Author/s:
Sri, Anna Ellen

Title:
Progressing antimicrobial stewardship in Australian veterinary practice through a One Health lens

Date:
2025

Persistent Link:
https://hdl.handle.net/11343/357233

Progressing antimicrobial stewardship in Australian veterinary practice through a One Health lens

By

Anna Sri BVSc (Hons) MPH

ORCID ID: 0000-0003-0843-4877

This thesis is submitted for the Doctor of Philosophy in Veterinary Medicine.

Melbourne Veterinary School, Faculty of Science &

National Centre for Antimicrobial Stewardship

February, 2025

This thesis is being submitted in total fulfilment of the Doctor of Philosophy in Veterinary Medicine.

Abstract

Antimicrobial stewardship in Australian veterinary practice has advanced significantly in the last decade. Availability of Australian-specific guidelines for the major domestic species have allowed appropriateness of antimicrobial use to be evaluated more effectively. However, understanding of antimicrobial use and support for antimicrobial stewardship is still lacking, especially in specific sectors. Veterinarians do not have to report their use of antimicrobials that are of high importance to human health. Neither is there regular monitoring of resistance patterns amongst bacterial species that are of significance to animal health.

Veterinarians have reported challenges to appropriate prescribing, including financial constraints of their clients, the costs of diagnostic tests, such as culture and susceptibility testing, and the influence of their colleagues and workplace cultures. In settings where these barriers are compounded due to systemic issues, practicing antimicrobial stewardship is even more challenging. Yet, at the same time, veterinarians also endure (often incorrect) comments in the media, from the public and even the human health sector about the negative impact of antimicrobial use in animals.

The studies described in this thesis aimed to progress antimicrobial stewardship in Australian veterinary practice while also using a One Health approach to increase collaboration, transdisciplinarity and equality. The attitudes of Australian veterinarians were sought via an online survey about the use of antimicrobials of high importance to human health. Overall, Australian veterinarians agreed with some restrictions on the use of these antimicrobials. In particular, when presented with multiple scenarios, in all cases, the majority of veterinarians thought use of high importance antimicrobials was reasonable if culture and susceptibility testing results suggested resistance to low- and medium-rated antimicrobials that could be used to treat the case.

Subsequently, a Delphi consensus-building study involving human and animal health experts built upon the results obtained from the first survey. Eight consensus statements were agreed upon about the use of high importance rated antimicrobials in animals and how this use could be deemed appropriate. Some of these included recommendations around reporting use and how veterinarians should record and justify their use in their medical records.

Both the survey of veterinarians and the Delphi consensus-building study suggested a significant role of culture and susceptibility testing in guiding and classifying antimicrobial use as appropriate, yet no guidance was available for domestic settings without easy and affordable access to this diagnostic testing, such as remote Indigenous communities. Consequently, a pilot surveillance study of prevalence and resistance patterns of *Staphylococcus spp*. isolated from dogs in a remote Indigenous community in Australia was undertaken to address the data gap in this area. Results suggested low levels of antimicrobial resistance. In-depth interviews with fourteen participants who worked in remote Indigenous communities (nurses, doctors, Aboriginal health workers, veterinarians and antimicrobial stewardship pharmacists) were also conducted to explore under-investigated topics of AMR and AMS as they relate to medical and veterinary practice. Staff shortages and overwork, interpersonal relationships and trust with community members influenced the practice of good AMS principles. Concerns around surgical site infections in settings where ongoing clinical monitoring opportunities were limited were a high driver of antimicrobial use for veterinarians. Several enablers for AMS were identified including the positive influence of local Aboriginal health practitioners and their equivalents in animal health and a willingness to collaborate. An openness by participants to improve their practices was also consistent with the results from the initial survey of veterinarians.

This study expands the scope of veterinary antimicrobial stewardship in Australia. The impact of considering upstream influences on AMR and being guided by the principles of One Health has resulted in practical guidance for veterinarians, policymakers and other stakeholders in addressing the super-wicked problem of antimicrobial resistance.

Declaration

This thesis comprises only the original work toward the Doctorate of Philosophy in Veterinary Medicine except where indicated in the preface.

Due acknowledgement has been made in the text to all other material used.

The thesis is fewer than the maximum word limit in length, exclusive of tables, maps, bibliographies and appendices as approved by the Research Higher Degrees Committee.

Preface

All of the work presented henceforth was approved by the University of Melbourne's Human Research Ethics Committee (Chapters 2, 3 and 5) or Animal Ethics Committee (Chapter 4). Research for Chapter 5 was also approved by the Human Research Ethics Committee of the Northern Territory.

Chapter 2 was published by the Journal Antibiotics on 10/11/2022: Anna Sri, Kirsten E Bailey, James R Gilkerson, Glenn F Browning, and Laura Y Hardefeldt. *Attitudes towards Use of High-Importance Antimicrobials—A Cross-Sectional Study of Australian Veterinarians*. Antibiotics, 2022. **11**.
Anna Sri: Conceptualisation, data curation, formal analysis, investigation, methodology, visualisation, writing – original draft, writing – review & editing.
Kirsten E. Bailey: Conceptualisation, methodology, supervision, writing – review & editing.
Ri Scarborough: Conceptualisation
James R. Gilkerson: Conceptualisation, supervision, writing – review & editing.
Karin Thursky: Conceptualisation.
Glenn F. Browning: Conceptualisation, writing – review & editing.
Laura Y. Hardefeldt: Conceptualisation, funding acquisition, methodology, supervision, writing – review & editing.
All authors have read and agreed to the published version of the manuscript.
This study was funded by the National Health and Medical Research Council of Australia through the Centres of Research Excellence Scheme, Grant no. 1079625 (National Centre for Antimicrobial Stewardship). L.H. is funded by the Australian Research Council through the Discovery Early Career Research Award program. A.S. was a recipient of an Australian Postgraduate Award scholarship.
We would like to thank the veterinarians who took part in this survey and those who facilitated it by sharing the survey link with their colleagues.

Chapter 3 was published by the Journal One Health on 26/08/24: Anna Sri, Kirsten E Bailey, Ri Scarborough, James R Gilkerson, Karin Thursky, Glenn F Browning, Laura Y Hardefeldt. *Reaching consensus amongst international experts on the use of high importance-rated antimicrobials in animals – a Delphi study.* One Health 2024. **19**.
Anna Sri: Conceptualisation, data curation, formal analysis, investigation, methodology, visualization, writing – original draft, writing – review & editing.
Kirsten E. Bailey: Conceptualisation, methodology, supervision, writing – review & editing.
Ri Scarborough: Conceptualisation
James R. Gilkerson: Conceptualisation, supervision, writing – review & editing.
Karin Thursky: Conceptualisation.
Glenn F. Browning: Conceptualisation, writing – review & editing.
Laura Y. Hardefeldt: Conceptualisation, funding acquisition, methodology, supervision, writing – review & editing.

This study was funded by the Australian Research Council through the Discovery Early Career Research Award program DE200100030 awarded to L.Y.H. A.S. and R.S. were the recipients of Australian Postgraduate Award scholarships. K.B. was supported through NHMRC CRE Application 1079625.
We would like to thank all the participants of the study for contributing their time and expertise. We would also like to thank the following Delphi process participants who consented to being acknowledged publicly.
Dr Ray Castle BSc BVMS (Hons)
Dr Tim Nuttall BSc BVSc CertVD PhD CBiol MRSB MRCVS
Dr Ross Cutler BVSc PhD
Professor Darren Trott BSc (Hon), BVMS (Hon), PhD
Dr Jo Coombe BSc (Hons), BVSc (Hons), PhD
Dr David Singleton BVSc MSc PhD MRCVS
Dr Tina Moeller Soerensen DVM, PhD

Chapter 4 is in preparation for publication: Anna E Sri, Kirsten E Bailey, Amy Hii, Joan Malku Dhamarrandji, James Bayung Garrawitja, Joanne L. Allen , Rhys N. Bushell , Marc S. Marenda, James R Gilkerson, Glenn F Browning, Laura Y Hardefeldt. *Antimicrobial resistance of canine staphylococci isolates from a remote Indigenous community: Is this an emerging One Health issue?*
This work was completed with the support of Yalu Aboriginal Corporation. We would like to thank Yalu Aboriginal Corporation community reference group members, Cyril Bukulatjpi, Brando Yambalpal, Evelyn Djotja and Yunggirnga Bukulatjpi, as well as all the members of the community and their lovely dogs who took part in this study. Thanks also to East Arnhem Regional Council Animal Management for use of the vehicle and general support.
L.H. was funded by the Australian Research Council through the Discovery Early Career Research Award program. A.S. was a recipient of an Australian Postgraduate Award scholarship.
Anna Sri: Conceptualisation, data curation, laboratory work, formal analysis, investigation, sample collection, methodology, visualization, writing – original draft, writing – review & editing.
Kirsten E. Bailey: Conceptualisation, supervision, writing – review & editing.
James R. Gilkerson: Conceptualisation, supervision, writing – review & editing.
Amy Hii: Assistance with laboratory work
Joan Malku Dhamarrandji: Communication with community members, conceptualisation, sample collection
James Bayung Garrawitja: Communication with community members, conceptualisation, sample collection
Joanne L. Allen: Methodology for laboratory work
Rhys N. Bushell: Methodology for laboratory work
Marc S. Marenda: Methodology for laboratory work
Glenn F. Browning: Conceptualisation, writing – review & editing.

Laura Y. Hardefeldt: Conceptualization, funding acquisition, supervision, writing – review & editing.

Chapter 5 is in preparation for publication: Anna Sri, Laura Hardefeldt, James Gilkerson, Kirsten Bailey
A One Health approach to AMS in remote Indigenous communities
This work was completed with the support of Yalu Aboriginal Corporation.
Anna Sri: Conceptualisation, data collection, data curation, formal analysis, investigation, methodology, sample collection, transcription, visualization, writing – original draft, writing – review & editing.
Thanks to all the participants who generously gave their time and provided their views.
Kirsten E. Bailey: Supervision, writing – review & editing.
James R. Gilkerson: Supervision, writing – review & editing.
Laura Y. Hardefeldt: Conceptualization, funding acquisition, supervision, writing – review & editing.

