) + \beta_3 \log(x_{i3}) + \varepsilon_i$$

Where;

y_i = Animal daily doses per 100 animals per day

x_{i1} = Farm size expressed by number of calf and young stock year-animals

x_{i2} = Proportion crossbred of bull calves

x_{i3} = Maximum number of suppliers per site

Model reduction was performed using backwards elimination based on Akaike's Information Criterion (Akaike, 1974). Changes in estimates were assessed after each elimination step and changes in estimates of +/- 20 % was set as criteria for keeping an explanatory variable in the model due to confounding. Interactions which were considered biologically plausible were tested. An interaction was kept in the model if significant at $p < 0.05$. Confounding was assessed, additionally, by introducing the explanatory variables not included in the initial model one at a time to the final model and checking for a change in the estimates of more than +/- 20 %.

2.6. Tools

All data management and analyses were performed using the statistical software R version 4.3.2 (2023–10–31 ucrt) (R Core Team, 2023) and R-Studio version 2023.9.0.463 (Posit team, 2023). The package tidyverse (Wickham et al., 2019) was used for data management, ggplot2 (Wickham, 2016) was used for visualisation. For analyses the packages epitools (Aragon, 2020), epiDisplay (Chongsuvivatwong, 2022), ResourceSelection (Lele et al., 2023), and broom (Robinson et al., 2023) were used.

3. Results

3.1. Descriptive statistics

A final dataset with 154 sites distributed in 119 productions was obtained. On these farms 87,355 calf and young stock year-animals were housed. A total of 653,673 ADDs were prescribed for the study population, corresponding to an average of 7.5 ADDs per year-animal, or on average 2 % of the animals across all farms and the full year being prescribed a standard day dose of antimicrobials. This average does not reflect fluctuations in AMU across a production cycle or the season. Data was summarised for a year to correct for potential effect of season.

3.1.1. Characteristics of included farms

Large variations were seen on the investigated explanatory variables across the included farms (Table 1). The distribution of the response variable was left skewed. A square root-transformation was carried out (ADD100SQRT). Normal distribution was obtained visually for the outcome ADD100SQRT, and a Shapiro-Wilk normality test confirmed this with a $p = 0.60$.

The farms ranged in size from 203 to 4749 year-animals, with 25 farms having more than 1000, and 60 farms having fewer than 500. The number of suppliers ranged from 1 to 280, with 33 farms having fewer than 10 suppliers and 25 having more than 50. In total, 84 farms consisted of one site, and the maximum number of sites was four (in two of the farms).

The on-farm animal composition varied considerably. The numbers went from less than 1 % heifer calves on 19 of the included farms to nearly exclusively heifers in one farm. Seven farms had less than 10 % crossbred bulls and eight farms had more than 50 %.

Mortality expressed as proportion of dead animals relative to number of animals leaving the farm for slaughter or as dead ranged from 1 % to 22 % with 17 farms having a mortality higher than 10 %.

The annual AMU varied markedly between farms from the lowest value (0.05 ADD100) to highest value (7.64 ADD100). The highest observed ADD100 exceeded second highest observed ADD100 by more than 60 % and was recipient of 20.3 % of the AMU doses prescribed for the entire study population. This is realistic but for modelling purposes we considered this extreme and excluded the farm from further analyses after our initial population characterisation seen in Table 1. The final data set used for modelling contained 118 farms on 151 sites. These farms received 41.43 % of the ADDs prescribed for calves and youngstock in Denmark in 2020.

Table 1
Characteristics of the study population with 119 Danish rosé veal farms. The distribution of observations for each variable is listed with minimum, 1st quartile, median, mean, 3rd quartile, and maximum values.

	Min	Q25	Median	Mean	Q75	Max
ADD100[a]	0.05	0.58	1.14	1.41	1.91	7.64
Farm size[b]	203	321	483	734	867	4750
Percent crossbred bulls[c]	6 %	19 %	25 %	29 %	36 %	83 %
Number of suppliers[d]	1	9	19	35.19	43	280
Percent heifers[e]	0 %	6 %	12 %	14 %	18 %	99 %
Mortality[f]	1 %	4 %	5 %	6 %	7 %	22 %
Number of sites[g]	1	1	1	1.39	2	4

[a] Animal Daily Doses per 100 animals per day
[b] Number of year-animals per farm
[c] Percent crossbred bulls relative to total number of bulls
[d] Maximum number of suppliers registered on a single site of the farm during the study period
[e] Percent heifer calves relative to total number year-animals
[f] Calculated as percent dead animals relative to number of animals leaving the farm for slaughter or as dead carcasses
[g] Number of sites per farm

3.2. Univariable analyses

All potential explanatory variables were plotted against ADD100SQRT and assessed for linear relationship and distribution of data. A linear relationship between ADD100SQRT and farm size, proportion of crossbred bulls, and number of suppliers, respectively, could be obtained through log-transformation.

For proportion of heifers and mortality no linear relationship could be obtained. For both variables clusters and outliers in data could be identified visually, thus data were categorised. Number of sites per farm were dichotomized into one or multiple sites.

For all variables converted into categories Bartlett tests of homogeneity of variances showed homogeneity of variance.

Univariable analyses were carried out for all potential explanatory variables with the applied transformations to the raw data and are listed in Table 2. Mortality and sites per production had a $p > 0.2$ against the outcome variable ADD100SQRT and were excluded from further analysis. Farm size was significantly associated with ADD100SQRT with $p < 0.05$. Proportion of crossbred bull calves and proportion of heifers had non-significant p-values in the univariable analyses but were eligible for inclusion in the multivariable model as $p < 0.20$ for both variables. For quantitative variables normality was found in visual examination of residual plots and in Shapiro-Wilk normality tests on the univariable model residuals.

3.3. Independence between explanatory variables

Proportion of crossbred bull calves was significantly correlated with proportion of heifer calves with a Pearson's correlation coefficient of 0.68 and $p < 0.001$. A X^2-test on categorised data resulted in $p < 0.001$. An increase in one corresponded to an increase in the other. Proportion crossbred bull calves had a $p = 0.060$ in the univariable analyses with ADD100SQRT and the categorised proportion of heifer calves had a $p = 0.124$. This led to the exclusion of the proportion of heifers from the multivariable model according to the chosen methodology.

Farm size and number of suppliers were found to be correlated with a Pearson's correlation coefficient of 0.49 and $p < 0.001$. This was below the set threshold of 0.6 for Pearson's correlation coefficient and both were kept in the final model. Farm size and number of sites were found to be correlated in a X^2-test with $p = 0.001$. No other significant correlations were found between variables.

3.4. Multivariable analysis

Three variables were kept in the final model: farm size, proportion of crossbred bulls, and number of suppliers. All were log-transformed. No

Table 2
Outcome of univariable analyses of potential explanatory variables against the AMU expressed as animal daily doses per 100 animals per day for the farm square root transformed (ADD100SQRT).

Potential explanatory variables	Farms	(%)	Estimate[s]	[CI95 %]	SE	p-value
Farm size[t]	118	(100)	0.32	[0.23:0.42]	0.05	<0001
Proportion crossbred bulls[t]	118	(100)	−0.14	[−0.28:0.01]	0.07	0060
Suppliers[t]	118	(100)	0.17	[0.11:0.23]	0.03	<0001
Proportion heifers						0124
<8.09 %	38	(32.2)	1.16	[1.03:1.3]		
8.09–14.60 %	39	(33.05)	−0.04	[−0.23:0.15]		
>14.60 %	41	(34.75)	−0.18	[−0.37:0]		
Mortality						0694
<4.39 %	39	(33.05)	1.14	[1:1.27]		
4.39–6.29 %	39	(33.05)	−0.06	[−0.25:0.13]		
>6.29 %	40	(33.9)	−0.08	[−0.26:0.11]		
Sites per production						0672
1	91	(77.12)	1.34	[1.13:1.54]		
2+	27	(22.88)	0.09	[−0.33:0.52]		

[t] Log-transformed to obtain better linearity with outcome
[s] All univariable analyses were performed with a square root-transformed outcome (ADD100SQRT)

variables were eliminated from the final model expressed by *Equation 1*.

The model was run with and without the identified extreme value with the highest ADD100. The Multiple R-squared were reduced from 0.4017 to 0.3568 with the exclusion of the extreme value. The largest change in estimates observed were for farm size, where the estimate decreased by 11.20 % with the inclusion of the extreme value. Results from the model excluding the extreme value are presented in the following.

In the final model, farm size and number of suppliers were found to be significantly associated with increase in AMU, while increasing proportion of crossbred bull calves was significantly associated with lower AMU.

The model predictions on a back-transformed scale for the outcome with confidence and prediction intervals are illustrated in Fig. 2 for each explanatory variable. The model output is listed in Table 3.

No statistically significant interactions were identified during model assessment. During testing for confounding with the variables not included in the model, no confounding was identified. However, when introducing proportion of heifers using the raw non-categorised data a

Table 3
Estimates of AMU expressed as square root-transformed animal daily doses per 100 animals per day in a multivariable linear regression model with the explanatory the log-transformed variables proportion of crossbred bull calves, farm size, and number of suppliers.

	Estimate[s]	Standard Error	t value	Pr(>|t|)	
(Intercept)	−0.996	0.316	−3.151	0.0021	**
Farm size[t]	0.261	0.053	4.910	0.0000	***
Proportion crossbred bulls[t]	−0.139	0.059	−2.362	0.0199	*
Suppliers[t]	0.085	0.033	2.605	0.0104	*

Signif. codes: 0 < = '***' < 0.001 < '**' < 0.01 < '*' < 0.05
Residual standard error: 0.3407 on 114 degrees of freedom
Multiple R-squared: 0.3568, Adjusted R-squared: 0.3399
F-statistic: 21.08 on 114 and 3 DF, p-value: 0.0000
[t] Log-transformed [s] Square root-transformed

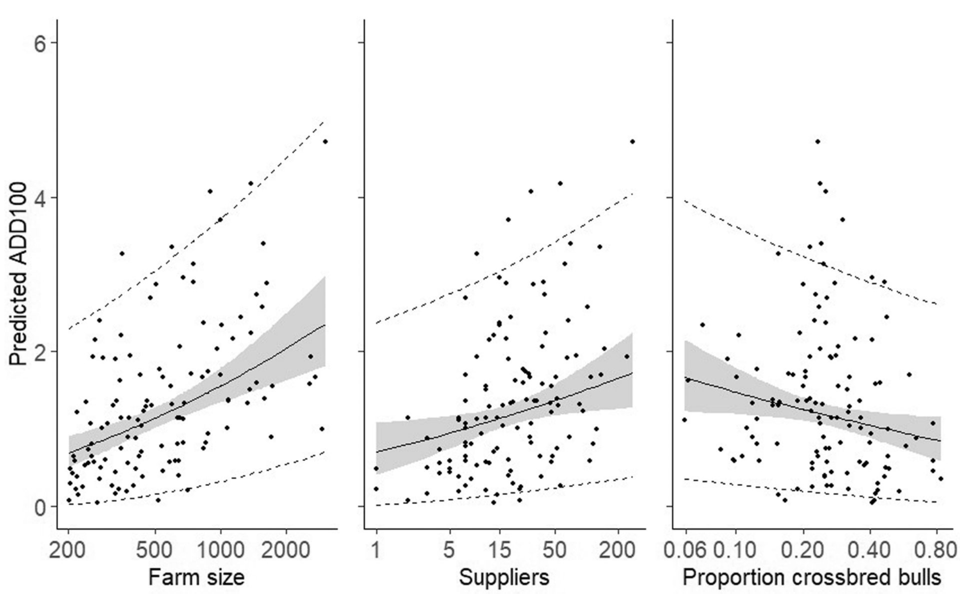

Fig. 2. Prediction line (—) of mean AMU expressed as square root-transformed Animal Daily Doses per 100 animals per day in a multivariable linear regression model with the explanatory log-transformed variables production size, proportion of crossbred bulls, and number of suppliers. The estimates are back-transformed and the x-axes are kept on the scale used for each explanatory variable in the model. The 95 % confidence interval on the model prediction line is marked by the grey band and the prediction interval is given in dashed lines (—). The original data (•) are plotted on top of the model data.

change of 112.09 % to an estimate of −0.066 ($p = 0.379$) were seen for the estimate for proportion of crossbred bulls. In the same model the estimate for proportion of heifers were −0.479 ($p = 0.112$). When running a model where proportion of crossbred bulls is replaced with the raw proportion of crossbred heifers the estimate for proportion heifers was −0.642 ($p = 0.007$). And running the model with total number of crossbreds across both sexes in addition to farm size and suppliers rendered an estimate for crossbreds (square root transformed) of −0.470 ($p = 0.0336$). No changes in the estimates for farm size and suppliers exceeding the previously noted 11.20 % were found in these alternative models.

4. Discussion

4.1. The study population

In this study, we found an association between AMU and increasing farm size and number of suppliers, as well as a lower proportion of crossbred bull calves. The study population consisted of 151 sites belonging to 118 rosé veal farms, including 82,605 year-animals in total. To the best of our knowledge, this is the first study to explore these explanatory variables aggregated at farm level in a multivariable model. Because the study was based on surveillance data for the entire Danish cattle population, we assume that the study is representative for farms that fall within the inclusion criteria under conditions similar to the Danish rosé veal production around year 2020.

In Denmark, Danish Holstein Friesian is the predominant dairy breed, followed by Danish Jersey and Danish Red (SEGES Innovation P/S/S/S, 2024). Crossbreeding primarily involves Danish Blue, Charolais, and Angus (Danish Agriculture and Food Council, 2021). Our primary interest was professional rosé veal farms. Fertner et al. (2016) used a threshold of 100 slaughtered bull calves in their study on the Danish rosé veal population. We chose a different threshold (200 year-animals), which was based on two key considerations; 1) The Danish legislation mandates VASCs for these farms and some types of VASCs allows farmers to carry out treatments themselves (for predefined herd diagnoses); 2) Expert opinion about the expected minimum size of a farm, which could correspond to one annual work unit. Additionally, the general trend in Denmark and across Europe is a decreasing number of farms and increasing farm size (Halasa et al., 2020; Neuenfeldt et al., 2019). We expect the farms to have increased in size since Fertner et al. (2016) carried out their study. They found that 325 rosé veal farms were responsible for 51 % of the antimicrobials prescribed for Danish calves and young stock in 2014. Despite our study including only 119 farms, before the exclusion of the extreme value, these were found to have received 52 % of the antimicrobials prescribed for calves and young stock in Denmark in 2020.

The farm type "starter farm" has previously been found to have a higher AMU compared to rosé veal full-line or finisher farms (Bos et al., 2013; Fertner et al., 2016). Fertner et al. (2016) included only "full-line" farms on one site, which were 183 farms out of the study population of 325 farms.

In our study, sites were grouped into farms by ownership, which led to inclusion of sites with "starter-farms". We also included the number of sites in our study as an expression of the level of sectioning as it has previously been documented that shared airspace is positively associated with level of AMU (Lava et al., 2016a). The number of sites showed correlation with the farm size but was not significantly associated with AMU.

Going forward, we suggest that the issue of the rosé veal production chain covering multiple sites is addressed, when evaluating AMU in the cattle sector.

Our final model had a Multiple R-squared of 0.3568, which explains the variation to a moderate degree. Reintroducing the outlier farm had little impact on the model results.

Our study population appeared very heterogeneous when the included variables were investigated (See Table 2). This issue in the Danish rosé veal population was also pointed out by Fertner et al. (2016). We attempted to reduce the heterogeneity prior to modelling by including only assumed professional rosé veal farms.

Other studies have documented large variations in AMU between rosé veal productions within the same population (Bos et al., 2013; Fertner et al., 2016). Potential confounders include: differences in housing, climate, logistics, management, feeding, vaccination strategies, and treatment practices (Lava et al., 2016a; Mallioris et al., 2022; Redman-White et al., 2023). Other factors potentially contributing to the spread of infectious diseases, and hence the AMU, could be proximity to other farms or local density of animals (Boklund et al., 2013), sharing of equipment, and social interactions between farmers (Brennan et al., 2008). Generally, disease occurrence and biosecurity are closely linked. Examples of important areas of biosecurity, which are not included in this study are animal movement, restrictions on visitors, management of direct and indirect animal contact, and cleaning and disinfection (Damiaans et al., 2019).

Finally, diverging attitudes towards AMU and AMR amongst farmers have also been suggested as an important area for further study, when examining differences in AMU between farms (Skjølstrup et al., 2021).

4.2. Effect of farm size and number of suppliers on AMU

Trading and movements of animals has been linked to the spread of infectious disease (Fèvre et al., 2006). Following this, farms would often have higher frequency and a more diverse presence of infectious diseases with increased trading of animals i.e. a larger number of suppliers. We expect an increased infection pressure with increased number of suppliers to be an important driving factor behind the demonstrated positive association between AMU and the number of suppliers. This association was also commented upon by Fertner et al. (2016).

The effect of the number of suppliers could be confounded by the disease status of the individual origin farms, where purchase from a farm with a high health status could result in a lower risk of introducing infectious diseases compared to a high disease prevalence herd (Mee et al., 2012).

Our finding of increasing AMU with increasing farm size was in accordance with similar findings from other studies (Fertner et al., 2016; Hommerich et al., 2019). If we consider farm size as an expression of the density of the host, frequently used to express the contact rate i.e. disease transmissions, it is worth noting that for different infectious agents and transmission routes the transmission rate will vary (Brooks-Pollock et al., 2015; Damiaans et al., 2019). In addition, previously mentioned confounders may also be important to consider here.

The farm size and the number of suppliers were found to be correlated in our study, but the correlation was below our chosen threshold for excluding variables. Fertner et al. (2016) excluded the number of suppliers due to correlation with the number of calves entering the farm. We ran two alternative models excluding the variables in turn and found the variables confounded the estimates of each other, which supported our decision to keep both variables in the final model. Had we removed one of these variables we would have underestimated the effect of the other. We tested for interaction between the two variables in our model and it was not significant. Our interpretation is that the effect of these two variables should be seen in combination. One could interpret the combined effect of number of suppliers and farm size on AMU as an expression of the combined effect of important external and internal biosecurity measures.

Concerning contact rates and transmissions routes for contagious diseases, it is relevant to look at other factors such as traffic within and between farms i.e. veterinarians, non-professional visitors, and trucks transporting e.g. manure or feed (Boklund et al., 2013). These factors may in some cases be correlated with farm size, as we expect more traffic in a larger farm.

Generally, there are few studies which address disease transmission within and between farms simultaneously (Brooks-Pollock et al., 2015). Thus, this would be an interesting area for further study.

4.3. Effect of breed and sex

We found that an increase in the proportion of crossbred bulls in the herd was associated with a reduction in the AMU, while the proportion of heifers did not show a significant association in the univariable analysis of the categorized variable. However, raw data analysis indicated a potential effect, suggesting that the categorization might have masked this association. On the other hand, the highly homogeneous breed composition of heifers (91 % crossbred) combined with the heavily left skewed heifer proportion distribution (i.e. 15.3 % farms with <1 % heifers) led us to focus on bulls to enable exploring potential associations between both breed and sex effects on AMU.