Acknowledgements

I would like to respectfully acknowledge the Gubbi Gubbi and Kabi Kabi people, the Traditional Owners of the Sunshine Coast area where I lived throughout my PhD and where I wrote and researched from home. I would also like to respectfully acknowledge the Wurundjeri Woi-wurrung and Bunurong peoples, the Traditional Owners of the unceded land where the University of Melbourne Parkville and Werribee campuses are located and where much of the laboratory and in-person work for this thesis took place. Also, without the inspiration and support from Yolngu community members from North-East Arnhem Land this work would not have taken place. I also respectfully acknowledge the Traditional Owners of that land.

I would like to thank and acknowledge my advisory committee chair Professor Andrew Fisher. I was so lucky to have such a kind and knowledgable person to help me navigate this PhD process. His sudden passing last year was a shock. He is fondly remembered with great respect by all those who knew him, however briefly. Thanks to Dr Andrés Diaz-Méndez for stepping in at short notice to fulfil the role and your support since, especially when I needed an extension at short notice.

Thanks to my brilliant supervisors. One could not wish for a better supervisory team with such complementary skills. Thanks to Assoc. Professor Laura Hardefeldt for initially inviting me to undertake this process, it was unexpected but turned out to be such a great experience. Your ability to just get things done is unsurpassed and the envy of many! Thanks to Dr Kirsten Bailey for your care, consideration and attention to detail. I appreciate all the time you have taken to help me improve my work and that you are always thinking about how to help others understand our research findings. Thanks to Professor James Gilkerson for never being phased by anything and saying yes to everything I wanted to do whether it be a conference in Italy or research in a remote community. I also appreciate your flexible approach to deadlines.

It has been amazing to work with so many skilled researchers as part of APCAH and NCAS. Thanks to Professor Glenn Browning for your support of my work and everyone who helped me in so many ways. Special thanks to Jo Allen for helping me with lab work when building 400 was so ghostly during the pandemic and Rhys Bushell for patiently teaching me in Werribee. Thanks to Ri Scarborough and Suzanna Richards for being so supportive and passionate about AMS from the very outset. To Amy Hii and Kim Carey, it's been so lovely to have fellow PhD candidates who understand whatever comes up. Amy, your help with lab work the second time around also made it much less overwhelming! Thanks to the AMROH-SEA team for being exceptional colleagues and helping me consolidate my understanding of AMR and AMS.

I would like to thank my family for all their support, especially my parents and my brother and his partner Anna. You always believe in me and have provided so much practical support. It has been great to discuss ideas and concepts with you. Thanks especially to Anna for providing insight and advice about the PhD journey before I decided to undertake it myself.

I'm so grateful to have such loving and supportive friends across the country and internationally. I would have to include many chapters to acknowledge all of you individually. Please know I appreciate all the calls, messages, meals, welcome distractions, places to stay and general support (including when I was unwell, during lockdown, or arriving and leaving from the airport). I am extremely thankful for all of you and love that we can always just pick up where we left off.

Dogs constantly brighten our days and bring out the best in us. I would like to give an acknowledgement to little Wren, a tiny, precious dog who will never understand her big impact and who continues to entertain us, to Doogal who was with me throughout the first years of my PhD and made working at home so enjoyable during difficult times, and to Meg, always, the perfect gift who inspired me to become a veterinarian.

It is fitting but distressing that I am finishing my thesis as South-East QLD is being impacted by its first cyclone in fifty years. In 2015, I witnessed the devastating and lasting impacts of Cyclone Lam and Cyclone Nathan while working in the Northern Territory. It prompted me to start an MPH after seeing there was inclusion of a 'One Health' course and a 'Health Impacts of Disasters' course. I felt that my work individually as a clinical veterinarian was going to be undermined by impacts of the climate crisis and rising inequality. In the face of multiple overlapping crises I want to acknowledge all the people working to address these problems in so many different ways. Keep doing whatever you're doing – providing support, developing solutions, advocating, agitating, locking on, and building stronger communities locally and globally.

Table of Contents

Acronyms

AHP	Aboriginal Health Practitioner
AMR	Antimicrobial resistance
AMS	Antimicrobial stewardship
AMU	Antimicrobial use
ASTAG	Australian Strategic and Technical Advisory Group
CARPA	Central Australian Rural Practitioners Association
CIAs	Critically important antimicrobials
C&S	Culture and susceptibility testing
ESBL	Extended-spectrum beta-lactamase
FAO	Food and Agriculture Organization
HIAs	High importance antibacterials (as per the Australian ASTAG rating system)
JETACAR	Joint Expert Technical Advisory Committee on Antibiotic Resistance
MIAs	Medically important antimicrobials
MRSA	Methicillin-resistant *Staphylococcus aureus*
MRSP	Methicillin-resistant *Staphylococcus pseudintermedius*
OHHLEP	One Health High-Level Expert Panel
UNEP	United Nations Environment Programme
WASH	Water, sanitation and hygiene
WHO	World Health Organization
WOAH	World Organisation for Animal Health

List of tables and figures

Introduction

Antimicrobial resistance (AMR) is well-established as a global challenge with profound impacts for nearly all living beings and the environments they inhabit [1]. Increasing levels of morbidity and mortality are expected into the future for humans and animals [2, 3]. A landmark report released in 2016 estimated that up to 10 million human lives could be lost due to AMR every year [1]; for context, approximately 7.1 million people have died due to the COVID-19 virus over a five year period [4]. The problems associated with AMR are only exacerbated by the lack of novel antibiotic drugs being brought to market [5]. In fact, the consequences of AMR are so pervasive, it has been termed by some as a 'super-wicked' problem requiring action from human, animal and environmental health spheres, government and non-government organisations, private business and society in general [6].

This thesis builds significantly on the work of Hardefeldt [7], which established the need for improved antimicrobial stewardship (AMS) practices across the Australian veterinary profession and identified the use of high importance antimicrobials (HIAs) as an area where the quality of prescribing could be improved. Some of the most significant AMR concerns relate to resistance development to HIAs, which are termed thus because there are no or very few treatment alternatives available for human infections if resistance develops to these antimicrobials [8]. As such, use of antimicrobials in this category is often the target of AMS activities, which aim to reduce the development of AMR.

AMR is further complicated by numerous other socio-cultural, political, and economic factors (also referred to as the social determinants of health and related inequalities) [9]. Simply imposing additional barriers to accessing antimicrobials, such as requiring a prescription or restricting use in animals, could result in worse human or animal health outcomes. However, a requirement in the future for more expensive antimicrobials or those requiring intravenous access for administration due to AMR may also have a greater negative impact on people disadvantaged by current systems [10, 11]. Therefore, effective AMS that does not unintentionally further perpetuate inequalities requires a conscious effort with an awareness of influencing factors that exist and persist beyond the general practice, hospital, or veterinary clinic. The use of an integrated One Health approach, which has at its core principles of equity, parity, equilibrium, stewardship and transdisciplinarity can assist such efforts [12].

The primary aim of this thesis is to progress antimicrobial stewardship in Australian veterinary practice by expanding its scope through a One Health approach. This includes a focus on equity and transdisciplinarity. Other objectives which support this aim include;

1. To improve understanding of the attitudes of Australian veterinarians about antimicrobial use particularly those with a high importance rating (HIAs)
2. Develop consensus across human and animal health experts around the use of HIAs in animals, including the appropriate circumstances and regulations surrounding their use.

3. Undertake surveillance in dogs from a remote First Nations community for resistant bacteria focusing on staphylococci.
4. To increase understanding of how antimicrobials are used in remote First Nations communities and the broader issues surrounding their use, with reference to One Health principles.

With increasing awareness of the serious threat posed by AMR, the field of AMS has emerged and gained traction, particularly over the last decade [13]. Although progress has been made with activities, policies and regulations falling under the sphere of AMS [1, 14, 15] the complex nature of the challenge means that current efforts are still insufficient. Early AMS efforts in the veterinary sphere understandably related to banning or further regulating the use of antimicrobials for growth promotion in livestock as this was a much greater concern than therapeutic use at the time [16, 17]. Recently Australian-specific antimicrobial prescribing guidelines have been developed for numerous domestic species, which dramatically improves the opportunity to improve the quality of prescribing, providing a clear standard against which prescribing choices can be evaluated [18-22]. However, a tendency to focus solely on terrestrial food-producing animals with less known about implementation of AMS practices in diverse veterinary settings, including those that treat companion animals, means that some opportunities to address AMR in a more holistic way are currently being missed [2, 16, 23]. There is an increased risk for transfer of resistant bacteria when people spend extended time with their companion animals, especially when involving close contact [24]. Antimicrobials, whether given to a food-producing or companion animal, also modify and interact with the environmental microbiome in soil or water, which in turn can have a flow-on impact on humans or other animals including wildlife [2, 25]. These are just two examples that highlight the need to look at but also beyond antimicrobial use in food-producing animals [26].

In an attempt to expand the sphere of discussion about AMS in veterinary practice to one that is more consistent with the key principles of One Health, this thesis takes the opportunity to examine drivers of AMR from a very broad perspective. It also adds to the body of work at a very granular level to fill gaps that exist particularly in animal health, where access to data to support decision-making is well behind that available for human health.

In Australia, any discussion of health and the interconnectedness of beings and their environment must acknowledge that these ideas have existed and persist in the current time due to the incredible resilience and generosity of the First Peoples of this country despite ongoing colonisation and injustices. Despite awareness of the social determinants of health and related inequalities, Western medicine both in a veterinary and human medical context persists with disconnected ways of thinking about and addressing illness. AMS in an Australian veterinary setting can be more effective when acknowledgement occurs of upstream drivers of AMR, which can include factors as diverse as access to infrastructure, workforce challenges, systemic racism, socio-economic status, and health system governance.

Considering that resistant bacteria or genetic elements can transfer from one practice type to another or between the spheres of human, animal and environmental health, it makes sense that stewardship activities across all types of practice must be considered. In addition, some veterinary clients, such as people on low incomes or Indigenous people may already be disproportionately impacted by AMR in relation to their own health. Prioritising and including these veterinary clients and their communities in establishing effective AMS programs whether they be veterinary focused programs or programs using a One Health framework is crucial in creating sustainable, effective change and addressing current inequalities.

Given the broadening nature of the topics of antimicrobial resistance and antimicrobial stewardship as well as the diverse ways of understanding the issues and the specialised language required, an overview of relevant terminology, and its use in this thesis is provided as part of the literature review in Chapter 1. Research will be situated amongst applicable themes, including how veterinary AMS is conceptualised and assimilated with concepts of One Health, the social determinants of health, and Indigenist Health Humanities.

Chapter 2 addresses a gap in knowledge about reasonable use of antimicrobials, particularly those with a high importance rating (HIAs), in veterinary practice in Australia. It explores veterinarians' attitudes towards their use in veterinary medicine, and determines levels of agreement amongst veterinarians about the introduction of restrictions and other conditions on their use.

Chapter 3 further defines the circumstances under which antimicrobials with high importance to human health can be used in animals by achieving consensus amongst human health and veterinary experts on key elements of antimicrobial use and stewardship. Recommendations are provided about reporting this use going forward.

Chapter 4 fills a data gap by describing a sampling and surveillance program for resistant bacteria in a remote community dog population. This type of active surveillance of all dogs in the community, not just those presenting for veterinary care, provides insight into future risks of development of AMR and its management.

Chapter 5 applies a One Health approach by undertaking qualitative interviews of Indigenous and non-indigenous human and animal health practitioners who had worked in remote Indigenous communities. It explores some of the practical challenges surrounding AMS in remote Indigenous communities and enables deep insights into current challenges, successful practices, and knowledge gaps.

Chapter 6 is a general discussion describing the outcomes and impact of this thesis. Viewing veterinary AMS as part of a holistic One Health approach acknowledges the disproportionate impact of AMR on some demographics and that veterinary AMS cannot be disconnected from wider AMS initiatives or the global impacts of AMR. This leads us to understand that AMS in veterinary practice should occur in a way that is grounded in social justice and equality.

Chapter 1 Literature review

Antimicrobial resistance

Antimicrobial resistance (AMR) refers to "a property of microorganisms that confers the ability to inactivate or elude antimicrobials or a mechanism that blocks the inhibitory or killing effects of antimicrobials." [27] Microorganisms can include bacteria, viruses, and fungi. Throughout this review, the microorganisms being referred to are generally bacteria and the antimicrobials referred to are usually antibacterial medications that kill bacteria or stop their growth. This follows the actions of the World Health Organisation and other leading organisations to use the term antimicrobial more widely than antibiotic or antibacterials in order to draw attention to the issues relating to resistance to all antimicrobials. For example, antifungal resistance has not yet attracted the same level of concern as that of antibiotic resistance, but it is an emerging problem [28]. The use of a broader term also helps maintain collaboration between various stakeholders working with different antimicrobials and may also include antiseptics and disinfectants [29].

The World Health Organisation published a *Global Action Plan on Antimicrobial Resistance* in 2015 to coordinate and guide international action addressing AMR [29]. It encouraged countries to create their own national action plans, with reference to the global plan, and recommended numerous actions including the collection of data and implementation of stewardship programs [29].

Annual additional deaths due to AMR in the future could reach over 10 million globally and this was calculated with acknowledgement that downstream impacts such as not being able to safely carry out surgical procedures were not assessed [1]. Procedures such as orthopedic surgery and caesarean sections, as well as organ transplantation, cancer chemotherapy and the care of premature babies, are all at risk [30]. This is consistent with the views of World Health Organization (WHO) director-general Dr Tedros Adhanom Ghebreyesus who described AMR as "a slow tsunami that threatens to undo a century of medical progress" [31]. The ramifications of the COVID-19 pandemic on all spheres of life, including health systems, have also slowed progress in addressing AMR [32, 33].

In Australia, there is generally low use of antimicrobials in animals and low levels of resistance in people and animals particularly compared to low- and middle-income countries [34]. Low levels of resistance to fluoroquinolones in the Australian human population have also been linked to the strict regulation of this antimicrobial for both human and food-producing animal use [35, 36]. AMR mortality in people in Australia is also relatively low – approximately 1000 per year [37]. However, without significant and sustained action this could increase over the next thirty years to 10 000 deaths per year [33].

Many changes thus far in relation to antibiotic use in animals in Australia are in line with the recommendations made by the Joint Expert Technical Advisory Committee on

Antibiotic Resistance (JETACAR) in 1998, which was established by the Australian Government [16, 17, 38, 39]. The role of the committee was to investigate and recommend risk management strategies in relation to the threat of resistant bacteria spreading from food-producing animals to humans, with particular focus on the use of antibiotics as growth promotants [16, 39]. JETACAR made twenty-two recommendations and although they have not all been implemented, they have provided the basis for some important actions such as the removal of label claims for growth promotion on all medically important antibiotics and that fluoroquinolones have never been permitted in food-producing animals in Australia [16].

A conservative approach to antimicrobial registration has been adopted by the Australian Pesticides and Veterinary Medicines Authority (APVMA) which is the agency responsible for registering medicines for use in animals [16, 40]. Australia's long-running national residue survey, in place since the 1960s, also plays a significant role in detecting antimicrobial residues in food-producing animals in Australia and these data are publicly available [41]. Strict compliance with withholding periods and residue monitoring has contributed to low use of many antimicrobials in food-producing animals in Australia. The Australian Government has also developed a *National Antimicrobial Resistance Strategy* [15] as a response to recommendations by the World Health Organisation. The *Australian Animal Sector National Antimicrobial Resistance Plan* [42, 43] has been in place since 2018 and while progress in some areas has been minimal, it has resulted in surveillance studies and sector specific plans, with significant opportunity to expand activities in the future.

Antimicrobial importance rating systems

Antimicrobial importance rating systems are classification systems based on pre-determined criteria. The purpose of an antimicrobial importance rating system is generally to provide guidance to stakeholders e.g. policymakers, regulators, and prescribers, about the risk of AMR developing with the use of antimicrobials. They incorporate available evidence about AMR but may also rely on expert opinion. Other criteria considered may include how important the antimicrobial is to human health and the likelihood of transmission of resistance, and how prevalent the conditions requiring antimicrobial treatment are in that country or region. Without rating systems it is difficult to assess whether antimicrobial use (AMU) is appropriate (sometimes referred to as the quality of prescribing).

Other antimicrobial rating or classification systems do not solely prioritise the risk of AMR developing but may also incorporate other criteria. For example, the importance of antimicrobials in maintaining animal welfare and food security in the face of serious animal disease is considered when determining which antimicrobials are included in the World Organisation for Animal Health (WOAH) List of Antimicrobial Agents of Veterinary Importance [44]. Some systems may prioritise more affordable medications or those that are readily accessible in low and middle income countries such as is the case for the WOAH List of Antimicrobial Agents of Veterinary Importance and the World Health Organization AWaRe (Access, Watch, Reserve) classification [45].

Critically important antimicrobials

Critically important antimicrobials (CIAs) refers to classes of antibiotics appearing on the WHO Critically Important Antimicrobials for Human Medicine list. This is essentially a global antimicrobial rating system. Criteria were used to group the antibiotics into ordered categories by considering their use in humans and animals, the seriousness of the diseases being treated, and the ramifications if there were no other alternative therapies available for human use due to antibiotic resistance developing [46, 47]. This list was created to allow more focused management strategies and guidelines regarding use of these antimicrobials in nonhuman sectors. At this stage, this refers to use in animal health (primarily food-producing animals). Data limitations and other factors have meant that antimicrobial use in the plant and crop sectors has largely been ignored [48]. The WHO intended that the CIA list be used by nations to assess their own use of antimicrobials in animals and adapt the list to consider resistance patterns and disease prevalence in their own country. Country-specific lists allow more nuanced assessment of new and existing drug applications. They also allow consideration of future consequences of resistance and risk management strategies for example, via restriction of use of antimicrobials in that country or having specific label restraints or prescription requirements [48]. In 2024, the WHO updated the CIA list and renamed it 'Medically important antimicrobials' (MIA), however the purpose is the same [46].

High Importance Antimicrobials

In Australia, antimicrobials are given an importance rating by the Australian Strategic and Technical Advisory Group on antimicrobial resistance (ASTAG). The ASTAG rating system is based upon, and considers, the WHO CIA list. However, ASTAG has rated some antibiotics differently given the local situation in Australia where resistance levels and disease prevalence are different to other parts of the world [8]. These importance ratings are published in a document that is publicly available and updated as required [14]. Ratings are given to antibacterials that are registered for use in Australia in either people or animals, as well as including some antibiotics that are not registered in Australia but may be in current use internationally or are otherwise relevant. The current importance ratings are low, medium and high and correspond to a colour-code of green, orange, and red respectively [8]. High importance antibacterials are, "essential for the treatment or prevention of infections in humans where there are few or no treatment alternatives for infections". HIAs in Australia are listed in Table 1 along with their registration status [8]. HIAs that are currently registered for use in food-producing animals include virginiamycin and ceftiofur. Some fluoroquinolones are registered for use in dogs and cats. In companion animal and equine practice polymyxin B is registered for topical ocular or aural use, as are third generation cephalosporins cefovecin (mostly used in cats) and ceftiofur (not widely used in dogs, but used in horses) [49].

In Australia, the term 'off-label' refers to a registered veterinary drug that is used for a different species or indication, at altered dose rate or treatment interval compared to that on the label. Or, 'off-label' can also refer to the use of a human registered antimicrobial for the treatment of an animal. There must be a clear indication for the off-label use, such as a veterinary labelled product for that species not being appropriate or available. Off-label use of amikacin and rifampicin has been reported in horses [50]. Ceftiofur and cefovecin are also used contrary to the label claims (without culture and susceptibility results) [50]. Sometimes off-label use is more appropriate when using antimicrobials at a higher more effective dose or different frequency to that described on the label [51]. The use of high importance antibacterials (HIAs) in animals in Australia is widespread, contentious, a focus for AMS activities and has been highlighted as an area where more research is needed to provide veterinarians with focused guidance [23, 52-57].