Unfortunately, it turned out that we were not able to separate the associations with AMU for breed and sex in the model, because these two explanatory variables were correlated to some extent. After several modelling steps, where we tested the different breed and sex-combinations, and log-transformed the variable proportion of crossbred bulls, the best fitting model was developed. An additional argument for using the proportion of crossbred males in our model is that they comprised 24.1 % of the population, compared to 12.5 % heifers. The use of sexed beef semen selecting for males will likely increase the crossbred male proportion even further in the future (VIKINGGENETICS innovative breeding, 2024).

Bokma et al. (2019) reported increased AMU for beef breeds (Belgian Blue) compared to crossbreeds (Holstein Friesians x Belgian Blue) and dairy calves (Holstein Friesians). Their multivariable model, which also accounted for effects of year, month of arrival and producer, showed overlapping confidence intervals for dairy and crossbred calves. Hence, they did not find much difference between the breeds relevant under Danish conditions.

Running our model with the total proportion of crossbreds instead of male crossbreds showed similar results, i.e. an increase in crossbreds associated with decreased AMU. Factors such as housing, management, or logistics could confound the observed association. For instance, Bokma et al. (2019) suggested different treatment thresholds based on calf worth, which might explain a higher focus on disease management for crossbred veal calves due to their higher value.

Diana et al. (2021) found lower treatment incidence in heifers versus bulls in beef cattle. However, their study on older beef breeds may not be directly relevant to our younger population, as Fertner et al. (2016) found Danish rosé veal calves to have a median age of approximately one month at entry into starter farms or full-line farms. This was confirmed in a Danish benchmarking report based on data from 40 Danish rosé veal farmers that noted a similar mean age at entry and reported a mean entry bodyweight of 66 kg for 2020 (Myhlendorph-Jarltoft, 2022).

To summarise, the observed effect of proportion of crossbred males on AMU for a rosé veal farm was correlated with the proportion of heifers present and should thus be interpreted with care. Further studies are warranted, ideally, in a setting where stratification of data by both sex and breed is possible, while also considering the potential effect of age.

4.4. Effect of mortality

We did not find an association between mortality and AMU-level. We wanted to relate mortality to the number of animals passing through the farm i.e. animals at risk. The number of year-animals could be significantly lower than animals at risk since the production cycle per fattened animal was less than one year. Data structure necessitated replacing number of animals entering the farm with the number of animals leaving the farm (animals which died on-farm from natural causes, were euthanised, or transported for slaughter) in our calculations of mortality. This did not account for live animals not intended for slaughter leaving the farm, but we expect this number to be negligible in professional Danish rosé veal productions.

Before the study, we hypothesized that increased occurrence of disease would lead to increased treatment frequency and mortality. This association has previously been documented (Jarrige et al., 2017; Santman-Berends et al., 2018). Bokma et al. (2020) documented both no association and a positive association between AMU and mortality in two different veal companies in the same study.

We also considered that the use of antibiotics could have a protective effect against death and thus, a low mortality could be seen with a high AMU. Opposite effect on mortality for different antibiotic classes has been documented (Bokma et al., 2019).

These conflicting findings of association between mortality and AMU emphasizes the complexity of this area. A potential association is likely influenced by several other factors such as when and how animals die during the production cycle. Mortality could be impacted by differences in farm-level management approaches to culling of e.g. chronically or severely infected animals and, additionally, by how (and if) euthanasia is recorded for a farm. Others have commented on farm-level management and housing information confounding the effect of mortality (Bähler et al., 2012; Bokma et al., 2019; Jarrige et al., 2017; Lava et al., 2016b).

Differences in calculations and definitions of mortality have been used (Bähler et al., 2012; Bokma et al., 2019; Jarrige et al., 2017; Lava et al., 2016b). This is an important consideration when investigating association with AMU. Understanding how and which data is recorded at the death of an animal and ensuring a uniform reporting of mortality would ease interpretation and comparison across studies.

4.5. Changes since 2020

From 2014 to 2022, daily doses for young stock younger than one year increased by 29.65 % (DANMAP, 2023). The Danish cattle sector has targeted a 10 % reduction of total AMU for the group from 2021 to 2023 (DANMAP, 2022). This goal has unfortunately not been met. However, the cattle sector has managed to phase out the use of 3rd and 4th generation cephalosporins as these have not been prescribed since 2019 and use of fluoroquinolones is close to zero (DANMAP, 2022). Despite not obtaining a reduction in AMU the sector attempts to mitigate AMR through other initiatives.

An EU regulation (Council Regulation (EC) 6/2019) implemented in Denmark by January 2022 and the Danish authorities' interpretation of it has sparked debate within the Danish cattle sector. Of particular concern amongst farmers and veterinarians is Article 106 stating that they cannot deviate from a product's marketing authorisation with respect to dose and treatment duration. According to some farmers and veterinarians this limits their action options cannot base their treatment strategies on professional knowledge and experience. One argument is that this will decrease the efficiency of treatment and increase the overall AMU. Future reports of AMU in Danish livestock will have to address this issue.

Fertner et al. (2016) found usage of vaccines against respiratory disease on only 9.3 % of their study farms and documented no effect of vaccination on AMU in 2014. Since 2014, the Danish cattle sector has worked towards a more systematic implementation of vaccine programs in an attempt to reduce AMU. Jourquin et al. (2023) documented significantly reduced prevalence of pneumonia long-term and increase in cold carcass weight in Belgian commercial Holstein-Friesian veal calves after vaccination against BRSV, BPI-3, and *Mannheimia Haemolytica* in a blinded, placebo-controlled, randomised clinical study. The effect of vaccination on AMU should ideally be assessed through studies of AMU on farms before, during, and after implementing a defined vaccination program. This would, partially, adjust for the large variation between farms demonstrated in this and other studies and thus provide a better assessment of the effect of vaccination.

4.6. Perspectives of the study experience

The idea behind the study was to explore the potential of using existing and continuously gathered surveillance data for the analysis. A benefit of using this type of data is that the study becomes easily reproducible with minimal data management required. In addition, it also reduces the cost of the analyses since minimal funding is required for obtaining data. However, a limitation to this is that the data structure does not allow for stratifying the outcome for each risk factor.

Access to the aggregated farm-level characteristics data supplied for this study from the *Salmonella* Dublin surveillance program (Conrady et al., 2024; Nielsen and Nielsen, 2015) for different time periods will require data agreements and have restrictions on data sharing, which may present barriers for others repeating our study. The data are however, based on data extracts from the CHR and can be reproduced using these data.

This study was done as a cross-sectional study with some inherent limitations. Data spanning longer time intervals and containing repeated records for each farm can be used for cohort studies and potentially reveal more causal effects. However, this could present a challenge with how to handle changes in ownership and in production, e.g. expansions, decrease or shifts in production.

An example of actions to improve current Danish surveillance is shifting focus from site-level to farm-business level. The documented associations could be included in risk assessments and aid decision makers in planning and performing targeted AMU benchmarking, surveillance, and control efforts.

Identifying and quantifying the effect of factors associated with AMU continuously by repeating the performed analyses could help further adapt the surveillance and control efforts.

5. Conclusion

In this study, we found increasing farm size, number of suppliers, and lower proportions of crossbred bull calves statistically associated with increasing AMU in 118 Danish rosé veal cattle farms. However, the proportion of crossbred bull calves was correlated with proportion of heifers on a farm, so separating the effect was not possible in our study setup. Mortality and number of sites in a farm was not associated with AMU. The results highlight an opportunity for continuous evaluation of the development in AMU at farm level and regular evaluation of the associations, which could be used to implement and adapt targeted AMU monitoring and control.

The main strength of the study was that it was done at aggregated farm level as opposed to individual farm site level. Reporting AMU for farms in a Danish setting allows the entire fattening period within each production to be assessed, which could improve benchmarking efforts and overall understanding of developments in AMU.

Ethics approval

Ethics approval has been obtained from the Research Ethics Committee for SCIENCE and SUND at University of Copenhagen [Journal no. 504–0330/22–5000]. The project is registered in the University of Copenhagen's joint record of biobanks and record of research projects containing personal data.

Data and code availability

Data cannot be provided, because they belong to the farmers and were obtained from the DCDB, supplied by SEGES Innovation P/S (https://segesinnovation.dk/) through a data sharing agreement with the University of Copenhagen, where data sharing with third parties was not permitted.

Questions regarding the software coding process and structure can be directed to Jeanette Kristensen at jp@sund.ku.dk

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CRediT authorship contribution statement

Liza Rosenbaum Nielsen: Writing – review & editing, Supervision, Project administration, Funding acquisition, Conceptualization. **Amanda Brinch Kruse:** Writing – review & editing, Supervision, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Anne Mette Hostrup Kjeldsen:** Writing – review & editing, Methodology, Formal analysis. **Jeanette Kristensen:** Writing – original draft, Visualization, Validation, Software, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Declaration of Competing Interest

The authors of this research article have no financial or personal interests that could have influenced the output of this paper.

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12.2. Manuscript III

Evaluation of the accuracy of a standard metric (ADD200) to monitor on-farm use of antibiotics for Danish rosé veal calves less than one year old

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Abstract

Antimicrobial resistance (AMR) poses a global threat to human and animal health. Antimicrobial use (AMU) is associated with AMR necessitating initiatives and interventions to ensure that it is prudent. Monitoring of AMU is frequently used as an important tool for planning and implementing these. This requires a nuanced understanding of the reflection of on-farm AMU in AMU monitoring. Typically, AMU monitoring features standardised metrics. The choice of metrics and their calculations has previously been shown to affect the succinct interpretations of on-farm AMU making it relevant to assess each metric used and the factors influencing it.

In this study, we evaluate of the accuracy of a Danish standard metric from the national monitoring system VetStat, Animal Daily Doses for 200 kg animals (ADD200), when it is used to monitor on-farm use of antibiotics. ADD200 should, ideally, express the number of daily treatments carried out. We compared ADD200 with treatment records from a study population of 27 Danish conventional rosé veal farms with digital recording of treatments of individual calves in the Danish Cattle database (DCDB). We divided the administered doses from the treatment records with the specific amount in an ADD200 given for each product in VetStat to calculate UDDprop. The median was 1.1 UDDprop and the mean was 1.27 UDDprop showing a general overestimation of the number of daily treatments with ADD200. The average age at treatment was 86 days at which the expected weight is substantially below 200 kg used in ADD200 calculations. This should theoretically have resulted in an underestimation of number of daily treatments in contrast to our findings. In univariable analyses, we found a positive association between calf age (proxy of weight) at treatment and log(UDDprop) and for antibiotic class of product, location of disorder treated, and route of administration used for treatment, log(UDDprop) was found to vary significantly between categories indicating an effect on UDDprop by all tested variables. We built a Linear Mixed-Effects Model on data with injection treatments of lung disorders, which included most of the treatment records and found antibiotic class and calf age at treatment significantly affecting UDDprop. The use of macrolides was overestimated with ADD200, and we suggest that the use of prolongated products may explain some of this. Farm was included as a random effect and explained 61.2% of the variation observed in our model study data, underscoring the relevance of addressing farm-level factors influencing AMU.

Key words

Antimicrobial use, Rosé veal, Bovine calves, Database, VetStat, Standard dose, Used dose, Linear mixed-effects model, Denmark

List of abbreviations

ADD: Animal Daily Dose per kg animal

ADD200: Animal Daily Dose per 200 kg animal (Danish standard weight for calves aged less than one year)

AMU: Antimicrobial use

AMR: antimicrobial resistance

ATCvet: Anatomical Therapeutic Chemical Classification System for veterinary medicinal products

CHR: The Danish Central Husbandry Register

DCDB: The Danish Cattle Database

DOT: Days of treatment

VetStat: The Danish Veterinary Medicines Statistics Program

1. Introduction

Antimicrobial resistance (AMR) claims an increasing number of lives globally each year, and this development is projected to continue unless we intervene (Naghavi et al., 2024). Combating AMR is a multifaceted challenge, but ensuring prudent antimicrobial use (AMU) is a key action point, as AMU is an important driver of AMR (Xiong et al., 2018). A robust and reliable system for monitoring AMU is essential for identifying usage patterns and understanding the driving factors (Werner et al., 2018). Thus, monitoring AMU serves as a critical tool for stakeholders seeking to design and implement effective regulations, initiatives, and policies that promote prudent AMU in both animal and human health contexts (World Health Organization, 2022; World Organisation for Animal Health, 2022). However, accurate interpretation of AMU data depends on a nuanced understanding of how the monitoring data reflect actual use, including AMU practices in livestock farms.

Veal farms contribute greatly to the total AMU in Danish cattle; 127 veal farms were responsible for 52% of the total AMU in Danish cattle youngstock in 2020 (Kristensen et al., 2025), and similar results were reported by Fertner et al. (2016). At the same time, Carmo et al. (2018) found a potential for reducing AMU in the Danish veal production. Following this, we decided to focus this study on AMU in rosé veal calves, which is the primary meat type produced from cattle youngstock in Denmark.

Standardised metrics feature in most AMU surveillance and reporting, but unfortunately, standardisation varies between countries and sectors (Collineau et al., 2017; Merle et al., (2012); Postma et al., 2015). AMU is often reported as either dose-based or use-based, where dose-based reporting uses standard doses of specific product or active compound given per animal or kg animal, whereas use-based reporting counts the number of treatments given (Werner et al. 2018). Typically, AMU doses are related to the size of the population given as e.g. number of animals or by a population correction unit.

An example of an AMU surveillance system is the Danish VetStat database owned by the Danish Veterinary and Food Administration (DVFA). VetStat contains compulsorily collected records of all sales of prescription medicine for animals (Dupont & Stege, 2012). Data from VetStat is used for annual reporting of AMU in the Danish Integrated Antimicrobial Resistance Monitoring and Research Programme (DANMAP) and for farm-level continuous surveillance of AMU-levels used mainly by veterinarians providing advisory services to farmers (DANMAP, 2023).

For cattle, another reliable source with information about farm-level AMU is the Danish Cattle Database (DCDB) (Frandsen, 2013). It is owned by the Danish Agriculture & Food Council (DAFC), who represent the farming and food industry, and managed by the private research and innovation company SEGES Innovation P/S. Records on medicine use in DCDB are private and for the most part voluntarily reported electronically; large proportion of Danish cattle farmers and their veterinarians record treatments in DCDB (Henningsen et al., 2024). Detailed and reliable on-farm treatment records have previously been underscored as important for evaluation of AMU metrics (Redding et al., 2020). Access to data from both VetStat and DCDB offers a unique possibility for comparing the standard doses used in VetStat with the recorded on-farm AMU listed with specific doses per treatment.

In VetStat, a dose-based measure, Animal Daily Doses (ADD), is defined for marketed products containing antimicrobials based on their Summary of Product Characteristics (SPC), which contain the recommended dosage. ADD is reported by species and age groups with standardised weights, both in VetStat and in other countries. Different classifications of cattle into subgroups are used around the globe, and the assigned standard weights differ markedly (Lardé et al., 2020). In VetStat, the standard dose to treat cattle less than one year old is calculated using the standard weight 200 kg (ADD200). This weight is most likely an overestimation of the mean weight at treatment in veal production, because most calves are treated young when they weigh less than 200 kg, and this would lead to an underestimation of number of treated calves, when using ADD200 to monitor AMU. Jarrige et al. (2017) estimated the mean weight at treatment in French white veal calves to be 100.4 kg overall, but with different mean weights at treatment depending on the antibiotic class used for treatment. The impact of the animal weights on AMU metrics has previously been demonstrated in other countries (Brault et al., 2019; Jarrige et al., 2017). Fertner et al. (2016) hypothesised an issue with standard weights in a Danish context, but it has not been further investigated.

Another issue is that the standard doses, such as ADD200, may not always reflect the on-farm used daily doses per animal (UDD) (Apley et al., 2023). The relationship between used doses and standard doses has previously been shown to vary between antibiotic classes (Becker & Meylan, 2021; Redding et al., 2020; Timmerman et al., 2006), and the product indication has been suggested to affect the ranking of farms when different AMU metrics were applied (Apley et al., 2023). The route of administration is frequently considered when developing standard doses (Becker & Meylan, 2021; Lardé et al., 2020; Postma et al., 2015). Finally, different farm characteristics, such as organic status, size of production, breed, sex and arrival time, number of calves introduced, mixing of calves, biosecurity, nutrition, housing, and farmer and veterinarian attitudes have also been found to influence AMU (Kristensen et al., 2025; Redman-White et al. 2023). Becker & Meylan (2021) investigated agreement between on-farm and standardised treatments in 38 Swiss veal farms, while stratifying by antibiotic class and route of administration. They found the agreement to be affected by both, but they did not address the effect of farm. Jarrige et al. (2017) found that “farmer” introduced in a linear mixed effect model explained a significant part of the variation in the AMU metric “number of antimicrobial treatments prescribed per calf”. They did, however, not stratify by antibiotic classes and their data were based on veterinary prescriptions and dispensing records instead of treatment records.

The purpose of our study is to facilitate the implementation of relevant and efficient initiatives promoting prudent AMU. Building on insights from previous studies, we aim to improve the understanding of factors affecting the relationship between on-farm used doses and standard doses in veal calf production. This will improve the overall understanding of AMU practices and implications for AMU surveillance. The specific objective is to evaluate the Danish metric ADD200 with particular focus on its accuracy in describing the doses used for daily on-farm treatments and factors affecting the accuracy. Our approach was to compare VetStat standard doses with treatment records from a study population of Danish conventional rosé veal farms with digital recording of treatments of individual calves in the DCDB using a linear mixed model.

2. Materials and methods

The core of evaluating methods for standardising AMU reporting is understanding the link between the AMU on-farm and the calculated AMU using standardised metrics. We have conducted a quantitative study, where information on farm-level treatments is translated to standardised metrics and the relationship with potential influencing factors examined using a multivariable linear mixed effect analysis.

The metric evaluated in this study was ADD200, and the two key components used in calculating it were (Equation 1):

Equation 1: $ADD200 = ADD_{Product} * Weight_{Standard}$

Where,

ADD200: Standard dose in VetStat to treat one animal for one day

$ADD_{Product}$: Standard dose in VetStat to treat one kg animal per day assigned to each unique product

$Weight_{Standard}$: Standard weight of an animal in VetStat; 200 kg for calves and youngstock

We evaluated both ADD and weight. We did not have access to data on weight at treatment for the animals, as these are not routinely and systematically recorded. The age of the calves at treatment was chosen as a proxy for animal weight.

2.1. Study design and data collection

The study was a cross-sectional study on digital farm-level treatment data collected from January 1st, 2023, to December 31st, 2023, and stored in the DCDB. The source population was professional Danish rosé veal farms. The study population was identified using data from the Danish Central Husbandry Register (CHR), which contain mandatory records for all Danish livestock farms. The farms had: one or more herds (separately registered group of animals in CHR) registered as veal productions with 200 or more calves/youngstock stabled, no changes in owner or affiliated veterinary practice, and changes in herd size not exceeding 25%. From the farms eligible for inclusion 60 farms were selected randomly and recruiting was done by phone. The recruiting and interview process is further detailed in Kristensen *et al.* (n. d.).