Table 1: High importance antimicrobials in Australia

Antimicrobial	Class	Registration status
Piperacillin with tazobactam Ticarcillin with clavulanic acid Ceftolozane with tazobactam	ß-lactamase inhibitor combinations	Human use
Amikacin	Aminoglycoside	Human use
Clofazimine Dapsone	Antileprotics	Human use
Isoniazid Ethambutol Pyrazinamide Cycloserine p-aminosalicylic acid Prothionamide Capreomycin	Antimycobacterials	Human use
Imipenem Meropenem Ertapenem	Carbapenems	Human use
Ceftriaxone Cefotaxime	3rd generation cephalosporins	Human use
Ceftiofur	3rd generation cephalosporins	Not used in humans Approved for use in cattle, dogs and horses Label restraints: Do not use for mass medication; individual animal treatment only. Do not use by intramammary, topical or oral route in food producing animals. Do not use for the treatment of mastitis in dairy cattle.
Cefovecin	3rd generation cephalosporins	Not used in humans Approved for use in dogs and cats Label restraints: Do not use in food producing species of animal or guinea pigs. For use only in dogs and cats where indicated by antibiotic sensitivity testing according to the principles of prudent use.
Ceftazidime Cefepime	4th generation cephalosporins	Human use
Ceftaroline	Anti-MRSA Cephalosporins	Human use
Fosfomycin	Fosfomycins	Human use
Sodium fusidate	Fusidanes	Human use Approved as a topical treatment of skin in animals
Vancomycin Teicoplanin	Glycopeptides	Human use
Tigecycline	Glycylcyclines	Human use
Daptomycin	Lipopeptides	Human use
Fidaxomicin	Macrocyclic lactones	Human use
Aztreonam	Monobactams	Human use
Nitrofurantoin Furazolidone Nitrofurazone	Nitrofurans	Human use

Linezolid	Oxazolidinones	Human use
Polymyxin B	Polymyxins	Registered for use in humans Approved for topical ocular and aural use in cattle, sheep, horses, dogs and cats
Colistin	Polymyxins	Human use
Norfloxacin Ciprofloxacin Moxifloxacin Ofloxacin Levofloxacin	Quinolones	Human use
Enrofloxacin Enrofloxacin+Silver Sulfadiazine Ibafloxacin Marbofloxacin	Quinolones	Approved for use in dogs and cats Label restraints: Do not use in food producing animals. For use in companion animals where culture and sensitivity testing indicate no suitable alternative.
Orbifloxacin	Quinolones	Approved for use in dogs and cats Label restraints: Not for use in food producing species.
Pradofloxacin	Quinolones	Approved for use in dogs and cats Label restraints: Do not use for any purpose, or in a manner, contrary to this label. For use only in dogs and cats which have responded poorly to other classes of antimicrobials and where culture and sensitivity testing indicate no suitable alternative
Rifampicin (Rifampin) Rifabutin Rifaximin	Rifamycins	Human use
Quinupristin with dalfopristin Pristinamycin	Streptogramins	Human use
Virginiamycin	Streptogramins	Approved for use in cattle, sheep, meat chickens (broilers) and horses. Label restraints: Not to be used for any purpose, or in a manner, contrary to this label. Do not feed to laying birds. Do not use in horses that may be slaughtered for human consumption. Prudent use: Prior to using virginiamycin investigate the use of non-antibiotic options. If virginiamycin is indicated and selected for use, prescription must be consistent with the AVA Code of Practice for Prescription and Use of Products which Contain Antimicrobial Agents. Dosage regimens should be designed for each situation with an appropriate duration and frequency to minimise treatment failure while minimising the emergence of resistance. Review farm records on the use of product containing virginiamycin to ensure compliance with prescribing instructions.

Antimicrobial Stewardship

Antimicrobial stewardship (AMS) is used in different contexts and can mean different things to different people [58]. The term has been in use over the past twenty-five years amongst health practitioners, researchers and policy makers, with wider understanding becoming more common over the past ten years in line with an exponential increase in publications on this topic [13]. AMS can describe specific activities that improve the appropriateness of antimicrobial use and aim to reduce the development of AMR in a clinical setting for example, audit and feedback, decision support tools, or point-of-prescribing nudges[59, 60]. More broadly it can be thought of as a concept or multifaceted approach that has the ultimate goal of reducing pressure on the development of AMR and may include aspects of client communication, disease prevention, biosecurity and animal husbandry [7, 58, 61].

In the Australian veterinary profession at present, most focus is on stewardship activities relating to antibacterials, although this may change in future [62, 63]. Antivirals and antifungals are used much less frequently than antibacterials in Australian veterinary practice, however emergence of resistance to both types of antimicrobials in human health suggests proactive action may be beneficial [28, 64-66]. Principles developed for stewardship of antibacterials could be adapted to antiviral and antifungal stewardship to preserve the efficacy of these drugs for as long as possible.

For many years Australia has been one of the countries at the forefront of addressing AMR and implementing AMS strategies [34, 36]. Since the release of the JETACAR recommendations in 1999 the use of HIAs in Australian animals has been debated and discouraged [23, 52, 67-70].

In Australia, HIAs such as fluoroquinolones and third generation cephalosporins can be legally used in companion animals and equine practice, whereas fluoroquinolones are banned, and third generation cephalosporins are highly restricted, in food producing animals [52-57]. Use of HIAs in food-producing animals in Australia is largely restricted to streptogramins (of which only virginiamycin is used) and third generation cephalosporins (ceftiofur in individual pigs or cattle only) [8, 16]. Veterinarians working in this sector have a more limited range of antimicrobials to choose from for treatment or prevention of disease [16, 71]. However, there is likely still scope to improve the quality of prescribing in food-producing animals in Australia. Publicly-available surveillance of AMU, including the indication for AMU are necessary to better understand and improve the quality of prescribing [72].

Companion animal and equine sectors have not been operating under the same strict regulations as veterinarians treating livestock in Australia. The range of practice is wider and AMR is potentially a higher risk for direct transmission to humans due to the close contact people have with companion animals including horses [73-78]. There is potential for improvement in prescribing and guideline compliance in these areas of practice with the implementation of AMS programs [79]. There is also evidence that, with the introduction of guidelines for some of these sectors, improvement has already been seen [52-54, 78, 80, 81].

Prescribing Guidelines and Decision Support Tools

Many veterinarians are keen to use prescribing guidelines to improve their practice [57, 80, 82-84]. To support AMS in Australian veterinary practice, country-specific, independent antimicrobial prescribing guidelines for all major domestic species would be helpful for prescribers [7, 23, 51, 80]. Some guidelines are currently in progress, with guidelines already released for sheep, poultry, dairy cattle, feedlot cattle and pigs [7, 19, 21, 22]. Research has shown that the use of HIAs in veterinary practice in Australia requires more guidance given the frequent unjustified use of these medicines [23, 51-54, 56, 57, 71, 78, 80]. This is particularly the case for companion animal practice given the high rates of use of third-generation cephalosporins, particularly amongst cats [68, 71, 78, 85]. There is a need for easy-to-use tools that complement guidelines, which could assist veterinarians in their day-to-day veterinary practice [7, 86, 87]. Decision support tools have been shown to be beneficial in medical practice by reducing errors and improving prescribing [87, 88]. Veterinarians unfamiliar with such tools may be wary of relying on their outputs, particularly if recommendations differ from what they would usually prescribe – this has been an issue in human hospitals with the use of decision support tools [89]. However, if introduced in the right way, potentially using implementation science techniques such as co-design to provide ownership, they could provide a sense of support and confirmation of the veterinarian's own treatment plan.

In human health sectors prescribing guidelines and decision support have been particularly helpful in remote settings where doctors are not always physically present. One example is the Central Australian Rural Practitioners Association (CARPA) manual [90], which provides decision support and treatment options for general practitioners as well as nurse practitioners, nurses and Aboriginal health practitioners (AHPs) who have been given limited prescribing rights when using this manual in the Northern Territory of Australia. Identifying barriers to appropriate antimicrobial use and addressing them with provision of prescribing resources could be a cost-effective way to improve AMS in resource-limited settings such as remote Indigenous communities and may work synergistically with other stewardship interventions [11, 91]. There are currently no specific AMS resources for veterinarians practicing in remote Indigenous communities.

Restrictions

All antimicrobial use potentially selects for resistance. Antimicrobials are not always prescribed appropriately by veterinarians, with inappropriate prescribing likely contributing to the unnecessary development of AMR [54, 71, 80, 92-94]. Regulating the use of antimicrobials has been shown to reduce inappropriate prescribing in humans [95, 96]. Veterinarians in Australia are supportive of additional antimicrobial stewardship (AMS) measures, but individual small businesses often lack the resources required to make effective change [97]. Sectors that could benefit most include companion animal and equine practice as there is a lack of restrictions on prescribing in these sectors, and unnecessary use of HIAs [52, 54, 71, 78]. Implementing restrictions on new classes of antimicrobials not currently registered for animals is likely to be more easily accepted than removing access to antimicrobials currently registered in animals and used regularly by veterinarians [11]. In relation to the use of HIAs in veterinary practice, further research in this area, particularly around the need for and feasibility of implementing restrictions, would benefit AMS planning in Australia as well as potentially be useful to other countries wanting to investigate similar actions [95].

Some countries have already progressed further along the path of implementing bans or restrictions, however this has sometimes been driven by consumer preference and public perception [98]. For example, in France, consistent with European Parliament legislation, veterinarians must now perform culture and susceptibility testing (C&S) before prescribing a MIA [99, 100]. This has resulted in reduction in use of medically important antimicrobials (MIAs), however care must be taken to avoid unintended impacts on animal welfare, food security and food safety if there is excessive focus on reduction of use instead of appropriateness of use [11, 101]. A balance needs to be found between implementation of restrictions, education of health practitioners, in this case veterinarians, and the provision of guidelines and tools to help with clinical decision-making, as well as addressing other factors that influence prescribing such as time pressures on prescribers [84, 102, 103].

One Health

The intersections between human and animal health, plus the connections with environmental health have been evident since the beginning of time. The purposeful naming of 'One Health' as an approach or concept to address issues is more recent and originated in the early 2000s with numerous definitions evolving over that time [29, 34, 104, 105]. In 2021 the Food and Agriculture Organisation (FAO), the United Nations Environment Programme (UNEP), WHO, and WOAH (now known collectively as the quadripartite) formed the interdisciplinary One Health High-Level Expert Panel (OHHLEP). This panel prioritised developing a consensus definition for One Health to support a common understanding and drive collaboration [12].

One Health is an integrated, unifying approach that aims to sustainably balance and optimise the health of people, animals, and ecosystems. It recognizes the health of humans, domestic and wild animals, plants, and the wider environment (including ecosystems) are closely linked and interdependent. The approach mobilizes multiple sectors, disciplines, and communities at varying levels of society to work together to foster well-being and tackle threats to health and ecosystems, while addressing the collective need for healthy food, water, energy, and air, taking action on climate change and contributing to sustainable development.[12]

This definition is now widely accepted and will be used as the primary definition of One Health throughout this thesis. Several key principles fundamental to a One Health approach are also clearly stated, including;

> *Equity between sectors and disciplines;*
> *Sociopolitical and multicultural parity (the doctrine that all people are equal and deserve equal rights and opportunities) and inclusion and engagement of communities and marginalized voices;*
> *Socioecological equilibrium that seeks a harmonious balance between human–animal–environment interaction and acknowledging the importance of biodiversity, access to sufficient natural space and resources, and the intrinsic value of all living things within the ecosystem;*
> *Stewardship and the responsibility of humans to change behaviour and adopt sustainable solutions that recognize the importance of animal welfare and the integrity of the whole ecosystem, thus securing the well-being of current and future generations;*
> *Transdisciplinarity and multisectoral collaboration, which includes all relevant disciplines, both modern and traditional forms of knowledge and a broad representative array of perspectives. [12].*

Recognising the deficiencies of current public health and social sciences approaches, Indigenist Health Humanities has emerged as a new field of research, which foregrounds Indigenous sovereignty. It aims to develop 'a deeper understanding of the human experience of health' and 'a greater understanding of the enablers' [106]. Indigenist Health Humanities goes beyond the multidisciplinary and transdisciplinarity that has been practiced in earlier enactments of a One Health approach with Indigenous communities [107], and also deprioritises scientific and epidemiological methods where necessary to make room for different knowledge systems.

"The transdisciplinarity required to effect change requires more than a bringing together of different methodologies—it demands attention to different ways of knowing and being in a relational, rather than hierarchical, manner, recognising the limitations of different knowledge systems as well as their strengths, so that the most appropriate conceptual tools are brought to bear in addressing the grand challenges we face both now and into the future." [106]

The research methods used in this thesis attempt to expand and prioritise the principle of transdisciplinarity to be more consistent with the aims of Indigenist Health Humanities. Although the OHHLEPP definition of transdisciplinarity considers modern and traditional forms of knowledge, the inclusion and foregrounding of Indigenous sovereignty was seen as essential given that colonial denial and silencing of First Nations perspectives is the basis for many existing inequalities for Indigenous people today [108].

Use of a One Health approach to implement AMS

An urgency to implement AMS using a One Health lens exists because current progress has been slow with a lack of coordination and consistency between human, animal and environmental health sectors [34, 96]. Significant discrepancies in funding exist between sectors and are worsened by funding arrangements that discourage collaborative research and program implementation [105]. In recent years, antifungal resistance due to agricultural use of antifungals and subsequent persistence in the environment has also highlighted the need for increased investment and focus on the environment [28, 64]. The benefits of using a One Health approach include increased collaboration among experts and the community, and encouraging knowledge sharing in a transdisciplinary way [104]. Environmental contamination with antimicrobials or resistant bacteria is also an emerging concern for human and animal health (including wildlife) and, in most cases, is not being monitored [28, 109-113]. Our understanding of how AMR persists and spreads between people, animals and the environment is still developing [34, 113-115].

However, the One Health approach does not necessarily translate into the required outcomes or clear responsibilities going forward, and like AMS, a similar 'umbrella' term, understandings of One Health as a concept can vary between people [116, 117]. Using a One Health approach can help unite disparate stakeholders [117], a common aim of using the approach [34], but outcomes or policy creation still depend on the right conditions and ideas, including adequate funding, governance, human resources and expertise. Current structural inequalities result in some communities suffering the worst impacts of AMR, while also creating the conditions for further resistance to develop due to a lack of appropriate resourcing and prioritisation [10, 91]. Using a One Health approach can be beneficial in these contexts to enable advocacy based on the unique requirements of stakeholders and to highlight holistic and transdisciplinary solutions [10, 96, 104].

AMS integrates well with One Health because there is increasing awareness of the way different spheres – animals, the environment or humans can act as reservoirs for AMR. A significant challenge for researchers has been the difficulty of demonstrating that restricting antimicrobial use in animals directly reduces resistance in the animals themselves and people [118, 119]. This is because a reduction in AMR may not occur until years after the use of specific antimicrobials has reduced or ceased and can be impacted by the presence of mobile genetic elements, the use of other agents (such as heavy metals) that select for resistance and the "cost" of maintaining resistance in a bacterial genome [94, 120-123]. However, a recent systematic review concluded that restrictions on antimicrobial use in animals does reduce AMR in animals and, by extension, people [118].

It is also important to address resistance that develops primarily in human or environmental settings. In human hospital settings, use of high importance antimicrobials alongside other drivers of resistance such as immunocompromised patients, longer hospital stays (compared to companion animal health) and inadequate hand hygiene, promote the development of AMR, which may then be shared with animals, other people, or the environment when people return to the community [24, 124]. Resistant bacteria or bacterial genetic elements can persist in an environment such as a sewerage plant, on a dog's coat, or in a biofilm on a hospital surface [125-127]. Due to all these complexities, it makes sense to address AMR concurrently across sectors otherwise deficiencies in one sector can lead to resistance in another [24, 34, 36, 110, 112, 122, 128-130]. Surveillance and sampling across different sectors can also be used to inform progress. In fitting with a One Health approach, studies in wildlife have shown that historical samples from wildlife can be used as indicators of human-associated AMR contamination of the environment, which could be helpful in monitoring success of AMS programs or interventions over time [122]. A current lack of surveillance data, particularly in animal and environmental health, makes monitoring and evaluation of interventions difficult.

AMS in Australian veterinary practice can benefit from a One Health approach by learning from more established human medical AMS programs and also contributing new knowledge and expertise, which naturally comes from continually working across the species divide [7, 27, 34, 96]. Veterinarians can also maximise the use of resources, to prevent duplication and enable a clear understanding of the situation at the community level, for example, by being involved in integrated surveillance programs [15, 34, 72].

In its most recent progress report, the Australian Government claimed to be using a One Health approach, in line with the *Global Action Plan on Antimicrobial Resistance* [29] but animal industries and veterinarians have not received key support from the government to implement recommended interventions [29, 38, 39]. For example, updated independent antimicrobial use data for the Australian livestock sector has not been provided despite over ten years passing since this information was last released [14, 38]. This raises concerns that Australia could be losing its former reputation as a leader in addressing AMR, rather than investigating and acting on recommendations based on a true One Health approach [33, 117]. Some of our low resistance rates are related incidentally to our strict biosecurity and remote population, rather than any specific actions of government or prescribers. Nevertheless, this reputation could be at risk if Australia falls behind other nations and is no longer seen to be taking a proactive approach [98, 131].

The benefit of national integrated surveillance systems for antibiotic use and resistance in informing AMS is well accepted [132, 133]. The European Union has well-implemented programs and up to date data on antimicrobial use and resistance and these systems are being constantly improved [134-136]. The EU conducts mandatory active surveillance for resistant bacterial isolates in healthy animals at the point of slaughter and in food, however prior to the pilot testing of their European AMR Surveillance network in veterinary medicine (EARS-Vet) reported in 2023, AMR data from sick animals compiled at an EU level was missing [136]. The goal of EARS-Vet[137], is to improve over time. Challenges remain regarding data variability and like Australia, the frequency of AST being performed on sick animals can be highly variable. The introduction of data from more EU countries and further clarification of reporting processes will enable future actions such as providing data for risk assessments, evaluation of antimicrobial registrations, and improvement of antimicrobial treatment guidelines[136].

The need across Australian veterinary practice for consistency through long-term surveillance of antimicrobial use and resistance has been described [7] and an integrated system of surveillance declared a 'national priority' [72]. There have been 'proof of concept' studies [38] and more recently, in 2022, a report was released which explored mechanisms for collecting AMU data from Australian veterinary practices and animal industries [138]. This report proposed the development of an Integrated National System for AMU in Animal Health (INSAAH) [138]. Many sources of AMU data that could be used for AMU surveillance across Australian animal sectors were well-described in this report, however implementation of an INSAAH is still dependent on significant funding and further stakeholder consultation. For example, the initial survey of veterinarians to assess attitudes to recording and benchmarking AMU only included 114 general practice veterinarians. There were also limited respondents from more remote parts of Australia such as the Northern Territory, Western Queensland and significant parts of Western Australia. Future investigation into an integrated surveillance system may require targeted discussions with stakeholders whose views and unique challenges may otherwise be overlooked.

The current lack of adequate AMU and AMR surveillance in Australia hampers AMS attempts such as using detailed data for the creation and revision of antimicrobial treatment guidelines or other decision support tools for prescribers. Without AMU and AMR surveillance, the gap in knowledge around the ecology of AMR in Australian animals and people remains, particularly for the veterinary sector where antimicrobial culture and susceptibility testing rates are low [68, 83, 84]. Some sectors of the human population also have limited access to healthcare and antimicrobial susceptibility data, which compounds the difficulties of implementing One Health AMS activities [139, 140].

Justice and equality

The rational use of antimicrobials must be equitable, and populations should not be placed at risk due to factors such as low socioeconomic status or reduced access to more advanced and often more costly diagnostic or treatment options [132]. Viewing AMS as an ethical issue makes sense because the ramifications of AMR are not just medical in nature [3, 6, 141, 142]. This poses particular challenges for veterinary medicine in Australia because generally it is fee for service, and there is no, or very little, government subsidised veterinary care for animals [84, 102, 103]. Defining and agreeing on conditions under which HIAs should or should not be used may help veterinarians communicate with clients about the need for diagnostic testing, but also with government bodies and non-government organisations regarding funding for AMS interventions such as surveillance. It is clear that over-prescribing promotes resistance, yet under prescribing for fear of driving AMR can also lead to undesirable health and welfare impacts [143]. In order to meet priority areas for action in the *National Antimicrobial Resistance Strategy*, we must consider whether high levels of AMS practice and engagement are going to be context dependent or equitable across the country [6, 15].

There are some contexts in Australia where veterinarians practice with minimal guidance or support in antimicrobial stewardship due to the lack of access to affordable diagnostic tests and limited research related to effective treatments or preventative approaches. From a justice perspective, it is not ethical to have a multi-tiered system of either healthcare or veterinary services in a wealthy country like Australia. Indigenous communities and their animals could be better served by veterinary AMS research and programs while maintaining cultural integrity, and this would also better support veterinarians who are currently working in suboptimal conditions [144, 145].

Establishing guidelines around the use of antimicrobials and implementing AMS programs that rely on diagnostic tests such as culture and susceptibility testing will not be effective for areas of Australia which lack these capabilities or lack access to veterinary care. Meagher et al. states that, “The promise of better diagnostics cannot be fulfilled without access to subsequent care” [146]. This is pertinent to veterinary practice in remote Indigenous communities. Allowing for some delays due to the challenges of remoteness, a reasonable standard of practice and access to diagnostic and treatment services would ideally be accessible to all animal owners. A lack of appropriate veterinary services in remote areas also impacts biosecurity, animal welfare, and disease preparedness [147]. Considering the other multiple health challenges faced by communities in remote areas, research to monitor and prevent antimicrobial resistance could provide multiple flow-on benefits [91, 140, 148, 149]. Ideally, veterinary AMS projects would occur concurrently with the other cross-sectoral projects to improve AMS across Australia [34, 91].