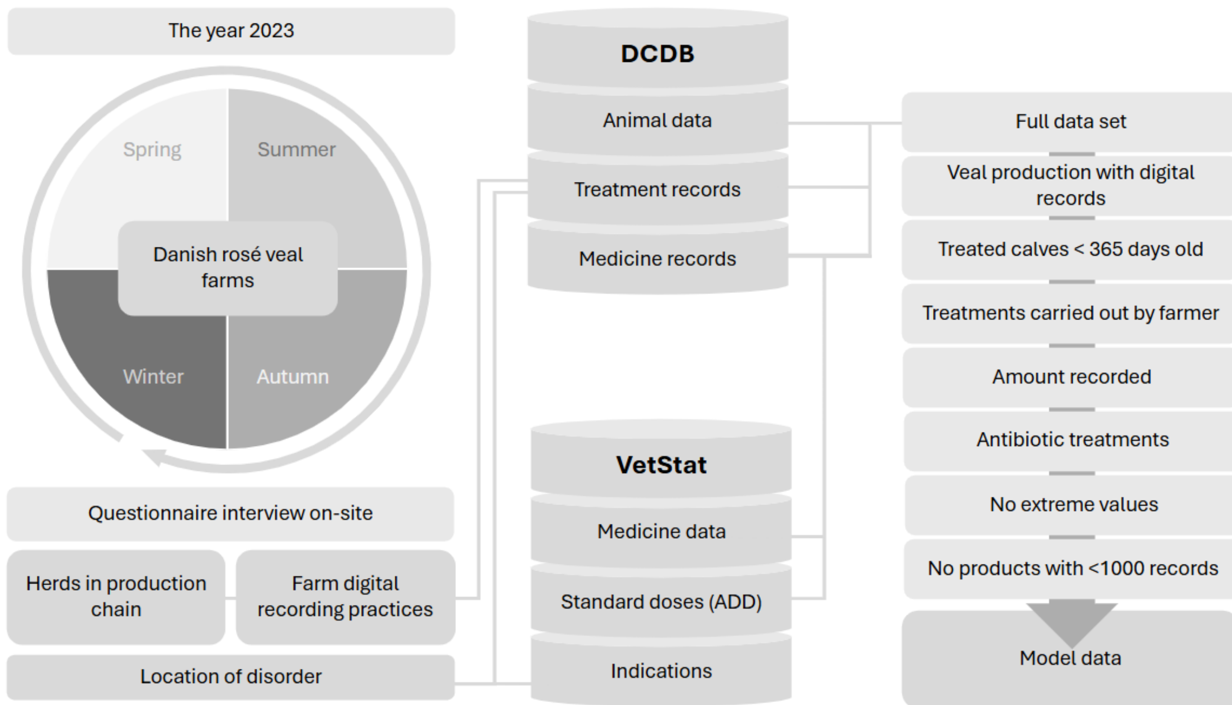

Figure 1: Study design illustrating origin of data and the process of merging and applying inclusion criteria to model data

An on-site questionnaire-based interview was conducted by the first author on the study farms during spring and early summer 2023. Only farms reporting routine use of digital treatment recording in DCDB were included, and from these farms only herds, which were identified by the interviewees as part of the production chain, were included in the study.

Data were extracted from DCDB and provided by SEGES Innovation P/S in May 2024 as three datasets: one containing information on individual animals (herd, animal, birthday), one containing data on treatments (herd, animal, treatment date, treatment responsible, diagnosis), and one linking treatment records to products and amounts used (product, amount, indication). The products in the DCDB dataset were merged with product information and standard doses extracted from VetStat (product, antibiotic class, ADD200) to facilitate translation of used amounts for treatment to standard doses used in VetStat.

From the full dataset only records fulfilling the following criteria were included: age of the calf at treatment had to be less than 365 days; the treatment had to be carried out by the farmer; the amount used had to be listed; only treatments with antibiotic products having an ADD; only treatments within limits indicating extreme outliers; only records with products with 1000 observations or more. Data were assessed for extreme outliers, defined as amounts exceeding twice the 99th percentile observed for each product. These outliers were excluded from the analysis.

2.2. Study model data

Each treatment record included in the final study data contained: Treatment date, unique animal identification, birthday of animal, farm, diagnosis, location of disorder, and VetStat indication. If a treatment consisted of multiple products a separate row in data was included for each product. For all treatments each row had information on: amount used for treatment, product, antibiotic classification.

2.2.1. Outcome

The outcome variable used to express the relationship between observed amount used for treatment on-farm and the standard metric was defined as a proportion and calculated as (Equation 2):

Equation 2: $UDDprop = UDD_{amount}/ADD200$

UDD_{prop}: Proportion of an ADD200 per product used for a treatment of one calf for one day
UDD_{amount}: Amount of a specific product used to treat one animal for one diagnosis on one day according to data extracted from DCDB
ADD200: Standard amount of a specific product to treat one animal aged less than one year for one day extracted from VetStat

UDDprop is thus an expression of the number of VetStat standard doses used per performed treatment according to the record in DCDB.

2.2.2 Explanatory variables

The explanatory variables included in this study were: Age at treatment, antibiotic class, location of disorder and route of administration. Age at treatment was calculated from DCDB data as the time difference in days between the birthday of the animal and the treatment date. Only data where age at treatment was less than 365 days were included; veal is defined as meat of bovine animals less than one year of age in the European Union (Council Regulation (EC) 1308/2013).

Antibiotic class was extracted from the product data in VetStat and corresponds with the classifications used in the Anatomical Therapeutic Chemical Classification System for veterinary medicinal products Index (ATCvet) published by the Norwegian Institute of Public Health WHO Collaborating Centre for Drug Statistics Methodology (NIPH, n. d.).

DCDB treatment data contained diagnoses defined by codes unique to DCDB (LK codes). These were correlated with the DCDB medicine data to VetStat indications. An additional classification method was proposed based on the location of the disorder (Table 1). The main reason for adopting this approach was the diversity of diagnoses observed within the indication "Joints, limbs, hoof, central nervous system, skin". Significant differences in the used treatment protocols in this indication group were hypothesised.

Table 1: VetStat indications and corresponding locations of disorder which are based on diagnoses observed in DCDB.

VetStat indication	**Location of disorder**
Replacement code	Medicine, correction
Reproduction and urogenital system	Reproductive organs
	Urinary tract
Udder	Udder
Gastrointestinal disorders	Gastrointestinal
Respiratory disorders	Lungs
Joints, limbs, hoof, central nervous system, skin	CNS
	Ears
	Eyes
	Hoofs
	Limbs
	Skin
Metabolism, digestion and circulatory system	Digestion
	Metabolism
Other	Other
Vaccines and sera	Vaccination

2.3. Statistical methods

The statistical software R (4.4.2) and R-Studio (2024.12.0.467) was used for all data management and analysis (R Core Team, 2024; Posit team, 2024). The package "tidyverse" (Wickham et al., 2019) was used for data management and "ggplot2" (Wickham, 2016) and "patchwork" (Pedersen, 2024) were used for visualisation and "flextable" (Gohel & Skintzos, 2024) and "sjPlot" (Lüdecke, 2024) for tables. Statistical analyses were carried out using the packages: "car" (Fox & Weisberg, 2019), "lme4" (Bates et al., 2015), and "lmerTest" (Kuznetsova et al., 2017).

2.3.1. Descriptive statistics

Outcome and the continuous explanatory variable were assessed for distribution; relevant transformations were determined visually through histograms. Presence of extreme values was visually assessed. Separate visual analyses were conducted for all explanatory variables against UDD_{prop}. A scatterplot was created for age at treatment and violin plots were used for antibiotic class, location of disorder and route of administration.

2.3.2. Univariable analyses

Univariable analyses against the outcome was conducted for all explanatory variables with visual evaluation of the relationship. Linear regression was carried out for UDD_{prop} against age at treatment. For antibiotic class, location of disorder and route of administration ANOVAs were carried out. For the indication group "Joints, limbs, hoof, central nervous system, skin" differences in mean UDDprop between the four major locations: Ears, eyes, hoofs and limbs were tested with an ANOVA followed by a Tukey's Honest Significant Difference (HSD) test (Tukey, 1949).

2.3.3. Independence

The variables were tested pairwise for independence with a X^2-test; to allow this age at treatment was converted to categorical variable with four levels based on quartiles. All strata were examined pairwise for presence of records. Independence was defined as $p > 0.05$. If significant correlation was found between categorical variables, the variable deemed most relevant was kept in the model.

2.3.4. Linear mixed-effects model

A linear mixed-effects models was build adding farm as a random effect to account for similar observations within farm in the model. Both intercept and slope of the random effect was included in the model.

Equation 3:

$$\log(\mathit{Lungs}\mathrm{UDD}_{prop}) = \beta_0 + \log(\beta_{Age}) + \beta_{Antibiotic\ class} + \log(\beta_{Age})*\beta_{Antibiotic\ class} + \mu_{Farm} + \mu_{Farm}*\log(\beta_{Age})$$

> $\log(\mathit{Lungs}\mathrm{UDD}_{prop})$: Proportion of an ADD200 per product used for a treatment on lungs in one calf on one day, log-transformed in model.
> β_0: Intercept
> Log(β_{Age}): Age of calf at treatment in days, log-transformed in model
> $\beta_{Antibiotic\ class}$: Antibiotic class of the product based on VetStat antibiotic classes
> μ_{Farm}: Farm the treatment is carried out on (intercept)
> μ_{Farm*} log(β_{Age}): Farm the treatment is carried out on (slope)
> e: Residuals

The model was built following a forward stepwise approach (Dohoo et al., 2014). Firstly, based on univariable and independence analyses categorical variables eligible for inclusion in the model were identified and added to the model as fixed effects along with farm as a random effect. For farm expressions both different intercept and slope were included. The categorical fixed effects were antibiotic class, location of disorder and route of administration. Data was assessed for data distribution within strata of the different categorical variables. If a model could be built using data with one level of the variables not included in the model this was attempted: a model using treatment data for the location of disorder “Lungs” and route of administration “Injection”. Age at treatment was introduced to the model and independence between this variable and categorical variables was determined using variance inflation factors (VIF); a VIF <5 was criteria for keeping age in the model. Relevant interactions identified through visualisation of raw data were then introduced to the model and kept at a significance level of $p < 0.05$. Akaike Information Criterion (AIC) was calculated for each model step described and the model with the lowest AIC was selected (Akaike, H., 1974).

3. Results

3.1. Study population

3.1.1. Farms and herds

During a questionnaire interview in 36 Danish rosé veal farms conducted in the spring and early summer 2023, 28 farms reported use of systematic digital recording practices providing data into DCDB. One farm was later excluded, as it had no records in DCDB. The final study population therefore consisted of 27 farms. The full production chain of the 27 farms encompassed 46 herds. From these, 37 herds had both animal and treatment records in the DCDB during 2023. Five herds had missing animal data due to authority-approved combined production agreements ("Samdrift"), which allows for all data including animal location to be registered on one of the herds in the combined production. Two herds had animal data before but not during 2023. The final two herds were excluded due to missing treatment data.

3.1.2. Animals

In the DCDB animal data, 63,492 unique animals aged less than one year during 2023 were identified across the study farms, in total 26,552 animal-years; where animal-years is a sum of days present on-farm for all animals aged less than one year. Descriptive summaries of the study farms and herds based on DCDB animal data are given in Table 2. The calves were mainly crossbred bulls (32.9 %) and large-breed dairy bulls (32.4%). Large, crossbred heifers constituted 20.4%. The remaining calves were primarily small dairy crossbreds (11.3%). For farms consisting of multiple herds, one herd per farm had median age of calves at arrival ranging from 21 to 30 days corresponding to a starter stable. The other herds received calves with median ages ranging from 78 days to 243 days corresponding to middle or finisher stables.

Table 2: Summaries for farms with number of animal-years, herds and percentages for distribution on sexes and breed

Variable	Min	Q1	Median	Mean	Q3	Max
% of study population animal-years	1.0	2.0	2.0	3.7	5.5	12.0
Number of herds	1	1	1	1.4	2	4
Number of animal-years	206	488	620	983	1,442	3,191
% bulls	0.2	73.6	78.9	76.5	82.7	100.0
% large dairy	2.6	26.8	40.4	38.7	48.4	75.0
% cross-bred	25.4	50.5	59.5	59.8	70.5	97.3
% 'other' breed	0.0	0.0	0.1	1.5	0.6	28.3

3.2. Descriptive statistics

3.2.1. Antibiotic use and sale

During the study period a total of 203,371 ADD200 were recorded sold via a pharmacy to the study farms, which corresponds to 15.2% of the total number of ADD200 sold in Denmark to treat cattle aged less than one year. The recorded use on-farm by farmers for calves aged less than one year for the study population in DCDB was 3.9% lower than the sale recorded in VetStat; this number included extreme values excluded later in our analysis. A total number of 151,937 treatment records were identified. There was no sales data in VetStat from the six herds in combined production.

The percent difference between used and sold ADD200 varied between study farms; min (-26.8%), Q1 (-3.8%), median (2.4%), mean (5.1%), Q3 (14.3%), max (37.4%). The number of days of treatments (DOT) defined as one animal treated for one diagnosis for one day was 150,044 DOT. For Danish rosé veal cattle, the number of DOT will be close to number of treatment records as combination treatments resulting in multiple records per DOT are rarely. The summaries for the study population by antibiotic class can be found in Table 3.

Table 3: Daily doses of Antibiotics used and sold in the study population for calves aged less than one year by antibiotic classes

Antibiotic	ATCvet	DOT[1]	Used ADD200	Sold ADD200	% diff. sold vs. used ADD200	% of DK sold ADD200
Amphenicols	QJ01BA	57,695	82,089	78,883	-4	19
Beta-lactamase sensitive penicillins	QJ01CE	14,815	24,630	27,029	9	13
Combinations of antibacterials	QJ01RA	7,381	6,652	6,790	2	11
Sulfonamides and trimethoprim, combined	QJ01EW	2,004	952	963	1	3
Macrolides	QJ01FA	32,652	61,535	68,894	11	19
Tetracyclines	QJ01AA	36,293	18,221	19,142	5	14

[1] DOT: Each unique observation of one animal treated for one diagnosis on one day summarised per antibiotic class. The table only includes antibiotic classes with a minimum of 1000 days of treatment; excluded are QA07AA (42 DOT), QJ01CR (183 DOT) and QJ01CA (830 DOT).

3.2.2. Treatment records

From the combined DCDB treatment and medicine data, 285,535 treatment records from 2023 were extracted for the 27 study farms; of these 285,259 treatment records were treatments of animals aged less than one year. No records were lost during the merging of DCDB and VetStat medicine data. Four farms had records with another treatment responsible, primarily the veterinarian. These records constituted a minor proportion of the treatment records (0.8 %); 283,855 treatment records were recorded by the farm personnel, and 283,069 treatment records had an amount recorded. Duplicated records due to duplicated treatment IDs in the DCDB medicine data were negligible but present; 252 records were duplicated of these 240 records were painkillers, 11 records were antibiotics, and one record was ringworm treatment.

In total, 151,905 treatment records contained antibiotics with an ADD200 listed in VetStat medicine data, corresponding to 195,424 ADD200 used of 35 unique products and 150,013 DOT. These were distributed on following routes of administrations: 188,932 ADD200 and 135,082 DOT were injectable antibiotics, 6,491 ADD200 and 15,046 DOT were oral treatments in drinking water or milk, and 10 DOT were spray application products without an ADD. For antibiotics this means oral treatments constituted 3.3% of ADD200 and 10%

of DOT of the total AMU in the treatment records. Seven farms used oral treatment with antibiotics.

After exclusion of extreme values, 151,867 treatment records (99.98%), 194,832 ADD200 (99.7%) and 149,976 DOT (99.7%) remained.

The number of unique products with antibiotics used per herd ranged from 1 to 10 products with a mean of 5.3 products and a median of 5 products in the full data set (285,259 treatment records). A decision was made to exclude products with less than 1000 treatment records, which resulted in a slightly lower mean of 5.14 antibiotic products per herd. After this, the data set contained 150,464 treatment records corresponding to 191,764ADD200 and 148,591DOT with 24 unique products containing antibiotics. Oral antibiotic treatments were carried out on five farms and only for lung disorders: Macrolides (tilmicosin, 250 mg/ml) 1,297 ADD200 and 3,469 DOT and tetracyclines (doxycycline, 500 mg/g) 5,147 ADD200 and 11,352 DOT. Oral antibiotics accounted for 3.4% of the ADD200 and 9.97% of the DOT.

Table 4: Antibiotic treatments in the study farms by summarised as standard doses (ADD200) and days of treatment (DOT)

Treatment type	Dose measure	Min	Q1	Median	Mean	Q3	Max
Antibiotic, injection	ADD200	422	1,597	2,905	6,864	10,321	32,482
	DOT[1]	344	797	2,139	4,958	7,190	22,134
Antibiotic, oral	ADD200	578	719	872	1,289	1,957	2,318
	DOT[1]	1,116	2,353	2,584	2,964	3,035	5,733

[1] DOT: Each observation of one animal treated for one diagnosis on one day

The dataset used in table 4 fulfils all inclusion criteria listed in Figure 1 and corresponds to the data set used in the univariable analyses below.

Records of treatment of lungs constituted 80.34% of the treatment records fulfilling the inclusion criteria listed previously: 151,230 ADD200 and 119,615 DOT. Oral treatments were 4.3% of the ADD200 and 12.4% of the DOT for lung disorder treatments.

Injection treatments for lungs disorders with amphenicols constituting 35% of treatment records, tetracyclines 22.7%, and macrolides 20.8%. Hoof disorders treated with injection beta-lactamase sensitive penicillins constituted 8.4% of the treatment records.

3.2.3. Standard doses used per treatment (UDDprop)

The outcome variable UDDprop reflects the proportion of a VetStat standard dose ADD200 of a given product used per treatment record; calculation on treatment records as opposed DOT allowed stratification by antibiotic class if products from different classes were used in combination. UDDprop summarised across all 150,464 treatment records was; min (0.01), Q1 (0.60), median (1.1), mean (1.27), Q3 (1.8), max (12). The distribution of raw data was left-skewed. After log-transformation a normal distribution was obtained; assessed visually. Log(UDDprop) summarised across all treatments were; min (-4.6), Q1 (-0.5), median (0.1), mean (0), Q3 (0.6), max (2.5). Log(UDDprop) for lungs was; min (-4.6), Q1 (-0.7), median (0.1), mean (0), Q3 (0.6), max (2.5).

3.3. Univariable analyses

In addition to calf age at treatment, antibiotic class, location of disorder and route of administration was tested for correlation with UDDprop in univariable analyses. Violin plots of the raw data distributed in the different strata of the explanatory variables can be seen in Figure 2.

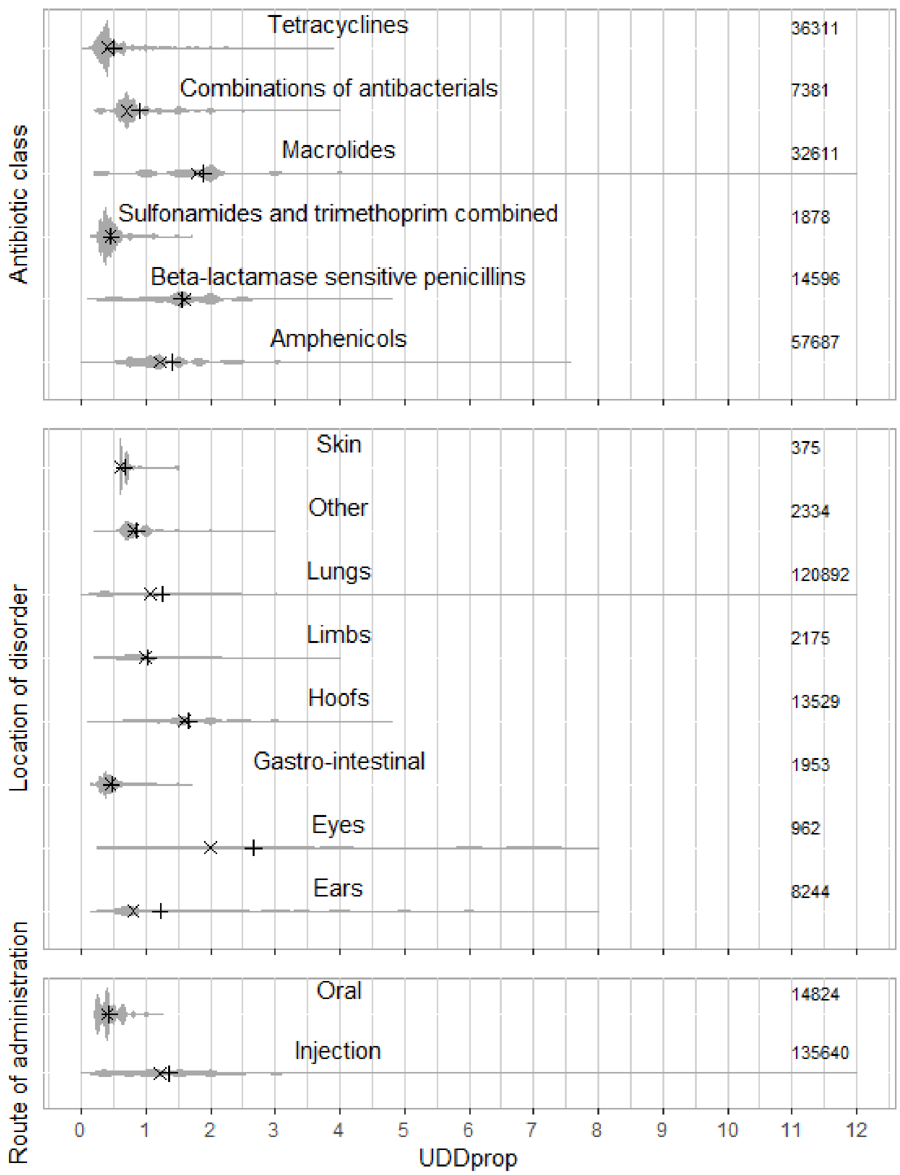

Figure 2: Distribution of used ADD200 per treatment record per antibiotic class, location of disorder and route of administration in violin plots with the antibiotic classes, (+) mean used ADD200, and (×) median used ADD200 layered on top. Numbers to the right are the number of treatment records per group.

UDDprop showed an increase with age in plots of the model data. Large variations in UDDprop were evident; if treatment ages were grouped by 10-day intervals the standard deviations on mean UDDprop in the groups varied from 0.56 UDDprop to 2.08 UDDprop. UDDprop exceeded 2 at ages below 100 days in 14.8% of the records.

A raw distribution of age at treatment showed a left-skewed distribution. After log-transformation a normal distribution was obtained; assessed visually.

A linear regression analysis was carried out on log(UDDprop) versus log(age at treatment). The resulting estimate was 0.27 indicating a positive association between age at treatment and UDDprop. The R-squared was 0.07, $p < 0.001$, and a SE of 0.69.

The UDDprop varied between antibiotic classes with macrolides and beta-lactamase sensitive penicillins having the highest median of 1.88 UDDprop and 1.56 UDDprop, respectively, and tetracyclines having the lowest median of 0.40 UDDprop. Amphenicols had a median of 1.21 UDDprop and a mean of 1.42 UDDprop and contributed with most records; 57,687 treatment records corresponding to 38.3% of the total records.

In an ANOVA, the log(UDDprop) was found to vary significantly between antibiotic classes ($p < 0.001$). The R-squared was 0.49 with a residual SE of 0.51.

The UDDprop varied between locations with eye and hoof disorders having the highest medians of 2.0 UDDprop and 1.60 UDDprop and gastrointestinal having the lowest median of 0.45 UDDprop. Lungs had a median of 1.06 UDDprop and a mean of 1.25 UDDprop and contributed with most records; 120,892 treatment records corresponding to 80.3% of the total records.

In an ANOVA, the log(UDDprop) was found to vary significantly between locations of disorders ($p < 0.001$). The R-squared was 0.06 with a residual SE of 0.70.

An ANOVA, using only data on ears, eyes, hoofs and limbs was carried out. Pairwise comparisons of locations found significant differences in mean between all pairs in a Tukey's Honest Significant Difference (HSD) test.

The mean UDDprop varied for oral and injection antibiotics with injection having the highest median of 1.21 UDDprop and oral having the lowest of 0.43 UDDprop. Injection treatments contributed with most records: 135,640 corresponding to 90.1% of total records. For lung treatments with macrolides the median UDDprop for injection treatments was 1.90 UDDprop and for oral treatments it was 0.30 UDDprop. For lung treatments with tetracyclines the median UDDprop for injection treatments was 0.35 UDDprop and for oral treatments it was 0.40 UDDprop

In an ANOVA, the log(UDDprop) was found to vary significantly between routes of administration ($p < 0.001$). The R-squared was 0.17 with a residual SE of 0.66.

An ANOVA with only records of oral and injection lung treatments with macrolides and tetracyclines resulted in a $p < 0.001$ with an R-squared of 0.16 with a residual SE of 0.78.

3.3.1. Correlation/Independence

The number of records per location and antibiotic class was stratified; 22 out of 48 strata were missing records reflecting that specific antibiotic classes are used for treatment at specific locations. For lungs, all antibiotic classes were present with a minimum of 1,008 records per strata, except "Sulfonamides and trimethoprim combined", which was not used for lungs.

When antibiotic class and route of administration was stratified, all antibiotic classes were used for injection treatments in a minimum of 1,878 records (Combinations of sulfonamides and trimethoprim). Only macrolides and tetracyclines were used for oral treatment with 3,469 and 11,355 records, respectively. Oral treatment was only recorded as carried out for lung disorders and constituted 12.3% of the treatment records for lung disorders.

The calf age at treatment was summarised for all included treatment records by antibiotic class, location of disorder and route of administration.

The mean calf age at treatment in days was 86 days: min (3), Q1 (39), median (66), Q3 (120), max (364). The calf age at treatment in days varied for different antibiotic classes, locations of disorder and routes of administration (Figure 3). For antibiotic classes, beta-lactamase sensitive penicillins had the highest median at 181.0 days and mean at 177.5 days and macrolides the lowest median at 34.9 days and mean 46.2 days. Amphenicols had median 80.0 days and mean 90.6 days. For all locations of disorder, except hoof and eye, the median age at treatment was below 100 days. Skin and gastrointestinal had the lowest medians, 36 and 42 days, respectively. For route of administration the median age was 91 days, with a median of 73 days for injection antibiotics, and 41 days with a median of 35 days for oral antibiotics. In X^2-tests log(age at treatment) grouped by quartiles was significantly correlated with antibiotic class, location of disorder and route of administration ($p < 0.001$). A similar significant correlation between age at treatment and antibiotic class or route of administration was also found when testing only records from the location "lungs".

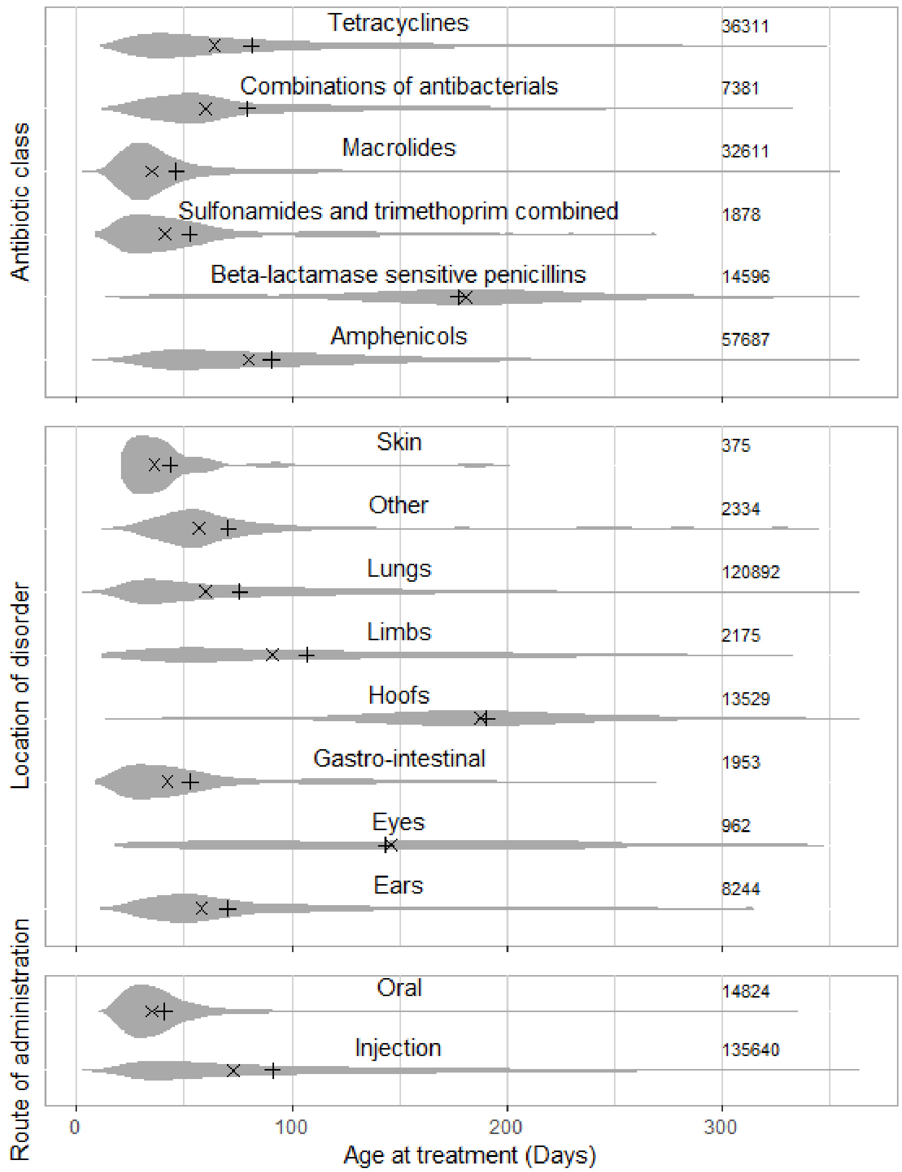

Figure 3: Distribution of calf age in days at treatment summarised per antibiotic class, location of disorder and route of administration in violin plots. (+) mean calf age at treatment, and (×) median calf age at treatment layered on top. Numbers to the right are the number of treatment records per group.

3.4. Linear Mixed-Effects Model

All explanatory variables were tested pairwise and found significantly correlated. Following this, a decision was made to focus on treatments on lungs with injectable antibiotics; 106,068 records. Both outcome and age at treatment were log-transformed in all steps of model-building.

Variance inflation factors (VIF) were examined after introducing both age at treatment and antibiotic class to the model. Using the package "car" a VIF = 1.41 was found; age at treatment was kept in the model. Following this step an interaction between age at treatment and antibiotic class was introduced to the model to allow different slopes of prediction lines for antibiotic classes. The interaction was statistically significant ($p < 0.001$). Farm was introduced as a random effect allowing different intercept and slope of prediction lines. AIC were determined for each step. The last model had the lowest AIC indicating the best model fit. The model parameters are given in table 5.

Table 5: Linear Mixed-Effects Model parameters for model examining the effect of antibiotic class and calf age at treatment on number of standard doses used per treatment while correcting for effect of farm

	UDDprop[1]		
Predictors	*Estimates*	*CI*	*p*
(Intercept)	-1.65	-1.96 – -1.35	**<0.001**
Age at treatment[1]	0.46	0.39 – 0.53	**<0.001**
Antibiotic [Beta-lactamase sensitive penicillins]	-1.32	-1.49 – -1.14	**<0.001**
Antibiotic [Combinations of antibacterials]	-0.18	-0.39 – 0.02	0.080
Antibiotic [Macrolides]	1.06	1.02 – 1.10	**<0.001**
Antibiotic [Tetracyclines]	-1.40	-1.45 – -1.35	**<0.001**
Age at treatment[1] × Antibiotic [Beta-lactamase sensitive penicillins]	0.13	0.09 – 0.17	**<0.001**
Age at treatment[1] × Antibiotic [Combinations of antibacterials]	-0.06	-0.11 – -0.02	**0.004**
Age at treatment[1] × Antibiotic [Macrolides]	-0.10	-0.11 – -0.09	**<0.001**
Age at treatment[1] × Antibiotic [Tetracyclines]	0.08	0.07 – 0.09	**<0.001**
Random Effects			
σ^2	0.09		
$\tau_{00\ \text{Farm}}$	0.64		
$\tau_{11\ \text{Farm*Age at treatment}}$	0.04		
ρ_{01}			
ρ_{01}			
ICC	0.87		
N_{Farm}	27		
Observations	106068		
Marginal R^2 / Conditional R^2	0.297 / 0.909		

[1] Log transformed

In Figure 4 the predicted average UDDprop across farms for each antibiotic class at a given age at treatment are presented. The prediction lines for the antibiotic classes show different intercepts and slopes. Predictions are only made for age intervals with data present in the study data used to create the model. The predicted number of standard doses per treatment exceeds one after around 6 days of age for macrolides, 36 days for amphenicols, 99 days for combination antibacterials, 153 days for beta-lactamase sensitive penicillins, and 285 days for tetracyclines. A figure M3S1F1 with 95% confidence intervals for prediction lines and raw data points is included in the supplementary material.

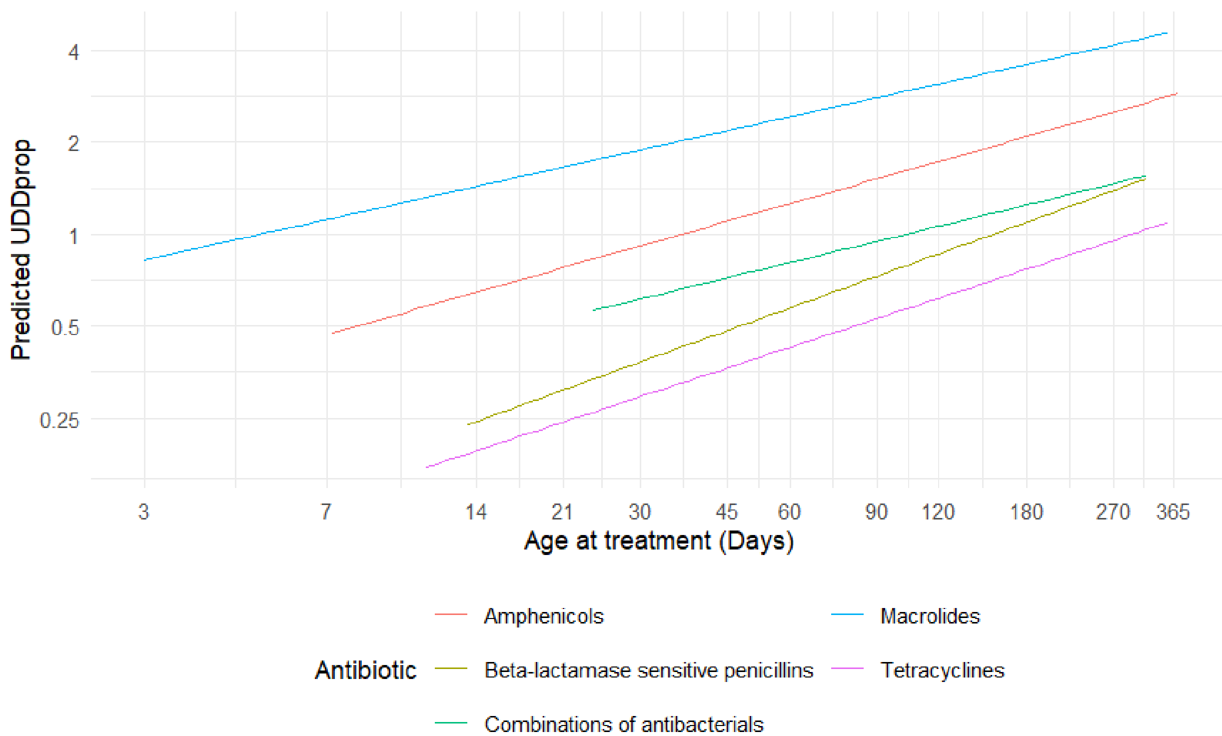

Figure 4: Predicted average number of standard doses used per treatment versus age at treatment in days for antibiotic classes administered as injection for lung disorders in the study population. Note that scales are log-transformed but labelled with non-log-transformed values.

The random effects of farm explain 61% of the variation observed in the model data used for our model. The number of farms with data in each antibiotic class varied: Amphenicols (26), beta-lactamase sensitive penicillins (5), combinations of antibacterials (2), macrolides (23), tetracyclines (17). In Figure 5 the prediction lines for the association between UDDprop and age at treatment for each farm are plotted for the antibiotic class

“Amphenicols”. The prediction lines show different intercepts and slopes. The plot includes only predictions for the age intervals with observations in each farm.