Bacteria with resistance genes are already present amongst the canine population in Australia at a level that indicates some selection pressure [150] and have been identified in remote communities [151, 152]. While the issue may not be as pronounced or difficult to manage in Australia in comparison to other countries [114, 153-155], knowledge of the natural history of bacteria and how resistance spreads suggests that without intervention it may only be a matter of time until cases of Methicillin-resistant *Staphylococcus pseudintermedius* (MRSP) and other resistant bacteria are more prevalent in human and animal infections in Australia [114, 156-158].

Studies of resistant bacteria, including staphylococci, have shown that in some settings such as veterinary clinics and households, there is carriage of the same strains of resistant bacteria between people and animals who have close contact, which suggests transfer between people and animals [159, 160]. This is a health risk for humans, especially those who are immunocompromised, as they may pick up resistant bacteria from their dogs and it may cause infection in the person [130]. Potentially the person could also then carry this bacterium into a healthcare setting like a clinic or hospital [153]. There is also a risk for pets that a person who carries a type of resistant bacteria, potentially from a hospital stay, could pass it on to their pet through skin contact or sharing bedding [24, 115, 153, 160], particularly if combined with another inciting factor such as skin allergies or parasite infestation that cause minor breaks in the dog's skin [161]. Therefore, research to improve knowledge of AMR and AMS in remote Indigenous communities is timely.

Social determinants of health

The relationship between health outcomes and inequality in a society is well understood [162]. In the USA, many risks for antibiotic-resistant infections are tied to the social determinants of health [163]. It is essential that these social determinants are addressed if AMS is to be successful [164]. Indigenous People in Australia are already impacted by higher rates of *Staphylococcus aureus* bacteremia than non-indigenous Australians [148]. If inequalities in implementation of AMS are not addressed, a system where there are high levels of antibiotic resistance in some communities, and low levels in others, could become entrenched [165]. While also being unjust, this creates the possibility for resistance to develop rapidly in some areas and then spread more widely, as was the case with the initial emergence of community-associated methicillin-resistant *Staphylococcus aureus* in Australia [149, 166].

Remoteness and by association, access to health and social services, has been identified as a risk factor for increased prevalence of third-generation cephalosporin-resistant *E. coli* in Northern Australia *[167]*. In the same study, socio-economic disadvantage and the average number of people per household did not correlate with increased risk of AMR. This may be due to the use of large-scale overlapping datasets that miss nuances in people's risk factors on a more localised level. The use of a strengths-based approach is highlighted by Indigenist Health Humanities as well as the need to include affected individuals in research so they can speak about their own lives and the strengths they have in addressing these challenges, not just for their communities but also to provide assistance to the wider Australian community. For example, the use of the CARPA manual has resulted in high levels of guidance-compliant prescribing practices across the Northern Territory when compared to other locations [91].

The integration of traditional disease surveillance with other data sets to better understand the risk posed by AMR to remote communities could be further enhanced by qualitative research and community-led approaches. More granular data would be beneficial to better understand people's exposure to antimicrobials, time spent in areas with a high risk of AMR (such as hospitals), immune status, and exposure to infectious diseases, as well as protective factors such as access to water, sanitation and hygiene, safe and nutritious food, and secure housing. Movement of people over longer periods of time, for example, from remote communities into towns with more available medical treatment may confound results that are reliant on large datasets, as would generalisations made on averages, such as the number of people per household. In many remote communities the housing mix can vary widely between local families and those living in the regions for shorter periods of time for service provision such as doctors, nurses, teachers and contract workers – who may have smaller, even individual, households [167]. It is likely some upstream drivers for AMR are external to the communities they ultimately impact, for example, systemic racism, inadequate and biased service provision and funding allocation by government [10, 108].

Veterinary service provision to remote Indigenous communities is generally infrequent (a few times per year), non-existent or on an 'as-needs' basis when animal populations become unmanageable [144, 168, 169]. A history of culling, sometimes without owner consent, in many communities has also added to the complexity of veterinary service provision given the significant role that animals, especially dogs, have for many Indigenous people [145, 170]. Dogs in remote communities have been implicated in the persistence of public health challenges such as strongyloidiasis, scabies, and scavenging through waste [152, 171]. Whether they play a significant role in transmission of AMR to people, other animals or the environment is unknown. It is also difficult to investigate this issue due to lack of funding, remoteness, and the complexity of bacterial ecology.

Indigenous people in Australia have been disproportionately impacted by methicillin-resistant *Staphylococcus aureus* (MRSA) [148]. Community-acquired strains of MRSA have also emerged in Indigenous and First Nations communities overseas due to drivers such as over-crowding and lack of access to water, sanitation and hygiene (WASH) [166, 172]. Given that people and dogs can share some species of bacteria and resistance genes, an understanding of the prevalence and resistance rates of staphylococci from dogs in remote Indigenous communities is important in addressing AMR. Currently, only two studies have been undertaken investigating the prevalence of resistance in staphylococci species from dogs in remote Indigenous communities and both have used convenience sampling, which makes estimation of prevalence uncertain [151, 152]. It is possible due to the large distances between communities, local variation in geography and movement of people and animals between communities as well as numerous other known and unknown factors, that the ecology of AMR could vary in different regions or even at the individual community level.

Identified Gaps

Australia is fortunate that effective legislation regulating use of antimicrobials in food-producing animals has been enacted for decades, and that the majority of antimicrobial use in animals in Australia requires a veterinary prescription. Given this strong foundation, antimicrobial stewardship in veterinary practice thus far has rightly focussed on improving the prescribing behaviour of veterinarians at the individual or clinic level. However, our current enviable position in Australia with relatively low levels of AMR could be at risk. Upstream interventions and guidance by government to support veterinary AMS is still lacking when viewed in relation to the massive disruption to healthcare that is projected with increasing levels of AMR. There is a lack of knowledge about how HIAs are currently used, particularly in the companion animal and equine sector. Previous research to better understand AMU has relied on survey data of veterinary practitioners or farmers and data such as pet insurance data, both of which can have biases due to practitioners self-reporting or the demographics of clients who have pet insurance [173, 174]. Without a surveillance or reporting system for AMU, it will be difficult to target this area for further

AMS interventions. As a veterinary profession, lack of data about AMU also undermines our ability to speak authoritatively about AMS practices and how veterinarians are tackling the super-wicked problem of AMR. Understanding what veterinarians' attitudes are towards these antimicrobials is also helpful if any restrictions are to be placed on the use of HIAs in future and to ensure that any changes are made collaboratively and with the support of the profession. Research specifically asking veterinarians about HIAs has not been carried out in Australia previously.

Currently there is a gap not only in knowledge of AMR and AMU in animals from remote Indigenous communities, but there is also a lack of process in being able to collect this data in future. AMS generally in remote communities would benefit from greater focus and resourcing. Further research relating to AMR and AMS in veterinary practice in remote Indigenous communities will be beneficial in ensuring equitable use of AMS practices and continued access to antimicrobials when required, particularly in areas already disproportionately impacted by AMR [148]. At present, research about AMS in remote communities is restricted to human health [175].

Greater awareness of systemic barriers to AMS whether they be regulatory, economic, political or social, and creating strategies to address these could progress veterinary AMS further without undue pressure on individual prescribers. Using a One Health approach when considering AMS also safeguards against areas of veterinary practice being left behind or unsupported. It promotes multi-sectoral collaboration so that decision-making occurs with mutual support and understanding to drive progress on AMS.

Chapter 2 Published Paper

Attitudes towards use of high importance antimicrobials – a cross-sectional study of Australian veterinarians

Anna Sri, Kirsten E. Bailey, James R. Gilkerson, Glenn F. Browning, Laura Y. Hardefeldt
National Centre for Antimicrobial Stewardship
Asia-Pacific Centre for Animal Health, Melbourne Veterinary School, Faculty of Veterinary and Agricultural Sciences, University of Melbourne, Melbourne, VIC, Australia

Abstract
Timely implementation of antimicrobial stewardship interventions could delay or prevent the development of higher levels of antimicrobial resistance in the future. In food-producing animals in Australia, the use of high importance antimicrobials, as rated by the Australian Strategic and Technical Advisory Group (ASTAG), includes virginiamycin and third generation cephalosporins (in individual pigs or cattle). Use of high importance antimicrobials in companion animals is more widespread and less regulated. There is no national antimicrobial use surveillance system for animals in Australia. Consequently, there is a gap in knowledge about reasonable use across all sectors of veterinary practice. This study explored attitudes towards use in veterinary medicine of antimicrobials with high importance to human health, and determined levels of agreement about the introduction of restrictions or other conditions on this use. An online survey was distributed via social media and email from June to December 2020 to veterinarians working in Australia. Of the 278 respondents working in clinical practice, 49% had heard of the ASTAG rating system, and 22% used a traffic light system for antimicrobial importance in their practice. Overall, 61% of participants disagreed that veterinarians should be able to prescribe high importance antimicrobials without restrictions. If there were to be restrictions, there was most agreement amongst all respondents for only restricting high importance antimicrobials (73%). There is a need for education, guidance, and practical support for veterinarians about prescribing high importance antimicrobials alongside any restrictions.

Keywords: stewardship; antimicrobial resistance; critically important antimicrobials, antibiotic, companion animals; food-producing animals; restrictions; rating system

Introduction
Antimicrobial resistance (AMR) is now well-established as a global problem with profound impacts on nearly all living beings and the environments they inhabit [1]. It is a multigenerational challenge, with increasing levels of morbidity and mortality expected into the future for humans and animals [2, 3]. A landmark report released in 2016 estimated that up to 10 million human lives could be lost every year due to AMR by 2050 [1], over half the number of deaths attributed to the COVID-19 pandemic (18.2 million) in

the one year period from January 2020 to January 2021 [176]. In the recent 2021 Global Antimicrobial Resistance and Use Surveillance System report, many countries reported high rates of resistance to high importance antimicrobials [177]. Given the extremely serious future consequences of AMR and the dynamic situation we face today, it is important that all sectors take responsibility for mitigating the further development of AMR. Timely implementation of antimicrobial stewardship (AMS) interventions could delay or prevent the development of increased levels of AMR in animals and people in the future [118, 122].