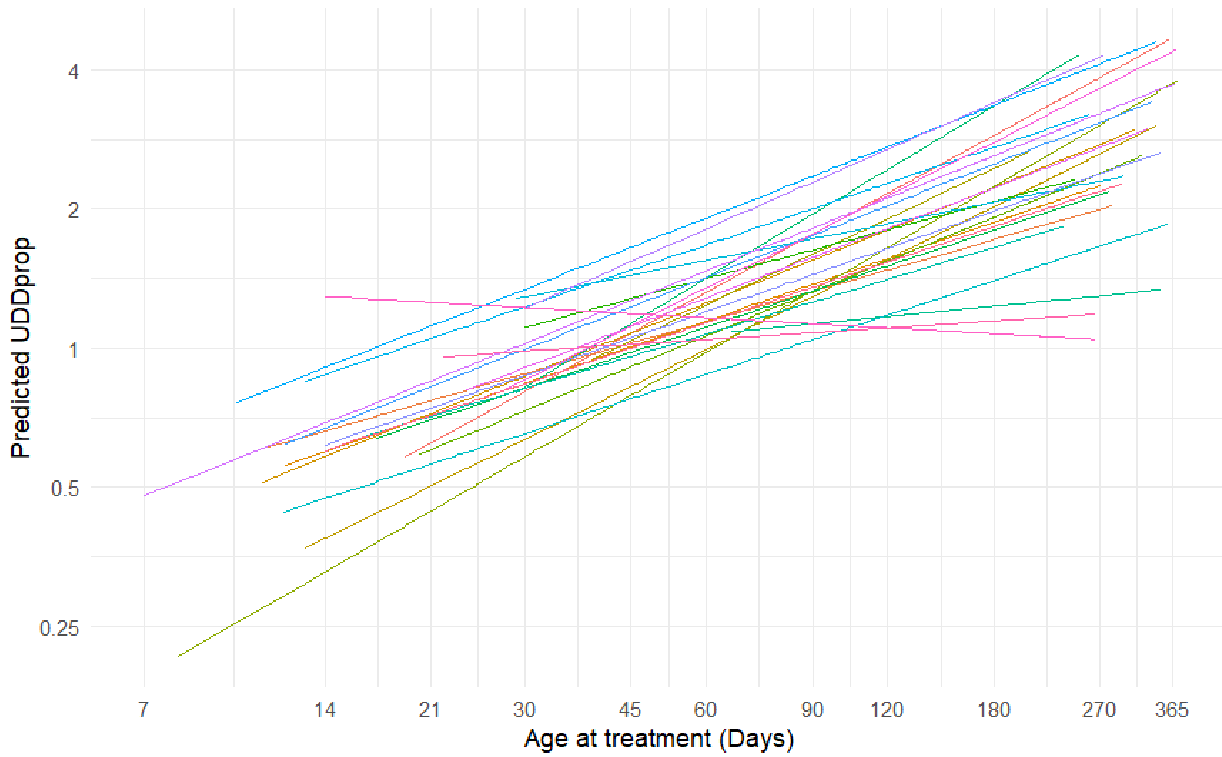

Figure 5 Predicted number of standard doses used per treatment versus age at treatment in days per farm for the antibiotic class ”Amphenicols”. Each line represents predictions for a single farm. Note that scales are log-transformed but labelled with non-log-transformed values.

4. Discussion

In this study, ADD200 did not correspond to the daily doses used on farm in Danish rosé veal cattle below one year of age. On average, the used doses were higher than the calculated ADD200, and therefore, using summaries of the ADD200, in Danish AMU surveillance, overestimate the number of daily treatments carried out in rosé veal farms. This discrepancy depended on several factors: calf age (as proxy for animal weight) at treatment, antibiotic class of the product used, route of administration, location of the treated disorder, and last, but not least, marked variation in AMU practices between farms.

Fertner et al. (2016) hypothesised an underestimation of calves treated when using solely VetStat data and ADD200 as a measure of AMU in Danish starter herds compared to finisher herds. By combining treatment records and VetStat data, we were able to add more nuances to the overall discussion of ADD200 as a measure of AMU.

The average calf age at treatment was found to be below 3 months (mean of 86 days, median of 66 days). If we assume an average daily weight gain like the one reported by Sandelin et al. (2021) (i.e. 1.074 kg per day) and a birthweight around 50 kg, the body weight of an average treated calf in our study population was around 142 kg. A challenge with this approach is the dependence on the assumption that the growth curves for all the calves in the study are alike. Our estimated weigh is relatively close to the standard weight of 140 kg used by the European Medicines Agency to calculate population correction unit (EMA/ESVAC, 2019). Lava et al. (2016) found the mean age at treatment to be 51 days and estimated the mean weight at treatment around 80-100 kg in Swiss veal calves. Their lower estimate is likely linked to Swiss veal calves being slaughtered earlier than Danish veal calves, but differences in production systems may also influence this. Ultimately, the standard weight of 200 kg used in VetStat is too high for our study population and likely for veal production in general. A standard weight of 200 kg should theoretically result in the standard daily doses being higher than the used daily doses (UDDprop below 1), when the calves weigh less than 200 kg at the average age at treatment. This was opposite of what we found for most antibiotic classes. If we adjusted the standard weight downwards, we would see an even higher discrepancy between number of standard and used doses, indicating that we have an issue with how the doses are defined and/or used in practice. Animal weight at time of treatments has previously been described as important for the performance of AMU metrics in describing actual use (Apley et al., 2023; Lava et al., 2016) In our study, age at treatment was significantly associated with UDDprop ($p < 0.001$), but the low R^2 (0.07) in the univariable analysis suggests that age alone is a weak predictor of dose variation. Age may not be a perfect predictor of weight, but more likely there are other explanations for the low predictive value of age such as the large variations seen within age groups across antibiotic classes. Antibiotic class was shown to significantly impact the relationship between standard and used doses in the univariable analysis with an R^2 of 0.49. The slopes of the lines presented in the illustration of our model results (Figure 4) illustrate the effect of age and antibiotic class in combination, and with a meaningful, significant interaction term between these two variables.

Generally, standard doses were higher than used doses for tetracyclines and lower for macrolides and amphenicols. Becker & Meylan (2021) had similar findings for some macrolides (tylosin and spiramycin), while only small differences were observed for other macrolides (tilmicosin and tulathromycin) This contrasts with the findings of Jarrige et al. (2017), who reported that prescribed doses of tetracyclines were higher and macrolides slightly lower than the recommended doses. We looked up products with dosage intervals listed in the SPC that had only a single value ADD in VetStat. This was relevant for the antibiotic classes beta-lactamase sensitive penicillins, combinations of antibacterials, and tetracyclines. For beta-lactamase sensitive penicillins, the ADD corresponded to the middle of the interval; for combinations of antibacterials (benzylpenicillin and dihydrostreptomycin) it corresponded to the lowest interval limit; and for tetracyclines, it matched the highest limit. The latter may explain why our results differed from Jarrige et al. (2017).

One factor potentially contributing to the variations seen between antibiotic classes is the long-acting effect of some products. For macrolides in our study, tulathromycin was the most frequently used active compound. This has a long-acting effect with a defined daily dose of 0.3mg/kg and a defined course dose (DCD) of 2.5mg/kg (EMA/ESVAC, 2016). This corresponds to an effect lasting for 8.33 days with a single injection of the recommended dose in the SPC for the products Tulaven 100 mg/ml and Macrosyn 100 mg/ml. However, the ADD is 0.5mg/kg in VetStat, which would then result in a long-acting effect of five days. Some products were registered with a dose for both intramuscular (IM) injection and subcutaneous (SC) injection such as Flordofen 300 mg/ml (Florfenicol). Here the ADD is 9.9mg/kg in VetStat contrasting the13mg/kg recommended by EMA/ESVAC (2016). The recommended dosage in the SPC is either 20mg/kg IM with a long-acting effect of two days or 40mg/kg SC with a long-acting effect of four days. Several products, in our study had long-acting active compounds and in many cases the ADD, DDD and SPC recommended dosages differed. Thus, ADD200 corrects for long-acting effect to some extent, but we found a lack in transparency about the duration of long-acting effects and how these were determined. Brault et al. (2019) summarised different scientific approaches to determining duration of effect (DOE) for tulathromycin and found it to range from 3 to 14 days. The authors underscored the profound effect the DOE can have on AMU metrics. Our observations about long-acting effect are in line previous statements emphasizing the need to address this factor in AMU monitoring (Apley et al., 2023; Lardé et al., 2020; Postma et al., 2015; Taverne et al., 2015). We expect that the used daily doses exceeding the standard doses in our study can be largely contributed to ADD200 correcting for long-acting effects, in other words a single treatment likely corresponded to multiple standard doses.

Jarrige et al. (2017) found that farmer and veterinarian explained a significant proportion of the variation observed in their dataset on French veal calves, when they investigated association of a range of factors with the outcome number of treatments per calf. In our models, farm introduced as a random effect explained a large proportion of the variation observed in our dataset. The substantial inter-farm variability has implications for the interpretation of surveillance results at national level. It underscores the need to address and investigate on-farm conditions, protocols and practices influencing the AMU. Supplementing AMU monitoring with farm-relevant context may help farmers and their advisors chose relevant treatment protocols and strategies when working towards prudent AMU. The association between AMU and farm conditions has been shown before. In a study population which also included the study farms from this study, Kristensen *et al.* (2025) found that the level of AMU increased with increasing farm-size and number of suppliers and demonstrated a potential effect of on-farm distribution of breed and sex. These findings were in line with findings from other studies (Bokma et al., 2019; Diana et al., 2021; Fertner et al., 2016; Hommerich et al., 2019).

Regarding on-farm protocols and practices influencing the AMU, farmers attitudes may be an important consideration (Skjølstrup et al., 2021). These attitudes have been demonstrated to be influenced by farm conditions such as size and organic status of farm, social and demographic factors such as education of farmer and age of the farmer and economic factors (Borelli et al., 2023). Borelli et al. (2023) found the role of the farm-veterinarian as an advisor on AMU to be significantly associated with better knowledge of AMU and AMR for farmers.

We tested effect of location of disorder and route of administration on UDDprop in our initial analyses. The two variables were, however, highly correlated with antibiotic class and therefore excluded from our model. We decided to reduce our dataset to include only injection treatment on lungs to correct for the potential effect of these factors in our multi-variable modelling. This can make our specific findings less relevant in an international context, where oral treatments or different location of disorders may be more predominant; in our study lung disorders contributed with 79% of the ADD200 and of these

4.3% of the ADD200 were oral treatments. Lava et al. (2016) found the majority of treatments carried out in Swiss veal calves to be group treatments with oral medication, and the main indication in their study was bovine respiratory disease. Oral treatments also constituted 73% of the standard doses in the study on Swiss veal calves by Becker & Meylan (2021). Apley et al. (2023) also reported predominantly oral treatments of U.S. feedlot calves with macrolides, and Bokma et al. (2019) reported mainly oral treatments in Belgian veal calves. However, we expect the correlation between - and correction for these - factors will be relevant and recommend including them in future studies to improve the understanding of how to ensure prudency in the use of antibiotics for cattle. The low use of oral antibiotics found in our study population is likely caused by targeted efforts and campaigns to promote prudent AMU in Denmark by minimising group treatments.

In univariable analyses, we found a significant association between the number of standard doses per treatment and route of administration. Interestingly, the median UDDprop was higher for oral treatments compared to injection treatments for tetracyclines, while the opposite was true for macrolides. Timmerman et al. (2006) found oral treatments to be generally underdosed in pigs, while comparing used daily doses to standard doses. Based on our findings we suggest adjusting for antibiotic class, or splitting the analyses by antibiotic class, when evaluating the effect of route of administration on AMU metrics.

The number of standard doses used per treatment was significantly different between locations of disorders, potentially reflecting different treatment strategies for different disorders, typically occurring at different locations. The correlation with antibiotic class reflects the use of specific antibiotics for specific disorders, e.g. sulfonamides and trimethoprim combinations were solely used for gastrointestinal disorders, while tetracyclines were used at all locations included in our study. Similarly, location of disorder was correlated with age at treatment reflecting specific disorders often occurring in specific age groups. Following this, the influence of location of disorder on number of standard doses per treatment was not further validated in the present study.

Different locations of disorder have previously been introduced, but the grouping and labels vary. Apley et al. (2023) categorised these into four categories: liver abscess control, lameness, bovine respiratory disease, and other. Redding et al. (2019) collected disease frequencies for calf diarrhoea, foot disease, calf respiratory disease, and other diseases. For both studies, bovine respiratory disease corresponds to our classification lung disorders. Our initial argument for introducing “locations” was the low granularity of the indications used in VetStat monitoring in the indication group “Joints, limbs, hoof, central nervous system, skin". Like Redding et al. (2019), we also wished to separate out hoof disorders as these contributed with most records after lung disorders in our dataset.

We found significant differences between all locations within "Joints, limbs, hoof, central nervous system, skin", supporting our initial assumption that AMU was different for the multitude of diagnoses included in this broad group ranging from omphalitis to interdigital phlegmon. If indication groups are used to make inference about the occurrence of different disorders and the corresponding AMU, care should be taken when grouping disorders. A benefit of keeping a low granularity of data used for monitoring is easier overview and simpler reporting with lower risk of misclassification. But with higher granularity of data, better targeted initiatives and benchmarking relevant to the farmer becomes possible. In all cases, accounting for effect of indication is relevant when reporting and analysing AMU and AMU metrics. Transparency in how grouping is carried out and the diagnoses included in each indication group would improve possibilities for international comparisons.

When making inference about occurrence of different disorders, another factor not included in our study is crucial. Different treatment strategies have been reported for veal calves; routine prophylactic and metaphylactic treatments, as well as group versus individual treatment regimens (Brault et al., 2019; Lava et al., 2016; Lowie et al., 2024; Pardon et al., 2012). Use of these strategies will also affect the overall AMU. A major concern with routine prophylaxis and metaphylaxis is the selection for AMR (Crosby et al., 2023). It is a limitation in our study that we could not include the type of treatment strategies used on each farm, and for the individual treatment record. Hence, ideally, evaluation of AMU and AMU metrics should be stratified by treatment strategy, but it would either require more extensive data collection or including this information into treatment recording or surveillance.

There were a few additional strengths and limitations in our study: First, we only included farms with digital recordings to enable the comparison between two databases. The study farms were in general larger compared to the target population. The minimum and maximum farm size included corresponded well to the target population, indicating an inclusion of the full range of sizes, but the quartiles in the study population were higher than in the target population. Larger farms are more likely to use the farm management system interface of DCDB, which can be used for both treatment recording and other management tasks, e.g. economy and feed optimisation (SEGES Innovation P/S. n.d.). This might be important for the interpretation of our results, because Danish veal farms of a larger size have been found to have a higher AMU than smaller farms (Fertner *et al.*, 2016; Kristensen *et al.*, 2025). Thus, some selection bias is a relevant concern for our study. One of our most important findings was the high inter-farm variability. Had more farms been included, we would likely have seen an even bigger variability across farms, further underscoring the need for addressing factors influencing AMU at farm-level.

Second, the dataset used was based on routine registration practices already in place on each farm. The farm personnel's familiarity with recording should minimize the risk of recording bias, though recording errors may still occur. Of particular concern is systematic recording errors on each farm, which can be hard to detect during data management. We have mitigated the risk of gross recording errors by removing the few extreme, unrealistic values (0.02%) identified in the dataset used for modeling. Total amounts sold for the study farms in VetStat were less than 4% higher than total amounts used, indicating a relatively good agreement between the two values, as some loss during treatment is to be expected. For amphenicols, we found use to be 4% higher than sales; this may be contributed to prescriptions sold before 2023 but used during the study period, though recording errors cannot be ruled out. This explanation may also be relevant for farms with a generally higher use than sales. The opposite, where prescriptions late in the study period were not used until after the study period, is also a relevant consideration. The time difference between sale and use, including length of prescription period, should always be considered when comparing sale and use data. Another consideration is whether some of the prescribed (sold) antibiotics for calves were used for animals aged over one year. Some of the study farms had a production of beef heifers, which were slaughtered around 16 months of age (Danish Crown, n.d.). Despite these limitations, we generally assess the treatment data used in this study to be of good quality, and access to such a detailed level of treatment data in large quantity is an important strength of our study.

Third, in model building we had to make some choices: Age and antibiotic class were found to be correlated in a X^2-test but were both kept in the model due to low variance inflation factors. With the inclusion of the interaction between the two, the variance inflation factors increased markedly. This indicates a challenge with multicollinearity in our model. We decided to keep the interaction in the model after examination of plots of raw data. It was evident that the increase with age in used doses varied markedly for the antibiotic classes. Multicollinearity might have affected the coefficient estimates and standard errors presented for the model, but we expect the overall predictions to be reliable. The inclusion of farm as a random effect improved model fit. The raw data are included with our model predictions and 95% confidence intervals in Figure M3S1F1.

Harmonising AMU metrics and stratification methods for international comparisons is important, but our study illustrates that even farms with similar production conditions have different AMU patterns. Finding an AMU metric and relevant strata to allow detailed and farmer-relevant benchmarking and international comparisons is a challenge. When working towards prudent AMU, local knowledge of the on-farm treatment practices and factors influencing them could be central but may be difficult to capture in current database formats. Encouraging and enforcing accurate and detailed treatment recording like the treatment records used in this study is the first step.

Based on our findings and experiences from this study, our recommendations align with previous recommendations in this field. We have two major recommendations: I) Ensuring transparency in choice and calculations of AMU metrics and II) Ensuring relevant and transparent stratification of AMU.

5. Conclusion

ADD200 had a low accuracy in describing the daily doses used on farm in Danish rosé veal cattle below one year of age. We found an average age at treatment (86 days) at which the expected weight is substantially below 200 kg, raising concern for an underestimation of number of animals treated with ADD200. Despite this, ADD200 generally overestimated the number of calves treated due to ADD200 being lower than the used doses. The relationship between ADD200 and used doses, was found to be significantly affected by antibiotic class, calf age at treatment, location of disorder and route of administration in univariable analyses, but due to correlation modelling on all variables not feasible. In a Linear Mixed-Effects Model on data with injection treatments of lung disorders, constituting most treatments, we found antibiotic class and calf age at treatment significantly affecting the relationship. Especially the use of macrolides was overestimated with ADD200 and we suggest use of prolongated products may explain some of this. An important find, in our model was that the random effect farm explained a large proportion of the variation in our study data underscoring the relevance of addressing farm-level factors influencing AMU.

Declaration of Competing Interest

None of the authors have any financial or personal relationships that could inappropriately influence or bias the content of this paper.

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Author contributions

The authorship follows the Vancouver guidelines:

JK: Conceptualization, Methodology, Data curation, Formal analysis and Investigation, Software, Visualisation, Writing-Original draft preparation, Funding acquisition

ABK: Supervision, Methodology, Writing - Review & Editing

APS: Supervision, Methodology, Writing - Review & Editing

LRN: Methodology, Writing - Review & Editing, Funding acquisition and Project administration

Data and code availability

Data is the property of the participating farmers and cannot be shared. SEGES Innovation P/S (https://segesinnovation.dk/) supplied data under a data sharing agreement with the University of Copenhagen; third party data sharing was not permitted.

Questions regarding the software coding process and structure can be directed to Jeanette Kristensen at jp@sund.ku.dk

Ethics approval

The Research Ethics Committee for the Science and Health Faculties at University of Copenhagen has approved the study [Journal no. 504-0330/22-5000]. The project is registered in the University of Copenhagen's joint record of biobanks and record of research projects containing personal data.

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Appendix A

Supplementary material for Manuscript I

M1 Supplementary 1

English translation of questionnaire used field study conducted during spring 2023 and the full frequency analysis of collected categorical variables, including regrouping of answers into levels.

Medicine

Recipient	Fixed / Varying	Number	Owner / Employee	Frequency	
Use	Herd diagnoses / Outbreak / Veterinarian treatments		Presence		days /year

Storage

	Antibiotics: Unopened	Antibiotics: Open	Foto	Vaccines: Unopened	Vaccines: Open	Foto
Where?	Office/Stable/Other	Office/Stable/Other		Office/Stable/Other	Office/Stable/Other	
How?	Refrigerator / Other	Refrigerator / Other		Refrigerator / Other	Refrigerator / Other	
	Hygiene | Order	Hygiene | Order		Hygiene | Order	Hygiene | Order	

Thermometer		Alarm		Control procedure	If yes, describe	
Medicine not used for treatment	When? / Why?					