In Australia, the importance of antimicrobials is determined by the Australian Strategic and Technical Advisory Group on AMR (ASTAG) [8]. The use of high importance antimicrobials in Australian food-producing animals is limited to streptogramins (virginiamycin only) and third generation cephalosporins (in individual pigs or cattle only) [8]. The use of fluoroquinolones, gentamicin and colistin has never been permitted in food-producing animals in Australia [8, 16, 178, 179]. As a result of numerous factors, including good regulation and residue monitoring, a predominance of extensive, rather than intensive, animal production systems, and widespread use of biosecurity and vaccination, Australia's levels of AMR, particularly within domestic animal populations, are relatively low [36, 41, 180, 181]. The low levels of fluroquinolone resistance in the Australian human population compared to other countries could also be a result of well-regulated use of this class of antibiotics in people and domestic animals in Australia since the early 1990s [35, 36, 182].

As the development of AMR is a time-sensitive problem, it would be wise to act quickly across all sectors, rather than waiting until evidence is clearer but resistance is more widespread [132]. At present, there is sufficient evidence that all antimicrobial use in domestic animals, humans or agriculture drives resistance at some level [39, 183-187]. Therefore, improving the quality of prescribing for therapeutic use and reducing unreasonable use of antimicrobials is of utmost importance. Unfortunately, assessing the quality of prescribing, particularly in a private veterinary setting, can be difficult. Gaps in knowledge about what is considered 'reasonable use' exist across all sectors of veterinary practice. Currently, there is no regular, systematic ongoing surveillance of antimicrobial use or resistance in animals in Australia [72]. There is scope to improve the quality of prescribing in food-producing animals in Australia [55], but more publicly-available knowledge about volumes of antimicrobial use and the disease presentations for which these antimicrobials are being used is also required. As the companion animal sector, including horses, has not been subject to the same strict regulations that govern veterinarians treating livestock in Australia, use of high importance antimicrobials is common [23, 49, 52, 78, 173]. There is also potential for more rapid improvement in prescribing and guideline compliance in these areas of practice because much of the current use of high importance antimicrobials is not guideline compliant and other treatment options are readily available. These sectors have also not traditionally been the focus of significant educational, public, or regulatory pressures to reduce unnecessary antimicrobial use [52-54, 78, 80].

Restricting antimicrobial use has resulted in improvements in prescribing in a human inpatient setting, particularly when combined with other antimicrobial stewardship (AMS) interventions [95, 182, 188], and this has also been seen in food-producing animals [118, 189-192]. There has been very little research in Australia on the attitudes of veterinarians about the imposition of restrictions on antimicrobial use. Previous work has shown that veterinarians are concerned about AMR and are prepared to change their prescribing practices, but they face a number of barriers to implementing AMS practices [23]. These barriers include a lack of AMS governance structures, as well as other factors associated with the largely private nature of veterinary practice in Australia [23]. The use of restrictions as an AMS intervention has been rated as 'not helpful' in improving prescribing by Australian veterinarians, doctors and dentists [96], even though other research, particularly from European countries, has suggested that restrictions can result in improved prescribing with no or minimal adverse economic impact [135, 193, 194] and reduced contamination of the environment with bacteria resistant to antimicrobials or antimicrobial resistance genes [122]. The impact of restrictions also needs to be assessed alongside animal welfare outcomes, as there are significant gaps in understanding these interactions [195].

The purpose of this study was to improve understanding of the attitudes of Australian veterinarians about antimicrobial use, particularly regarding the use in veterinary medicine of antimicrobials with high importance to human health. An improved understanding of these attitudes will enable more targeted and effective AMS interventions and guide future policy development.

Results

Demographics/participant information

The survey was completed by 322 veterinarians, the majority of whom (71%, n=227) worked in general practice. An additional 16% of participants were engaged in other areas of clinical practice, including emergency (3.5%), referral (6.2%), or university practice (6.2%). The remaining participants worked in government (3.1%), industry/pharmaceutical (2.8%) or university teaching and research roles (7.8%). The distribution across the Australian states was generally consistent with the number of veterinarians registered in those states [196, 197], although Victoria was slightly over-represented and our survey population also included non-registered veterinarians, about whom there is limited demographic data available. Assuming a maximum population size of veterinarians in Australia of 15000, our 322 survey respondents yielded a confidence interval of 93%.

Respondents worked in rural (40%) and metropolitan locations (60%), with metropolitan areas defined as a population over 100,000 people. Survey respondents were largely graduates from the last twenty years (61%), but there were respondents from all graduation years between 1971 and 2019. Post-graduate qualifications were common among participants (40%), with membership of the Australian and New Zealand College of

Veterinary Science (34%) or specialist qualifications (20%) the most frequently attained. All the recent graduates (classes of 2016-2019) that responded to the survey were in clinical practice.

Knowledge and use of rating systems

Of the 278 veterinarians working in clinical practice, 49% (n=135) knew of the ASTAG antimicrobial importance rating system, and 22% (n=60) used a traffic light system for antimicrobial importance in their workplace. An example of a traffic light system for antimicrobial importance may include where antimicrobials held in the clinic are colour coded green, orange or red based on their ASTAG importance rating using a sticker or sign on the packaging or the shelf where the antimicrobials are stored. Of the 44 non-clinical veterinarians, 66% (n=29) knew of the ASTAG antimicrobial importance rating system, and 32% (n=14) used a traffic light system for antimicrobial importance in their workplace. Veterinarians with post-graduate qualifications working in clinical practice were 1.7 times (RR 1.7; 95% CI, 1.4-2.2; $p<0.05$) more likely to have known of the ASTAG rating system (67%) compared to veterinarians in clinical practice without post-graduate qualifications (39%), but differences in the use of a traffic light system for antimicrobial importance were not significant (RR 1.25; 95% CI, 0.79-1.97; $p=0.36$). Recent graduates were more likely to be aware of the ASTAG rating system compared (62%) to more experienced clinicians (46%) (RR 1.35; 95% CI, 1.0-1.8; $p=0.05$), but this did not translate into a significant increase in the use of a traffic light system in the workplace (RR 1.15; 95% CI, 0.7-2.0; $p=0.69$). There was no difference between rural clinicians and those in metropolitan areas in awareness of the ASTAG rating system (RR 1.04; 95% CI, 0.8-1.3; $p=0.08$), or in the use of a traffic light system in their workplace.

Agreement with restrictions

Overall, when asked whether veterinarians should be able to prescribe antimicrobials with high importance to human medicine *without* restrictions, 61% (n=196) of participants disagreed, while 35% (n=113) agreed that they should. Disagreement was highest for veterinarians not in clinical practice (73%, n=32), followed by recent graduates (65%, n=34) and clinical veterinarians (59%, n=164). Veterinarians with post-graduate qualifications who were working in a clinical role had higher agreement (46%, n=44) that veterinarians should be able to prescribe high importance antimicrobials without restrictions, whereas only 31% (n=10) of veterinarians with post-graduate qualifications working in a non-clinical role agreed with this proposition.

When all participants were asked, *'If there were to be restrictions placed on veterinary prescribing of antimicrobials, which antimicrobials should they apply to?'*, there was most agreement for restricting high importance antimicrobials (73%), followed by restricting high importance antimicrobials but excluding 3rd generation cephalosporins and fluoroquinolones from these restrictions (64%) (Figure 1). There was minimal agreement with restricting all antimicrobials (9%), and this option also elicited the most 'strongly disagree' responses (66%). For clinicians, only 6% agreed with restricting all antimicrobials and 89% disagreed or strongly disagreed with this proposition.

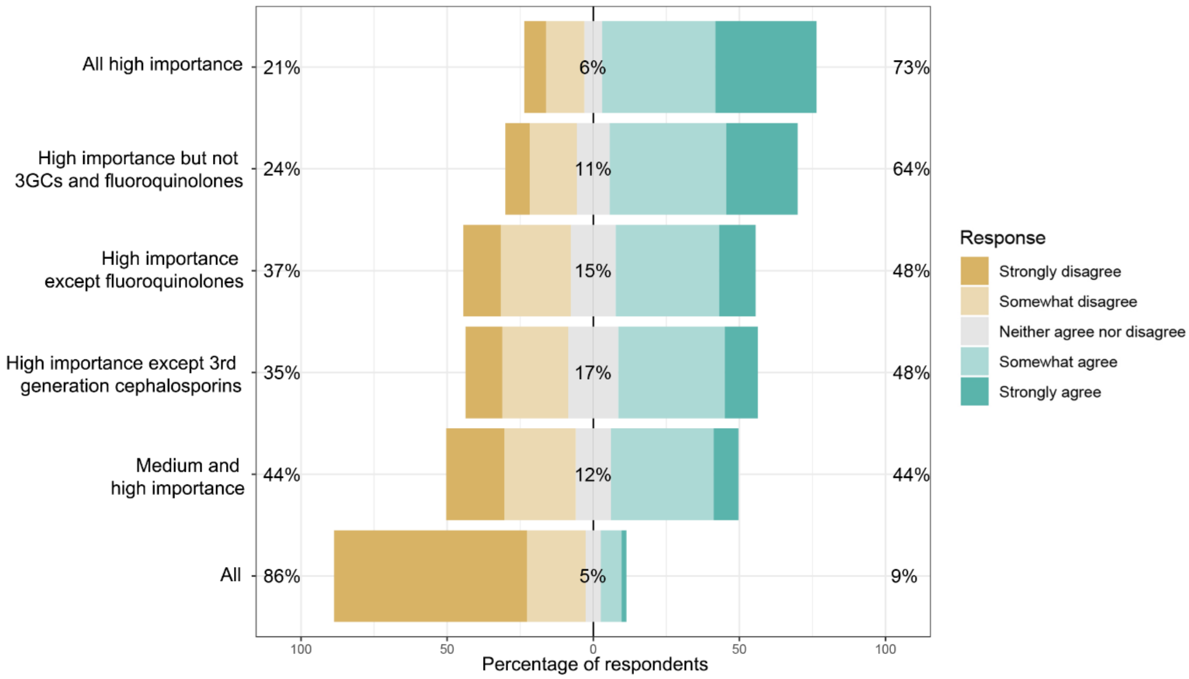

Figure 1 Responses of all participants to the question: "If there were to be restrictions placed on veterinary prescribing of antimicrobials, to which antimicrobials should they apply?"