Waste	Medicine containers, empty	Syringes	Needles
	No sorting/Environmental/Other	No sorting/Environmental/Other	No sorting/Environmental/Other

Medicine in the stable

	Starters	"Middle"	Finishers	Other
When? Always (A), During feeding (F), During treatment (T), Other (O)	A / F / T / O	A / F / T / O	A / F / T / O	A / F / T / O
How? Toolbox (TB), Bag (B), Pockets (P), Refrigerator (R), Other (O)	TB/ B/ P/ R/ O	TB/ B/ P/ R/ O	TB/ B/ P/ R/ O	TB/ B/ P/ R/ O
Hygiene / Order	Hygiene | Order	Hygiene | Order	Hygiene | Order	Hygiene | Order

Handling, requirements

Employees	Access to medicine		Treaters		Medicine handling course	Couse/Exempt due to experience
Treaters – attempted approach	Fixed / Work rotations / Varying / Other					
New treater	Oral review / peer-to-peer training / Irrelevant / Other		Time to unsupervised treatments	days		
	Other Training level, Language skills, Employment status, Irrelevant					
Treater's influence on farm	Economic / Procedure / None / Other					
New herd diagnosis	Veterinarian reviews orally / Treater(s) read(s) diagnosis text / Other					
Laboratory/Veterinarian diagnostics	Blood samples / Necropsy / Lung lavage / Other		Frequency	tests/year		

Handling, practical

Finding sick Specific task (SW), During feeding (F), Continuous (C) Other (O)	SW / F / C / O		Responsible for task Number employees. /Section	min/max		
Record of animals for/under treatment Telephone/tablet (T), Computer (C), Paper (P), Whiteboard (WB), Other (O)	For	T / C / P / WB / O	Stable / Office /Other			
	In	T / C / P / WB / O	Stable / Office /Other			
Follow-up on treatment	Fixed / Varying / Other | From treatment records / Memory / Other					
Follow-up on treatment history	times/nr. of animals	Reason	Routine/Diagnose/Poor condition/ Memory/Other			
Treater Number of employees. /Section	Day	min/max	Week	min/max	Month	min/max
Treatment omitted due to dangerous conditions	Yes / No		Frequency	times/year		

Recording Final left blank if only one recording step	Who?	Treater / Other	Time from treatment to final recording	timer
	Where? – 1st	Stable / Office /Other	How? – 1st	T / C / P / WB / O
	Where? - Final	Stable / Office /Other	How? - Final	T / C / P / WB / O
	Treatment records	Digital / Paper / Other		
	IT-Solutions	DMS Dyreregistrering / EasyCow / None / Other		
	Ear tags	Manual reading / Electronic reading		

Dosage

Choice of dosage If more records age group and diagnosis	Fixed / Visual weight estimation / Weight / Other		
Fixed dosage	Why/How are the fixed doses decided?		
Visual weight estimation	How/Which training?	Calibration frequency	/
Calculating doses	Fixed per section / Mental arithmetic / Digital tools / Other		

Syringe + dosage interval Automatic (A), Manual (M), Other (O)	Fixed / Varying	A / M / O	ml	Procedure nr. 1
	Fixed / Varying	A / M / O	ml	2
	Fixed / Varying	A / M / O	ml	3
	Fixed / Varying	A / M / O	ml	4

M1S1F1 English translation of semi-quantitative questionnaire covering farm-level medicine use

Treatment protocols with antibiotics									
Farm diagnose nr.	Diagnose	Product Name or Nordic product identification	Route of adm.	Dose	Unit	Animal	Unit	Number Doses total	Interval Between doses

M1S1F2 English translation of semi-quantitative questionnaire covering treatment protocols

Vaccination strategy

Diagnosis	Product	Route of adm.	Procedure nr.	Dose /Animal	Number Doses total	Time Interval between doses	Time Weeks from arrival	Animal group vaccinated	Strategy
				ml		min/max	min/max	N/A/BS/I/O	C/S/OB/I/O
				ml		min/max	min/max	N/A/BS/I/O	C/S/OB/I/O
				ml		min/max	min/max	N/A/BS/I/O	C/S/OB/I/O
				ml		min/max	min/max	N/A/BS/I/O	C/S/OB/I/O

Antibiotic treatments

Diagnosis Pneumonia (LU), Arthritis (LB), Interdigital phlegmon (KBB), Conjunctivitis (ØJ), Otitis (MØ), Contusion (T), Diarrhoea (D)	Farm diagnose nr.	Typical animal group Weeks from arrival	Diagnostics Visual specific clinical signs (VD) / Visual unspecific (VU) / Thermometer (T) / Other (O)	Diagnostics specific* (See table below)	Frequency of use	Status first choice (Numeric)	Number of treatments/treatment period (Days)	Treatment strategy Single-animal (E), Metaphylactic (MF) + Arrival (I), Pen-level (F), Other (O)	Procedure for dosage	Dosage in ml or g	Dosage animal /unit	Insufficient treatment effect *(See table below) Fixed procedure (FP), individual evaluation (I), Other
		min/max	VD/VU/T/O		dg/md		/	E/MF/F/O		min/max		FP/I/TF
		min/max	VD/VU/T/O		dg/md		/	E/MF/F/O		min/max		FP/I/TF
		min/max	VD/VU/T/O		dg/md		/	E/MF/F/O		min/max		FP/I/TF
		min/max	VD/VU/T/O		dg/md		/	E/MF/F/O		min/max		FP/I/TF
		min/max	VD/VU/T/O		dg/md		/	E/MF/F/O		min/max		FP/I/TF
		min/max	VD/VU/T/O		dg/md		/	E/MF/F/O		min/max		FP/I/TF
		min/max	VD/VU/T/O		dg/md		/	E/MF/F/O		min/max		FP/I/TF
		min/max	VD/VU/T/O		dg/md		/	E/MF/F/O		min/max		FP/I/TF
		min/max	VD/VU/T/O		dg/md		/	E/MF/F/O		min/max		FP/I/TF
		min/max	VD/VU/T/O		dg/md		/	E/MF/F/O		min/max		FP/I/TF
		min/max	VD/VU/T/O		dg/md		/	E/MF/F/O		min/max		FP/I/TF

*Notes: Diagnostics specific (D) Insufficient treatment (TF)	

M1S1F3 English translation of semi-quantitative questionnaire covering use of treatment protocols

M1S1T1 Frequency of answers to semi-quantitative questionnaire on farm medicine management, use and recording with variable used for coding and short definition (Variable), original answers (Questionnaire), regrouped answers (Level), number of observations (n) and percentage (%)

Variable	Questionnaire	Level	n	%
	Medicine entering the farm			
medicine_recipient_status: Status of recipients of medicine on farm	Fixed	Fixed	19	52.8
	Primarily fixed	Primarily fixed	2	5.6
	Varying	Varying	15	41.7
medicine_receipient_nr: Number of people who receives and stores the medicine	1	1	20	55.6
	2	2	9	25.0
	3	3 to 9	7	19.4
	4			
	9			
medicine_receipient_title: Who recieves/picks up the medicine and stores it by title	Owner	Owner	16	44.4
	Employee/Owner	Employee/Own er	13	36.1
	Employee	Employee	7	19.4
medicine_received_freq: Frequency of medicine recieved given as decimal per week	0	Varies	1	2.8
	2	2 weeks	2	5.6
	4	4 weeks/1 month	16	44.4
	4.3			
	6	6 weeks-2 months	12	33.3
	7.4			
	8			
	8.7			
	10.8	10-13 weeks	5	13.9
	13			
medicine_overall_use: What medicine is used for in the production	Treatment protocols	Treatment protocols	23	63.9
	Treatment protocols and veterinary treatments	Treatment protocols and veterinary treatments	13	36.1
	Medicine storage			
storage_ab_where: Where unopened antibiotics are stored	Anteroom		4	11.1
	Medicine room		2	5.6
	Milk room		4	11.1
	Milk room/Other		1	2.8

Variable	Questionnaire	Level	n	%
	Milk room/Stable/Anteroom		1	2.8
	Milking room		1	2.8
	Office		4	11.1
	Other		7	19.4
	Stable		6	16.7
	Stable storage room		1	2.8
	Storage room		5	13.9
storage_ab_how: How unopened antibiotics are stored	Fridge	Refrigerator	17	47.2
	Fridge/Closet	Refrigerator and other	4	11.1
	Fridge/Drawer			
	Fridge/Shelf			
	Closet	Other	15	41.7
	Fridge, turned-off			
	Other			
	Shelf			
storage_ab_open_where: Where opened antibiotics are stored	Anteroom		5	13.9
	Medicine room		2	5.6
	Milk room		5	13.9
	Milk room/Other		1	2.8
	Milk room/Stable/Anteroom		1	2.8
	Milking room		1	2.8
	Office		3	8.3
	Office/Stable		1	2.8
	Other		4	11.1
	Stable		10	27.8
	Stable storage room		1	2.8
	Stable/Storage room		1	2.8
	Storage room		1	2.8
storage_ab_open_how: How opened antibiotics are stored	Fridge	Refrigerator	12	33.3
	Tool box in fridge			
	Fridge/Closet	Refrigerator and other	4	11.1
	Fridge/Drawer			
	Fridge/Box			
	Fridge/Pocket			
	Closet	Other	20	55.6
	Fridge, turned-off			
	Shelf			
	Box			
	Tool box			
	Tool box, locked			

Variable	Questionnaire	Level	n	%
storage_ab_hygiene: Hygiene of storage of antibiotics 1: No visible contamination 2: Visible contamination	No visible contamination		21	58.3
	Visible contamination		13	36.1
	NA's		2	5.6
storage_ab_order: Order of storage of antibiotics 1: Clear and intutive order in storage 2: Less clear and intutive order in storage	Clear order		29	80.6
	Less clear order		5	13.9
	NA's		2	5.6
storage_vacc_where: Where unopened vaccines are stored	Anteroom		1	2.8
	Ceased			
	Horse Stable			
	Lunch room		2	5.6
	Medicine room			
	None		6	16.7
	Office		5	13.9
	Other		11	30.6
	Stable		3	8.3
	Stable storage room		1	2.8
	Storage room		3	8.3
storage_vacc_how: How unopened vaccines are stored	Fridge	Refrigerator	28	77.8
	None	None	7	19.4
	Ceased			
	NA's		1	2.8
storage_vacc_open_where: Where opened vaccines are stored	Ceased		1	2.8
	Lunch room		1	2.8
	Medicine room		1	2.8
	NA's		1	2.8
	None		29	80.6
	Office		1	2.8
	Other		1	2.8
	Stable		1	2.8
storage_vacc_open_how: How opened vaccines are stored	Fridge	Refrigerator	5	13.9
	None	None	30	83.3
	Ceased			
	NA's		1	2.8
storage_vacc_hygiene: Hygiene of storage of vaccines 1: No visible contamination 2: Visible contamination	No visible contamination		12	33.3
	Visible contamination		4	11.1
	NA's		20	55.6

Variable	Questionnaire	Level	n	%
storage_vacc_order: Order of storage of vaccines 1: Clear and intutive order in storage 2: Less clear and intutive order in storage	Clear order		12	33.3
	Less clear order		4	11.1
	NA's		20	55.6
thermometer: Presense of themometer in fridge for medicine storage	Yes		16	44.4
	No		17	47.2
	NA's		3	8.3
alarm: Presense of alarm on fridge for medicine storage	Yes		4	11.1
	No		29	80.6
	NA's		3	8.3
temp_control: Presense of control procedures of fridge for medicine storage	Control procedure		2	5.6
	Cooling determined upon access		20	55.6
	No		12	33.3
	NA's		2	5.6
	Medicine disposal			
discarded_medicine: Instances where medicine is discarded and reason	Yes	Yes	8	22.2
	Yes, delivered to pharmacy			
	Yes, discarded with waste for empty containers			
	Yes, expired			
	Yes, given to veterinarian			
	Yes, not antibiotics			
	No	No	26	72.2
	No, only dropped bottles			
	NA's		2	5.6
waste_empty_container: Waste handeling of empty medicine containers	Environmental waste	Sorted as 'Hazardous waste'	16	44.4
	Sorted waste	Other	5	13.9
	To herd veterinarian			
	Ordinary waste	Not sorted	15	41.7
waste_syringe: Waste handeling of discarded syringes	Environmental waste	Sorted as 'Hazardous waste'	6	16.7
	Sorted waste	Other	5	13.9
	To herd veterinarian			

Variable	Questionnaire	Level	n	%
	Iron recycling			
	Ordinary waste/Iron recycling			
	Ordinary waste	Not sorted	25	69.4
waste_needle: Waste handeling of discarded needles	Environmental waste	Sorted as 'Hazardous waste'	27	75.0
	Irrelevant	Other	6	16.7
	To herd veterinarian			
	Iron recycling/To herd veterinarian			
	Ordinary waste	Not sorted	3	8.3
	Medicine in the stable			
nr_storage_animal_adjacent: Number of medicine storages on a farm adjacent to stabled animals	0	0		
	1	1	23	63.9
	2	2	4	11.1
	3	3-5	6	16.7
	4			
	5			
medicine_starter_when: When medicine is present in the starter area	Treatment	During treatment	19	52.8
	Feeding	During feeding and treatment	7	19.4
	Feeding/Treatment			
	Feeding/Treatment/People in the stable			
	Always	Always	10	27.8
medicine_starter_how: How medicine is stored when present in the starter area	Closet	Stored in stable	9	25.0
	Fridge			
	Fridge, turned-off			
	Pocket/Closet			
	Tool box/Pocket/Closet			
	Tool box/Pocket/Fridge			
	Bag	On person	12	33.3
	Bag/Pockets			
	Belt bag			
	Pocket			
	Pocket/Vest			
	Tool box	In container	13	36.1
	Wagon			
	Bucket/Tool belt	On person and in container	2	5.6
	Tool box/Bag			

Variable	Questionnaire	Level	n	%
medicine_middle_when: When medicine is present in the middle area	Treatment	During treatment	24	66.7
	Feeding/Treatment	During feeding and treatment	1	2.8
	Always	Always	3	8.3
	Irrelevant	Not relevant	8	22.2
medicine_middle_how: How medicine is stores when present in the middle area	Fridge	Stored in stable	2	5.6
	Tool box/Pocket/Fridge			
	Bag	On person	15	41.7
	Bag/Pockets			
	Belt bag			
	Pocket			
	Pocket/Vest			
	Vest			
	Tool box	In container	8	22.2
	Wagon			
	Tool box/Bag	On person and in container	2	5.6
	Tool box/Pocket			
	Irrelevant	Not relevant	8	22.2
	NA's		1	2.8
medicine_end_when: When medicine is present in the end area	Treatment	During treatment	28	77.8
	Feeding/Treatment	During feeding and treatment	3	8.3
	Feeding/Treatment/People in the stable			
	During daily supervision			
	Always	Always	4	11.1
	NA's		1	2.8
medicine_end_how: How medicine is stores when present in the end area	Fridge	Stored in stable	3	8.3
	Pocket/Fridge			
	Bag	On person	17	47.2
	Bag/Pockets			
	Belt bag			
	Pocket			
	Pocket/Vest			
	Vest			
	Tool box	In container	12	33.3
	Wagon			
	Bucket/Tool belt	On person and in container	3	8.3
	Tool box/Bag			
	Tool box/Pocket			
	NA's		1	2.8
medicine_stable_hygiene: Hygiene of stable antibiotics 1: No visible	No visible contamination		14	38.9

Variable	Questionnaire	Level	n	%
contamination 2: Visible contamination	Visible contamination		14	38.9
	NA's		8	22.2
medicine_stable_order: Order of stable antibiotics 1: Clear and intutive order in storage 2: Less clear and intutive order in storage	Clear order		24	66.7
	Less clear order		4	11.1
	NA's		8	22.2
Handling, requirements				
nr_employee_medicine_access: Number of emploees with medicine access	1	1-2	17	47.2
	2			
	3	3-4	12	33.3
	4			
	5	5-12	7	19.4
	6			
	8			
	9			
	12			
nr_employee_medicine_use: Number of employees administering treatments to calves	1	1-2	19	52.8
	2			
	3	3-4	13	36.1
	4			
	5	5-9	4	11.1
	7			
	8			
	9			
perc_employee_medicine_access_use: Percent of employees with medicine access which also treats	25	0%-25%	1	2.8
	33.3	26%-50%	7	19.4
	50			
	55.6	51%-75%	6	16.7
	60			
	66.7			
	75			
	77.8	76%-100%	22	61.1
	100			
perc_employee_medicine_course: Percent of employees with medicine handling course	0	0%-25%	12	33.3
	20			
	25			
	33.3	26%-50%	8	22.2
	42.9			
	50			
	66.7	51%-75%	6	16.7
	75			
	87.5	76%-100%		27.8

Variable	Questionnaire	Level	n	%
	100		10	
perc_employee_medicine_experience: Percent of employees exempted from medicine handling course due to ancinnity	0	0%-25%	15	41.7
	12.5			
	25			
	33.3	26%-50%	6	16.7
	50			
	60	51%-75%	5	13.9
	66.7			
	75			
	100	76%-100%	9	25.0
	NA's		1	2.8
treatment_responsibility_strategy: How responsibility for treatment in each stable area is managed	Fixed	Fixed	26	72.2
	Fixed (owner treats 98% of time)			
	Fixed with some variation			
	Work-rotation	Work-rotation	6	16.7
	Varying	Varying	4	11.1
	Varying min. 2 per round			
new_treaters_training: Training of new employees in treatment procedures was reported as peer-to-peer training on all farms where this was relevant	*Qualitative text answers*			
new_treaters_independant: Days until new treateres perform treatments independantly	1	1-2 days	7	19.4
	2			
	<1-7	7-14 days	8	22.2
	7			
	14			
	7-30	>14-180 days	4	11.1
	17-90			
	30			
	180			
	1 treater	Only one treater	10	27.8
	Irrelevant	Irrelevant	6	16.7
	NA's		1	2.8
new_treaters_demands: Responders were asked about their requirements for new employees performing treatments. This question was perceived differently by responders	*Qualitative text answers*			

Variable	Questionnaire	Level	n	%
influence_production: Minimum level of influence on production exerted by people with treatment responsibility max: econimical min: procedure	(Economical)	Economic	14	38.9
	Economical			
	Procedure	Procedure	21	58.3
	None	None	1	2.8
		Laboratory or veterinary diagnostics		
diagnostics_performed: Types of diagnostic tests performed related to disease in the production	Blood sample/Lung fluid	Yes	29	80.6
	Blood sample/Nose swab/Lungs from dead/Necropsy			
	Blood samples			
	Blood samples/feces(/lung fluid)			
	Blood samples/Lung fluid/Lungs from dead			
	Blood samples/Necropsy			
	Blood samples/Necropsy/Nose swab			
	Calves to Kjellerup + AMR check			
	Feces			
	Feces/Blood samples			
	Feces/Lung fluid			
	Lungs from dead			
	Lungs from dead/Lung fluid			
	Necropsy			
	Necropsy/Lung fluid			
	Necropsy/Lungs from dead			
	Necropsy/Scanning			
	Nose swab/Feces/Lung fluid/Necropsy			
	None	No	7	19.4
diagnostics_freq: Times per year any type of laboratory or veterinary diagnostics is performed	0.3	Once per year or rarer	14	38.9
	<1			
	1			
	>1			
	2	2-7 times per year	13	36.1
	>4			
	4			
	<5			

Variable	Questionnaire	Level	n	%
	7			
	0	Never	7	19.4
	NA's		2	5.6
diagnostics_blood: Diagnostics performed on blood samples	Yes		10	27.8
	No		26	72.2
diagnostics_feces: Diagnostics performed on feces samples	Yes		7	19.4
	No		29	80.6
diagnostics_lungs: Diagnostics performed on lungs from deceased calves	Yes		12	33.3
	No		24	66.7
diagnostics_lung_fluid: Diagnostics performed on lung fluid samples	Yes		8	22.2
	No		28	77.8
diagnostics_nose_swab: Diagnostics performed on nose swab samples	Yes		3	8.3
	No		33	91.7
diagnostics_necropsy: Necropsy of deceased calves performed	Yes		9	25.0
	No		27	75.0
	Handling, practical			
finding_sick: Procedure for finding sick animals	Specific task	Specific task	26	72.2
	Specific task/Continuous			
	Specific task/Feeding			
	Feeding/2-3 daily rounds	Mixed approach	4	11.1
	Feeding/2 daily rounds			
	Feeding/5 daily rounds/Specific task during problematic periods			
	Feeding/Cleaning water dispensers(/Specific task)			
	Feeding	During other tasks	6	16.7
	Continous			
	Feeding/Continous			
	Feeding/Distributing straw			
nr_finding_sick_min: Minimum number of people responsible for finding sick animals in a section	1	1	31	86.1
	2	2	4	11.1
	NA's		1	2.8

Variable	Questionnaire	Level	n	%
nr_finding_sick_max: Maximum number of people responsible for finding sick animals in a section	1	1	5	13.9
	2	2	22	61.1
	3	3-4	8	22.2
	4			
	NA's		1	2.8
sick_for_treatment_log: How animals sick animals which have not yet recieved treatment are logged	Telephone	Digital log (phone)	6	16.7
	Telephone/Messenger			
	Oral/Paper	Physical log (paper or whiteboard)	18	50.0
	Paper			
	Paper/Other			
	White board			
	Memory	No log (oral or from memory)	3	8.3
	Oral			
	None	Not relevant	9	25.0
	Immediate treatment			
sick_for_treatment_log_where: How the log of sick animals which have not yet recieved treatment is stored	Stable	Stable	24	66.7
	Stable/Other			
	Milk room	Other location	3	8.3
	Office			
	None	Not relevant	9	25.0
	Immediate treatment			
sick_in_treatment_log: How animals sick animals in treatment are logged	Telephone	Digital log (phone)	6	16.7
	Paper	Physical log (paper or whiteboard)	21	58.3
	Paper and spray			
	Paper/Whiteboard			
	Paper/Telephone	Physical and digital log	7	19.4
	Telephone/Whiteboard			
	Irrelevant, only one-day treatments	No log	2	5.6
	Remembers			
sick_in_treatment_log_where: How the log of sick animals in treatment is stored	Stable	Stable	30	83.3
	Stable/Office			
	Other	Other location	5	13.9
	Milk room			
	Anteroom			
	Irrelevant, only one-day treatments	Not relevant	1	2.8
check_treatment_course: All responders replied that they checked daily to see if initiated treatment courses were completed for the calves			36	100.0

Variable	Questionnaire	Level	n	%
prev_treatment_action_freq: Frequency per treated calf of actions to check if it has been treated previously	0	Never	2	5.6
	1	1%-10%	18	50.0
	2			
	4			
	5			
	6.7			
	10			
	13.3	11%-90%	7	19.4
	33.3			
	50			
	80			
	90			
	100	Always	6	16.7
	NA's		3	8.3
prev_treatment_action_trigger: Triggers leading to actions to check if a calf has been treated previously	Routine		6	16.7
	Calf clinical signs			
	Memory of calf		10	27.8
	Clinical signs and memory of calf		12	33.3
	Never		2	5.6
treatment_omitted: Conditions where treatments are omitted	*All respondents replied that treatments of sick animals were never omitted due to dangerous conditions*			
nr_treater_day: Maximum number of people responsible for treatment in a stable area per day	1	1	14	38.9
	2	2	21	58.3
	4	>2	1	2.8
nr_treater_week: Maximum number of people responsible for treatment in a stable area per week	1	1	11	30.6
	2	2	15	41.7
	3	3-5	10	27.8
	4			
	5			
nr_treater_month: Maximum number of people responsible for treatment in a stable area per month	1	1	9	25.0
	2	2	14	38.9
	(2)			
	3	3-7	13	36.1
	4			
	6			
	7			
Medicine use documentation				

Variable	Questionnaire	Level	n	%
reg_who: Identity of person registering treatment in final medicine record	Other	Treater	22	61.1
	Treater			
	Treater/Fixed employee			
	Owner	Fixed person(s)	13	36.1
	Fixed 2 employees			
	Fixed employee			
	Fixed owner			
	Fixed?			
	NA's		1	2.8
h_treat_reg: Maximum hours from treatment to final registry of treatment	0	Immediately	8	22.2
	1	<24 hours	13	36.1
	2			
	7			
	8			
	12			
	24			
	48	48-72 hours	10	27.8
	72			
	120	>120 hours (5 days)	5	13.9
	168			
	1440			
reg1_where: Where first record of treatment is done. This is registered as "none" if only one registration process is performed	Stable	Stable	29	80.6
	(Stable)			
	None	Irrelevant	7	19.4
reg1_how: How first record of treatment is done. This is registered as "none" if only one registration process is performed	Paper/Telephone	Paper or digital	7	19.4
	Whiteboard/Telephone			
	Paper	Paper	22	61.1
	Paper/Whiteboard			
	(Paper)			
	None	Irrelevant	7	19.4
reg2_where: Where final record of treatment is done.	Stable	Stable	16	44.4
	Stable/Office			
	Office/Stable			
	Other	Other location	20	55.6
	Milk room			
	Office			
	Anteroom			
	Lunch room			
reg2_how: How final record of treatment is done	Computer	Computer	16	44.4
	Telephone	Telephone	13	36.1
	Telephone/Computer			
	Paper	Paper	7	19.4

Variable	Questionnaire	Level	n	%
reg_format: How treatment records are stored	Digital	Digital	16	44.4
	Paper	Paper	7	19.4
	Digital/Paper	Digital and paper	13	36.1
	Digital/Paper for previous 1 month			
it_solutions: IT solutions used in the production	DMS Dyreregistrering[1]	Computer program	10	27.8
	Excel			
	DMS Dyreregistrering[1] /EasyCow[2]	Computer program and phone app	19	52.8
	DMS Dyreregistrering[1] /EasyCow[2] /SmartKoen[3]			
	DMS Dyreregistrering[1] /SmartKoen[3]			
	EasyCow[2]			
	None	None	7	19.4
Dosage of medicine				
dosing_general: How dosing is done generally	Fixed doses per pen	Fixed doses per pen	6	16.7
	Visual weight estimation	Doses by animal bodyweight	14	38.9
	Fixed doses per pen with visual weight estimation for outliers	Mixed approach	16	44.4
	Visual weight estimation / fixed doses for finishers with foot rot			
	Visual weight estimation / fixed doses for starter calves			
	Visual weight estimation / fixed doses for starter calves with diarrhea and pneumonia			
	Visual weight estimation by intervals / fixed doses for starter calves			
	Visual weight estimation in 40 kg weight increments			
	Visual weight estimation/Fixed doses per pen			
weight_estimate_training: How treaters are trained in estimating weight of calves	Fixed doses per pen	Experience with weight of animals in pen	6	16.7
	Animals are sorted in pens by size			

Variable	Questionnaire	Level	n	%
	Based on experienced average weight of animals in the pen			
	Experience with weighings of animals in each pen and previous treatments			
	Experience with weight of animals in each pen			
	Experience and continued input from weighing at arrival	Weighing and experience	19	52.8
	Experience and experience from earlier weighings			
	Experience and previous weighings			
	Experience from earlier weighings			
	Experience/Measuring tape			
	Experience/Weighing at arrival and move from middle stable			
	Instruction of new emplyees and experience with start weight - rule of thumb 1 day = 1 kg			
	Present at weighing of calves			
	Weighing of starters			
	Weighing of starters/Measuring tape			
	Experience	Experience and/or peer-to-peer training	10	27.8
	Experience/Peer-to-peer training			
	Peer-to-peer training			
	NA's		1	2.8
weight_estimate_calibration: How and when calibration of weight estimation accuracy is performed	At arrivals	Every 1-3 weeks	14	38.9
	Every 14 days			
	Weekly			
	Weekly, bets on weighing results			
	Weighing every 3rd week			

Variable	Questionnaire	Level	n	%
	Weighing of starters and using meassuring tape 2 times per year			
	1 per 2 months	1-13 times per year	7	19.4
	4 times/year			
	Once per month			
	Weighing 1 time per year			
	Weighing every 4th week			
	None	Never	14	38.9
	NA's		1	2.8
calc_dosage: How treaters calculate dosage of medicine	Experience with dose for size	Mental arithmetic	23	63.9
	Fixed with addition substraction for outlier calves			
	Mental arithmetic			
	Mental arithmetic/Fixed doses per pen			
	EasyCow/Calculator	Aid from digital tools	4	11.1
	Mental arithmetic/Digital tools			
	Mental arithmetic/Digital tools/Experience			
	SmartKoen			
	Fixed doses per pen	No calculation	6	16.7
	Fixed dose per pen			
	NA's		3	8.3
syringes_used_ab: Type of syringes used for antibiotics	Manual	Manual	23	63.9
	Manual single-use			
	Automatic	Automatic	5	13.9
	Automatic/Roux syringe			
	Roux syringe			
	Manual/Automatic	Manual and automatic	7	19.4
	Manual/Roux syringe			
	NA's		1	2.8
dosage_interval_ab_min: Minimum dosage interval in ml for antibiotics	0.1	0.1ml to 0.5ml	7	19.4
	0.2			
	0.5			
	1	1ml	23	63.9
	1.5	1.5ml to 2ml	4	11.1
	2			

Variable	Questionnaire	Level	n	%
	NA's		2	5.6
dosage_interval_ab_max: Maximum dosage interval in ml for antibiotics	1	1ml	15	41.7
	1.5	1.5ml to 4ml	4	11.1
	2			
	4			
	5	5ml to 12ml	15	41.7
	6			
	8			
	12			
	NA's		2	5.6
dosage_interval: Difference in ml between min and max dosage interval for antibiotics	0	0ml	9	25.0
	0.5	<1ml	9	25.0
	0.9			
	1			
	3	3ml to 11ml	16	44.4
	4			
	4.8			
	6.5			
	7			
	11			
	NA's		2	5.6
syringes_used_vacc: Type of syringes used for vaccines	Manual	Manual	3	8.3
	Manual single-use			
	Automatic	Automatic	20	55.6
	Roux syringe			
	None	Not relevant	6	16.7
	NA's		7	19.4

[1]DMS Dyreregistrering: DMS is the most frequently used digital management tool in Danish cattle farms and exchanges data with DCDB. Some veterinarians have access to DMS and register treatment protocols directly in the tool. In these cases, a farmer can select the herd diagnose from a drop-down menu when recording a treatment and will only need to enter the date of treatment, identification of the animal, and the amount of drug used; the rest will be automatically entered in accordance with the diagnose.
[2]EasyCow: An app version of DMS available for phone or tablet
[3]Smartkoen: An app version of DMS available for phone or tablet

M1 Supplementary 2

The interviewees were asked to describe the clinical signs they observed in calves, which made them initiate a treatment of a calf/group of calves for the farm treatment protocols with antibiotics

M1S2T1 Calf signs used to evaluate need for treatment

Diagnosis by organ system or location		Symptoms in layman's terms identified and described by the farmer		Farms with diagnosis
		Do match symptoms for diagnosis found in literature	Do not match symptoms for diagnosis found in literature	Count (%)
Ears	**Otitis media**	**Drooping ears (uni-/bilaterally)**[2] Flickering ears Ear discharge Head shaking Head tilt Depressed/weak Fever "Confused"	Joint swelling Acute onset of panting and high fever	15 (41.7)
Eyes	**Conjunctivitis** **Infectious bovine keratoconjunctivitis**	**Eye discharge**[2] Frequent blinking Redness in eye "Spot" on cornea Squinting eyes Swelling around eye		13 (36.1)
Gastro-intestinal	**Diarrhoea** **Enteritis** **Calf Diphtheria**	**Diarrhoea**[2] (severe, bloody, watery, foul smelling or explosive) Depressed/weak Greasy tail and hind limbs Bloat Blood in feces Abscesses in jaw region Fever		26 (72.2)
	Coccidiosis[1]	**Diarrhoea**[2] Depressed/weak Greasy tail and hind limbs Blood in feces		26 (72.2)
Hoofs	**Interdigital phlegmon** **Interdigital dermatitis** **Digital dermatitis**	**Swelling above the hoof (in the coronary band)**[2] (ruptured, severe or mild)	Joint infection	36 (100)

Diagnosis by organ system or location		Symptoms in layman's terms identified and described by the farmer		Farms with diagnosis
		Do match symptoms for diagnosis found in literature	Do not match symptoms for diagnosis found in literature	Count (%)
		Lameness (mild to severe) Lesions in hoof gap		
Limbs	**Septic Arthritis "Swollen hock" "Limb disorder, other"**	**Joint swelling**[2] Lameness Fever	Pneumonia (2nd choice) Interdigital phlegmon (2nd choice)	22 (61.1)
Lungs	**Pneumonia (pre-weaned)**	**Panting**[2] Depressed/weak Nasal discharge Cough Fever (39.0, 39.3) Poor performance Stretching neck Changed breathing pattern Weight loss Sunken eyes Eye discharge Changed head position Sawbuck stand Sunken eyes Drooping ears	Interdigital phlegmon Unspecific depressed/weak "Calves from suppliers with joint infection problems" "...can be confused with middle ear infection"	36 (100)
	Pneumonia (post-weaned)	**Panting**[2] Depressed/weak Nasal discharge Cough Fever (39.0, 39.5) Thin Raised hair Dehydrated Eye discharge Drooping ears	Poor performance	36 (100)
Other	**Infection**[3]	Drooping ears Lung infection (3rd choice) Depressed/weak for multiple days		7 (19.4)
Skin	**Omphalitis**	Swelling around umbilicus		4 (11.1)

Diagnosis by organ system or location		Symptoms in layman's terms identified and described by the farmer		Farms with diagnosis
		Do match symptoms for diagnosis found in literature	Do not match symptoms for diagnosis found in literature	Count (%)
		Warm and hard umbilicus		

[1] Treated with antiprotozoals
[2] Most frequently mentioned symptom
[3] Unspecific diagnosis

Appendix B

Danish version of field study questionnaire and informed consent form used during field study conducted during spring 2023

Plan for dagens besøg:

Jeg vil gerne se, hvor medicinen opbevares

Jeg vil gerne gå en tur igennem hele bedriften, hvis muligt vil jeg gerne følge samme rute som en kalv bevæger sig gennem bedriften fra indsætning til slagt.

Undervejs vil jeg spørge til:

- Almindelig drift, primært med fokus på de nyindsatte dyr
- Hvordan medicin opbevares og håndteres
- Hvordan behandlinger foregår

Ved besøgets afslutning:

Set med dine øjne, hvad er så den største udfordring ift. at sikre ansvarligt antibiotikaforbrug på din besætning?

Basis information			
Dato		Postnummer	
Ejer			
Bedrift		CVR-nummer	
CHRnr	/	Besætningsnr	/
Kontaktperson			
Telefon		E-mail	
Titel	Ejer / Driftsleder / Fodermester / Andet		

Dyrlæge						
Navn		Praksis				
VASC	Ingen / Frivillig / Obligatorisk | Tværfaglig / Staldskole / Modul 1 / Modul 2					
Dyrlæge telefon		Dyrlæge e-mail				
Slagtekalverådgiver						
Navn		Firma				
Telefon		E-mail				
Andre rådgivere						
Udfyld med funktion og navn på bagsiden						
Erfagruppe	Ja / Nej	Antal årlige møder med deltagelse		Facilitator	Hvis ja, hvilken faggruppe?	

Bedriften						
Antal besætninger		Antal bygninger		Antal sektioner		
Produktionsstruktur	Tyre: Starter/Indsætter|Mellem|Slut|Andet **Kvier:** Starter/Indsætter|Mellem|Slut|Andet					
Bedriftsbesætning	1	2		3		
Produktionsstruktur	Starter|Mellem|Slut|Andet	Starter|Mellem|Slut|Andet		Starter|Mellem|Slut|Andet		
Ansatte I alt	Fuld tid | Deltid | Ungarbj.	Deles ansatte ml. besætninger		Ja | Delvist | Nej		
Levereres til biogas	Ja / Nej / Andet	Frekvens	Gange / Tidsenhed	Tilknyttet anlægget	Antal bes.	
Totalt antal flytninger per kalv per produktionscyklus						
Bygninger	min/max	Sektioner	min/max	Bokse	min/max	

Tegn kalvenes vej igennem besætningen / bedriften

Flytninger til ny sektion markers med pil og ny firkant. Hvis en bestemt gruppe flyttes f.eks. kvier noteres dette ved pilen

Antal kontakt adskilte sektioner der indsættes i tegnes som separate firkanter og min/max flytninger i sektion noteres

Ind **Ud**

Relevant ændring i produktion gnm. seneste år (+/- 10%) | Relevant ændring i produktion planlagt for næste år (+/- 10%)

Levering			
Leverandørprofil - tilstræbt	Fast / Kalveformidling / Andet	- opnået	Fast / Kalveformidling / Andet
Leverandørmøder	Fast / Sporadisk / Aldrig / Andet	Frekvens	Gange / Tidsenhed
Antal dyr leveret		Antal "læs"	
Leveringsansvarlig Hvem?	Henter / Bragt	Besætning / Vognmand / Kalveformidling /Andet	
Leveringsform Hvordan?	Kreaturvogn / Lastbil / Andet | Blandet / Sektioneret / Sektioneret leverandør		
Leveringssted Rækkefølge?	Fra transport til: Vægt / Opsamlingsplads / Boks / Andet		
Leveringsfrekvens Hvornår?	Hver 1. / 2. / 3. / 4. uge / Varierende / Andet | Afvigelser: gange / tidsenhed		

Kalvekrav ved ankomst		Vægt min	Alder min	Andet
	V			
	S			

Konsekvens v. manglende opfyldelse af krav	Ingen / Påtale, ved flere / Påtale / Andet	Salgskrav ved slagt	Dansk Kalv / Andet

Starter/Indsætterafsnit			
Definér sektion	Adskilt af Bygning / Mur / Port / Gangareal / Andet		
Antal sektioner i alt		Bokse/sektion	min/max
Antal kalve per boks	min/max	Antal leverandører per boks	min/max
Antal mælkefodrede	I alt	Antal fravænnede	I alt
Kontakt ml. bokse	Angiv primær og evt. sekundær None/Full/FNose/PN/Other		
Aflastning svage dyr	Mælkefodrede / Øvrige	Aflastning kapacitet	Mælkefodrede / Øvrige

Hygiejne	Dyr		Inventar		Foder		Vand		
Orden	Dyr, str.		Dyr, antal		Belægningsgrad		Inventar		
Bygning	Tag	F/H/O	Vægge	F/H/OP/O	Gulv	F /S /B /O | DB /LB /M /O	Ventilation	P/M	

Flytninger internt ekskl. Sygeboks					
Tid før 1. flyt i uger	min/max	Antal bokse blandet 1. flyt	min/max	Dyr per boks	min/max
Tid til 2. flyt i uger	min/max	Antal bokse blandet 2. flyt	min/max	Dyr per boks	min/max

Flyttes frem	Ja / Nej	Frekvens	antal / holdstr.	Flyttes tilbage	Ja / Nej	Frekvens	Antal / holdstr.

Mælkefodring			
Udfodringsmetode	Sutteautomat / Suttespand / Skål / Trug /Andet	Tildeling	Manuel /Automatisk / Andet
Adskillelse ved udfodring	Ingen / Skillevæg / Total / Varierende /Andet		
Fodringspladser/kalv	/ min | max /	Kilo mælkepulver per kalv	
MP produkter i brug	Foto	g pulver til 1 l vand	Sommer | Vinter

Antal Strategier og kriterier for inddeling

Antal		Vægt		Alder		Andet	

Kriterier for fravænning

Vægt		Alder		Andet		Fravænningsalder, min. i uger	

Mælkefodringsperiode Vinter blank hvis ens	Tid		Dagligt i l per kalv	
	Min	**Max**	**Min**	**Max**
Opstart	uger gl.	uger gl.	Sommer | Vinter	Sommer | Vinter
Mælketildeling max. Antal dage	Sommer | Vinter	Sommer | Vinter	Sommer | Vinter	Sommer | Vinter
Nedtrapning Antal dage	Sommer | Vinter	Sommer | Vinter	**Liter fjernet per reduktion**	
			Sommer | Vinter	Sommer | Vinter
Liter ved sidste tildeling			**Antal reduktioner i alt**	
Sommer | Vinter			Sommer | Vinter	Sommer | Vinter

Supplerende væsketildeling	l/kalv/dag mælkefodret |	l/kalv/dag fravænnet

Andet iblandet mælken		Hvornår?	

Medicin

Modtager	Fast / Varierende	Antal	Ejer / Medarbejder	Frekvens		
Anvendelse	Besætningsdiagn. / Udbrud / Enkeltdyrsbeh. v. dyrlæge			Forekomst	dage /år	

Opbevaring ankomst

	Antibiotika		Foto	Vacciner		Foto
	Uåbnet	Åbnet		Uåbnet	Åbnet	
Hvor?	Kontor/Stald/Andet	Kontor/Stald/Andet		Kontor/Stald/Andet	Kontor/Stald/Andet	
Hvordan?	Køleskab / Andet	Køleskab / Andet		Køleskab / Andet	Køleskab / Andet	
	Hygiejne / Orden	Hygiejne / Orden		Hygiejne / Orden	Hygiejne / Orden	

Temperaturmåler		Alarm		Egenkontrolprocedure	Hvis ja, beskriv
Medicin som ikke bruges til dyr?	Hvornår?/Hvorfor?				

Affalds- håndtering	Medicin beholdere, tomme	Sprøjter	Kanyler
	Alm. affald /Miljøaffald / Andet	Alm. affald /Miljøaffald /Andet	Alm. affald /Miljøaffald /Andet

Medicin i stalden

Hvornår? Altid (A), under fodring (F), kun ved behandling (T), andet (O)	Starter	Mellem	Slut	Andet
	A / F / T / O	A / F / T / O	A / F / T / O	A / F / T / O
Hvordan? Kasse (TB), taske (B), lommer (P), køleskab (R), andet (O)	TB/ B/ P/ R/ O	TB/ B/ P/ R/ O	TB/ B/ P/ R/ O	TB/ B/ P/ R/ O
Hygiejne / Orden	Hygiejne / Orden	Hygiejne / Orden	Hygiejne / Orden	Hygiejne / Orden

Håndtering, krav

Ansatte	Adgang til medicin		Behandler		Medicinhåndteringskursus	Kursus	Anciennitet
Behandlere – tilstræbt tilgang	Fast / I arbejdsrul / Varierende / Andet						
Ny behandler	Gennemgang / Sidemandsoplæring / Ikke relevant / Andet				Selvstændige behandlinger	dage	
	Andet uddannelsesniveau, sprogkundskaber, ansættelsesforhold, ikke relevant						
Behandler(e)s indflydelse på driften	Økonomisk / Procedurer / Ingen / Andet						
Ny besætningsdiagnose	Dyrlæge gennemgår / Læser diagnosen / Andet						
Prøver til sygdomsdiagnostik?	Blodprøver / Obduktion / Lungeskylning / Andet				Frekvens	gange/år	

Håndtering, praktisk

Fund af syge dyr Specifik opgave (SW), ved fodring (F), Medarb. Fortløbende (C) andet (O)	SW / F / C / O		Ansvarlige for fund Antal medarb. /sektion	min/max		
Oversigt over dyr til/i behandling Telefon/tablet (T), computer (C), papir (P), tavle (WB), andet (O)	til	T / C / P / WB / O	Stalden / Kontor /Andet			
	i	T / C / P / WB / O	Stalden / Kontor /Andet			
Tjek for dyr til efterbehandling	Fast / Varierende / Andet	I behandlingsoversigt / Fra hukommelsen /Andet				
Tjek tidligere behandling	gange/grp.str	Årsag	Rutine/Diagnose(angiv)/Utrivelig/ Hukommelse/Andet			
Behandler Antal medarb. /sektion	Dag	min/max	Uge	min/max	Måned	min/max
Behandling undladt grundet manglende mulighed for sikker håndtering?	Ja / Nej	Frekvens	gange/år			

Registrering Endelige efterlades blank, hvis der kun registreres 1 gang	Hvem?	Behandler / Anden	Tid fra beh. Til endelig	timer
	Hvor? – Første	Stald / kontor /andet	Hvordan? – Første	T / C / P / WB / O
	Hvordan? - Endelige	Stald / kontor /andet	Hvordan? - Endelige	T / C / P / WB / O
	Opbevaring medicinregistrering	Digitalt / Papirform / Andet		
	Benyttede IT-løsninger	DMS Dyreregistrering / EasyCow / Ingen / Andet		
	Øremærker	Manuel aflæsning / Elektronisk aflæst		

Dosering ved sygdomsbehandling

Valg af dosering Hvis fl. skriv aldersgrp.+diagnose	Fast til afsnit / Visuel vurdering vægt / Præcis vægt / Andet			
Fast dosering, fastsættelse	Hvorfor/hvordan er de faste doseringer valgt?			
Visuel vurdering, baggrund	Hvordan er behandler trænet?	Kalibrering frekvens	/	
Beregning af dosering	Fast til afsnit / Hovedregning / Digitale hjælpemidler / Andet			
Sprøjte + doseringsinterval Automat (A), manuel (M), anden (O)	Fast / Varierende	A / M / O	ml	Procedure nr. 1
	Fast / Varierende	A / M / O	ml	2
	Fast / Varierende	A / M / O	ml	3
	Fast / Varierende	A / M / O	ml	4

Vaccinationsstrategi									
Diagnose	Produkt	Adm. vej	Procedure nr.	Dosis /dyr	Antal Ds i alt	Tid Ml. doser	Tid Uger fra indsættelse	Dyr vacc.	Strategi
				ml		min/max	min/max	N/A/BS/I/O	C/S/OB/I/O
				ml		min/max	min/max	N/A/BS/I/O	C/S/OB/I/O
				ml		min/max	min/max	N/A/BS/I/O	C/S/OB/I/O
				ml		min/max	min/max	N/A/BS/I/O	C/S/OB/I/O

Antibiotikabehandlinger												
Sygdom Lungebetændelse (LU), Ledbetændelse (LB), Klovbrandbyld (KBB), Øjenbetændelse (ØJ), Mellemørebetændelse (MØ), Trykning (T), Diarré (D)	Bedriftens diagnose nr.	Typisk dyregruppe Uger fra indsættelse	Diagnostik Visuelle specifikke sygdomstegn (VD) / Visuel uspecifikke tegn (VU) / Termometer (T) / Andet (O)	Diagnostik specifikke krav* Fortløbende	Hyppighed for diagnosens anvendelse	Status førstevalg Angiv valg rækkefølge numerisk	Antal behandlinger/behandlingsperiode Antal gange ét dyr behandles dgl. og perioden i dage, hvor behandlingen anses for igangværende	Beh. Type Enkeltdyr (E), Metaphylaktisk (MF) + indsætter (I), Flokbehandling (F), Andet (O)	Procedure for dosering	Dosering i ml	Dosering dyr og enhed	Ved utilstrækkelig behandlingseffekt * Fastprocedure - overgang til 2. valg (FP), individuel vurdering (I), Andet (TF+fortløbende)
		min/max	VD/VU/T/O		dg/md		/	E/MF/F/O		min/max		FP/I/TF
		min/max	VD/VU/T/O		dg/md		/	E/MF/F/O		min/max		FP/I/TF
		min/max	VD/VU/T/O		dg/md		/	E/MF/F/O		min/max		FP/I/TF
		min/max	VD/VU/T/O		dg/md		/	E/MF/F/O		min/max		FP/I/TF
		min/max	VD/VU/T/O		dg/md		/	E/MF/F/O		min/max		FP/I/TF
		min/max	VD/VU/T/O		dg/md		/	E/MF/F/O		min/max		FP/I/TF
		min/max	VD/VU/T/O		dg/md		/	E/MF/F/O		min/max		FP/I/TF
		min/max	VD/VU/T/O		dg/md		/	E/MF/F/O		min/max		FP/I/TF
		min/max	VD/VU/T/O		dg/md		/	E/MF/F/O		min/max		FP/I/TF
		min/max	VD/VU/T/O		dg/md		/	E/MF/F/O		min/max		FP/I/TF
		min/max	VD/VU/T/O		dg/md		/	E/MF/F/O		min/max		FP/I/TF

*Beskrivelser: Diagnostik (D) krav og procedure ved utilstrækkelig (TF) behandlingseffekt	

Besætningsdiagnoser behandlet med antibiotika

Diagnose nr. Tildeles af interviewer	Diagnose	Produkt navn eller nordisk varenummer på AB produkt	Adm. Adm. vej	Dosis	Enh.	Dyr	Dyr enh.	Antal Ds i alt	Tid ml. doser

KØBENHAVNS UNIVERSITET
UNIVERSITY OF COPENHAGEN

VetStat Kvæg - Evaluering af dataopgørelser og forbedret kvantificering og forståelse af mønstre i medicin-forbruget i kvægbesætninger

Samtykkeerklæring	NEJ	JA
Jeg deltager frivilligt i projektet*		
Jeg er bekendt med at mit samtykke kan trækkes tilbage samt processen for dette (se bagsiden)		
Jeg er tilstrækkeligt informeret om projektets formål		
Jeg er informeret om at oplysninger indsamlet anonymiseres inden offentliggørelse i nogen form		
Jeg er informeret om at billedmateriale fra besøget ikke offentliggøres uden min skriftlige godkendelse for hvert billede.		
Jeg giver samtykke til at data indsamlet i spørgeskema og interview ved besætningsbesøget dags dato må anvendes i projektet		
Jeg giver samtykke til at ansvarlig for projektet må indhente relevante oplysninger (se bagsiden) om besætningen fra Kvægdatabasen i projektperioden via en legalisering ansøgt gennem SEGES		
Jeg giver samtykke til at der ved besøget må tages billeder af besætningens medicinopbevaring og behandlingsprocedurer		
Jeg giver samtykke til at data indsamlet ved besætningsbesøg må indgå i analyser med data fra VetStat.		
Jeg giver samtykke til at data indsamlet ved besætningsbesøg må indgå i analyser med data fra **Kvægdatabasen** og databasen VetStat.		

*"Projektet" dækker i denne erklæring over projektet "VetStat Kvæg - Evaluering af dataopgørelser og forbedret kvantificering og forståelse af mønstre i medicin-forbruget i kvægbesætninger" Se projektbeskrivelsen her: https://ivh.ku.dk/forskning/dyrevelfaerd-og-sygdomsbekaempelse/projektside/vetstat-kvaeg/

Jeg bekræfter ved underskrift på denne erklæring,

at jeg ____ Dags dato_________________

giver samtykke ovenstående

Behandling af personoplysninger i dette projekt sker i overensstemmelse med behandlingsreglerne i databeskyttelsesforordningens kapitel II. Denne erklæring er udarbejdet ud fra Datatilsynets Vejledning om Samtykke af Maj 2021.

KØBENHAVNS UNIVERSITET
UNIVERSITY OF COPENHAGEN

Hvad betyder mit samtykke?:
Dit samtykke betyder, at vi må anvende de data, som indsamles i dette projekt. Data vil indgå i opgørelser og analyser i en anonymiseret form, som ikke kan spores tilbage til din besætning.

Tilbagetrækning af samtykke:
Hvis du ikke ønsker at deltage i projektet alligevel kan dit samtykke trækkes tilbage. Dette sker ved at kontakte projektansvarlig Jeanette Kristensen på mail jp@sund.ku.dk. Din mail skal markeres tydeligt med hvem du er, dine kontaktoplysninger samt at du ønsker at trække dit samtykke tilbage. Hvis du ikke ønsker at dine data skal indgå i publikationer (altid i anonymiseret form) skal din tilbagetrækning ske inden 1. juli 2023.

Projektets formål:
Projektets overordnede formål er at evaluere og forbedre dataopgørelser samt at øge forståelsen af mønstre i medicinforbruget i danske kvægbesætninger. For at opnå dette har vi i projektet valgt en tilgang der kan beskrives som "kvæg til computer". Vi ønsker at klarlægge, hvordan medicinforbruget i kvægbesætningerne rent praktisk ser ud og følge det gennem diverse registreringer til opgørelserne i den nationale database VetStat som administreres af Fødevarestyrelsen. Dette gøres blandt andet med henblik på at klarlægge hvordan VetStat opgørelserne og deres opgørelsesmetoder afspejler medicinhåndtering og –forbrug på danske kvægbesætninger. I tillæg til dette vil vi i studiet kigge på mønstre i medicinforbruget samt forsøge at identificere faktorer som kan have indflydelse på valg af behandlinger herunder behandlings- og produktionsstrategier.

Data inkluderet:
Vi indhenter oplysninger om den enkelte besætnings behandlings- og produktionsstrategier – fokus er på strategier, der kan have betydninger for din besætnings nuværende sundhedsstatus og dennes udvikling over tid. Vi indhenter også oplysninger om aktuelle behandlings- og produktionsprocedurer på besætningen, altså hvordan tingene rent praktisk gøres. Alle disse oplysninger sammenholdes med VetStat oplysninger om indkøb af medicin samt behandlingsoplysninger fra kvægdatabasen, hvis disse foreligger (se nedenfor). Vi indhenter oplysninger fra VetStat og hvis muligt kvægdatabasen for hele år 2022 og 2023.

Relevante oplysninger fra kvægdatabasen
Relevante oplysninger fra Kvægdatabasen omfatter besætningsdiagnoser samt behandlings- og sundhedsregistreringer som gør det muligt at opgøre antal daglige enkeltdyrsbehandlinger i studieperioden per diagnose og produkt. I tillæg hertil indhentes oplysninger som gør det muligt at identificere mængde af antibiotikaholdige produkter eller vacciner brugt per daglige enkeltdyrsbehandling per diagnose.

Datahåndtering:
Alle dine data håndteres kun af projektansvarlig inden de anonymiseres. Data bliver opbevaret på et personligt drev, hvor kun projektansvarlig har adgang. Dine data vil ikke blive brugt i andre projekter uden dit samtykke.

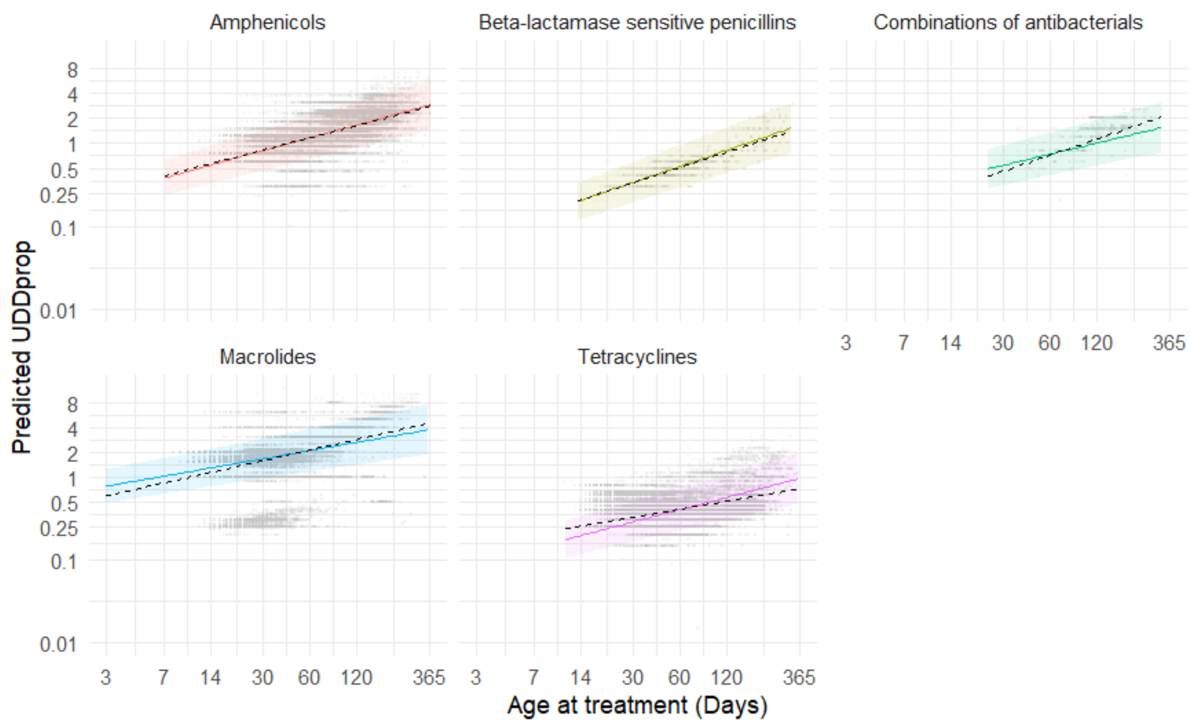
Anonymisering:
Dine data anonymiseres ved hjælp af en nøgle som giver dine data et ID-nummer i stedet for besætningsnummeret. Når projektet er overstået slettes nøglen og dermed kan data ikke kædes sammen med din besætning længere.

Appendix C

Supplementary material for Manuscript III

M3 Supplementary

We ran a generalised linear model excluding the random effect of farm to assess how it affected the model predictions. The R^2 decreased to 0.63 and the AIC was higher than for our presented model. Predictions were close to identical for amphenicols and beta-lactamase sensitive penicillins. Macrolides had a slightly steeper slope and tetracyclines a flatter slope in the simple model. These findings suggest that our model predictions are relatively robust and again underscore the differences between antibiotic classes.



M3S1F1: Predicted average UDDprop versus age at treatment in days for antibiotic classes used for lung disorders in the study population with 95% confidence intervals. The dashed lines show model predictions for a model which did not account for the random effect of farm. The grey points are the data values used for model building. Note that scales are log-transformed but labelled with non-log-transformed values.