More recent graduates (graduated in the years 2016-2019) agreed that restrictions should apply to all high importance antimicrobials (83%). This was a greater level of agreement than among experienced clinical veterinarians (greater than five years after graduation), 71% of whom agreed that restrictions should apply to all high importance antimicrobials. Experienced veterinarians that were not working in clinical practice had higher levels of agreement that restrictions should apply to high importance antimicrobials (76%) and had much lower levels of agreement that restrictions should apply to high importance antimicrobials but exclude third generation cephalosporins and fluoroquinolones (42% compared to 68% of experienced clinical veterinarians). Uncertainty around the option of excluding third generation cephalosporins from restrictions was pronounced among recent graduates (26% neither agreed nor disagreed) and non-clinical veterinarians (25%), whereas only 13% of more experienced veterinarians in clinical practice were uncertain about this option.

Participants were asked about the appropriateness of various restrictions if they were to be placed on the use of high-importance antimicrobials. Figure 2 shows the responses for all participants. There was most agreement (81%) for use to only be allowed after culture and susceptibility (C&S) testing confirmed that the pathogen was resistant to all low- and medium-rated antimicrobials that could be used to treat the case.

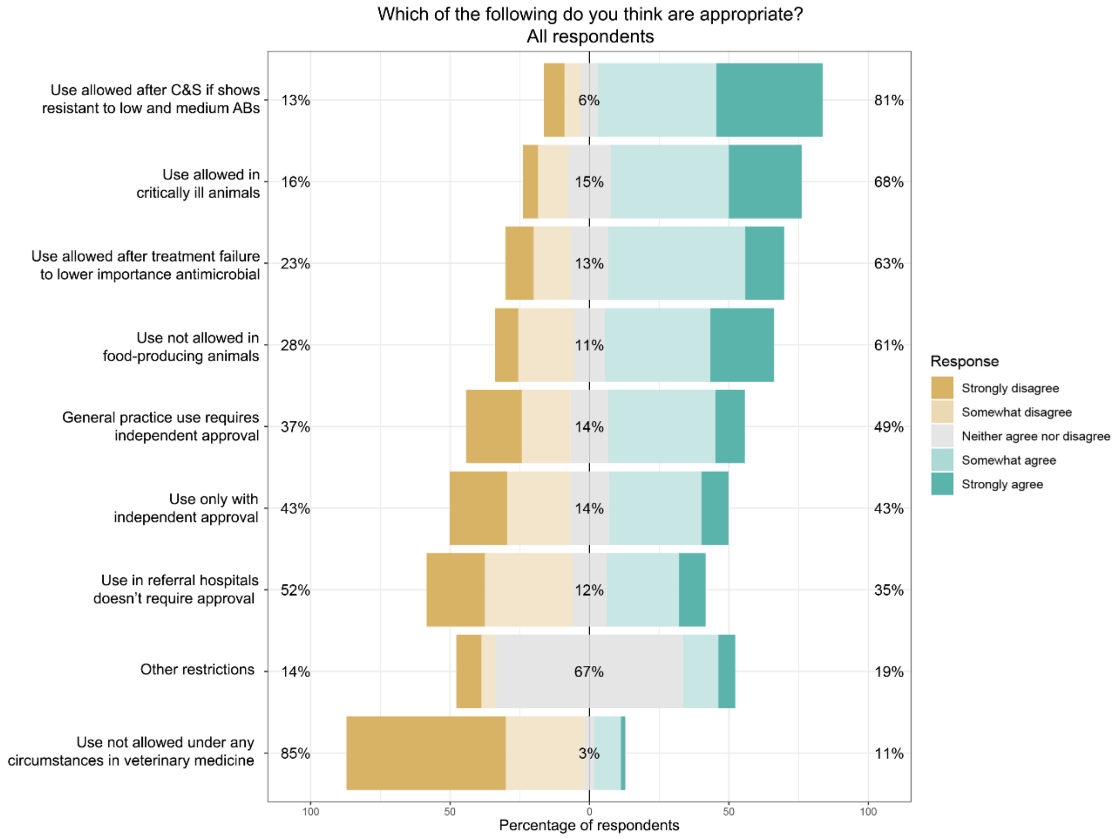

Figure 2 Responses of all participants to the question: "If there were to be restrictions placed on veterinary prescribing of antimicrobials with a high importance rating, which of the following do you think is appropriate?"

Support for other restrictions was noticeably different between veterinarians who were and were not working in clinical positions (Figure 3). Clinical veterinarians were more inclined to support use after the failure of treatment with low- and medium-rated antimicrobials (66% agreement compared to 47% agreement amongst non-clinicians). There was also more support amongst clinicians for use to be allowed in critically ill animals (72% agreement compared to 49% amongst non-clinicians). Clinical veterinarians were more likely to agree that use of high importance antimicrobials must never be allowed in food-producing animals, but can be allowed in other animals (62% compared to 55% of non-clinical veterinarians). However, 16% of non-clinicians agreed with restricting high-importance antimicrobials so their use was not allowed under any circumstances in veterinary medicine, whereas only 10% of clinicians supported this restriction. Almost half (49%) of veterinarians in clinical practice agreed with the restriction, 'Use in general practice requires approval from an independent office' and 13% neither agreed nor disagreed with this restriction.

For the small group of respondents in referral practice (n=20), the most agreement was for use being allowed in critically ill animals without restriction and use being allowed after culture and susceptibility testing confirmed that the pathogen was resistant to all low- and medium-rated antimicrobials that could be used to treat the case (83% in both cases). Fifty percent of referral veterinarians agreed or strongly agreed that use in referral hospitals should not require approval.

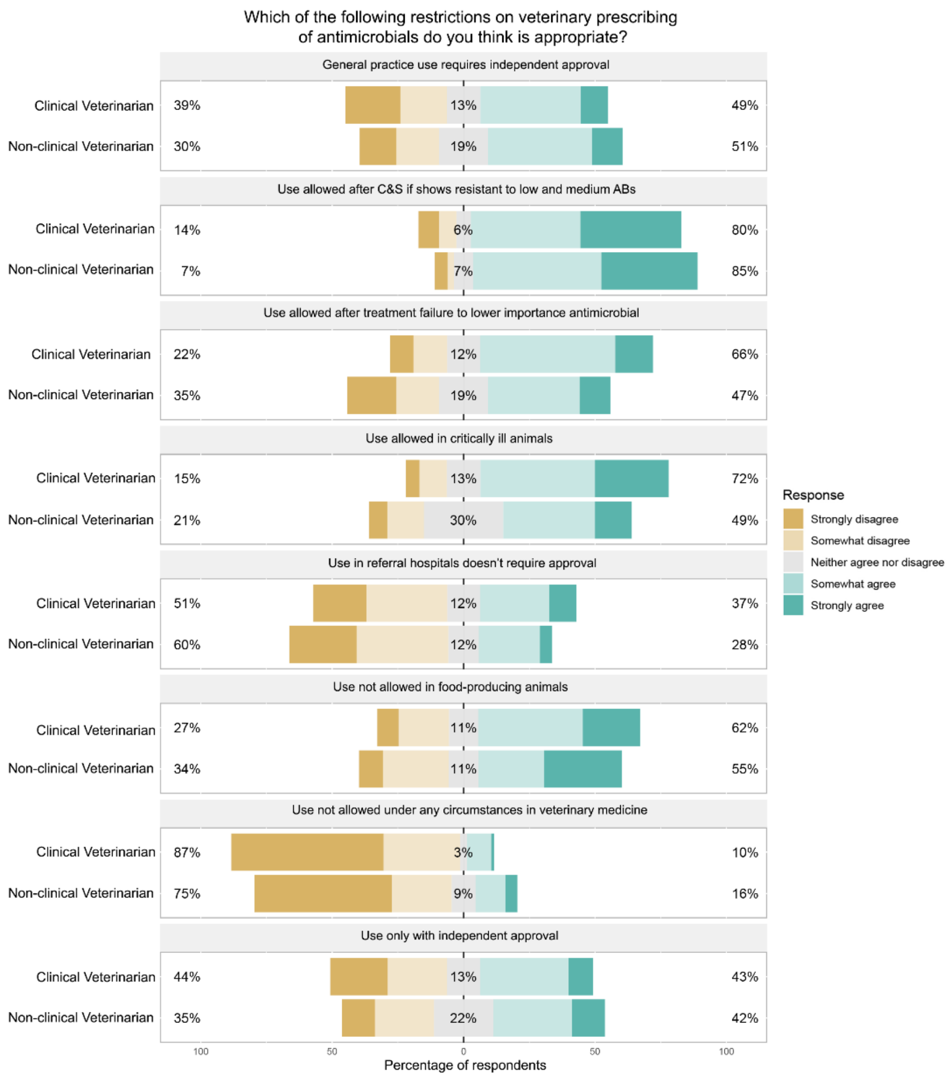

Figure 3 Responses of clinical and non-clinical veterinarians to the question "If there were to be restrictions placed on veterinary prescribing of antimicrobials with high importance rating, which of the following do you think is appropriate?

Three questions were asked to clarify whether respondents felt that certain conditions should preclude the need for approval (Table 1). If culture and susceptibility testing confirmed that the pathogen was resistant to all low- and medium-rated antimicrobials, most respondents (51%, n=160) indicated that approval should still be required for the use of high importance drugs.

Table 1: Scenarios requiring approval – responses of all participants

Question: Approval is still required prior to high importance drugs being used in veterinary medicine…	Agree (%)	Disagree (%)	Unsure (%)
…if culture and susceptibility testing confirms that the pathogen is resistant to all low- and medium-rated antimicrobials that could be used to treat the case	51	37	13
…if treatment has failed with a lower importance rating antimicrobial	45	28	26
… in critically ill animals	34	33	34

Case Scenarios and Reasonable Treatments

Participants were provided several case scenarios and asked whether use was appropriate or not.

Scenario 1 Cat: *A cat presents with a draining abscess on its face. While the cat is febrile and inappetent and you believe that antimicrobial therapy is indicated, you do not think that the infection is life-threatening. Under which circumstances is it reasonable to treat this cat with cefovecin (long-acting 3rd generation cephalosporin), an antimicrobial with a high importance rating?*

Veterinarians with knowledge of the ASTAG rating system had lower levels of agreement with the use of cefovecin in all the situations except when approval was given by an independent office (46% veterinarians with knowledge, 41% of those with no knowledge) and for the option of use never being reasonable (43% with knowledge, 32% with no knowledge) (Figure 4). Culture and susceptibility results suggesting resistance to low- and medium-rated antimicrobials was the situation in which the greatest proportion of respondents considered the use of cefovecin to be reasonable.

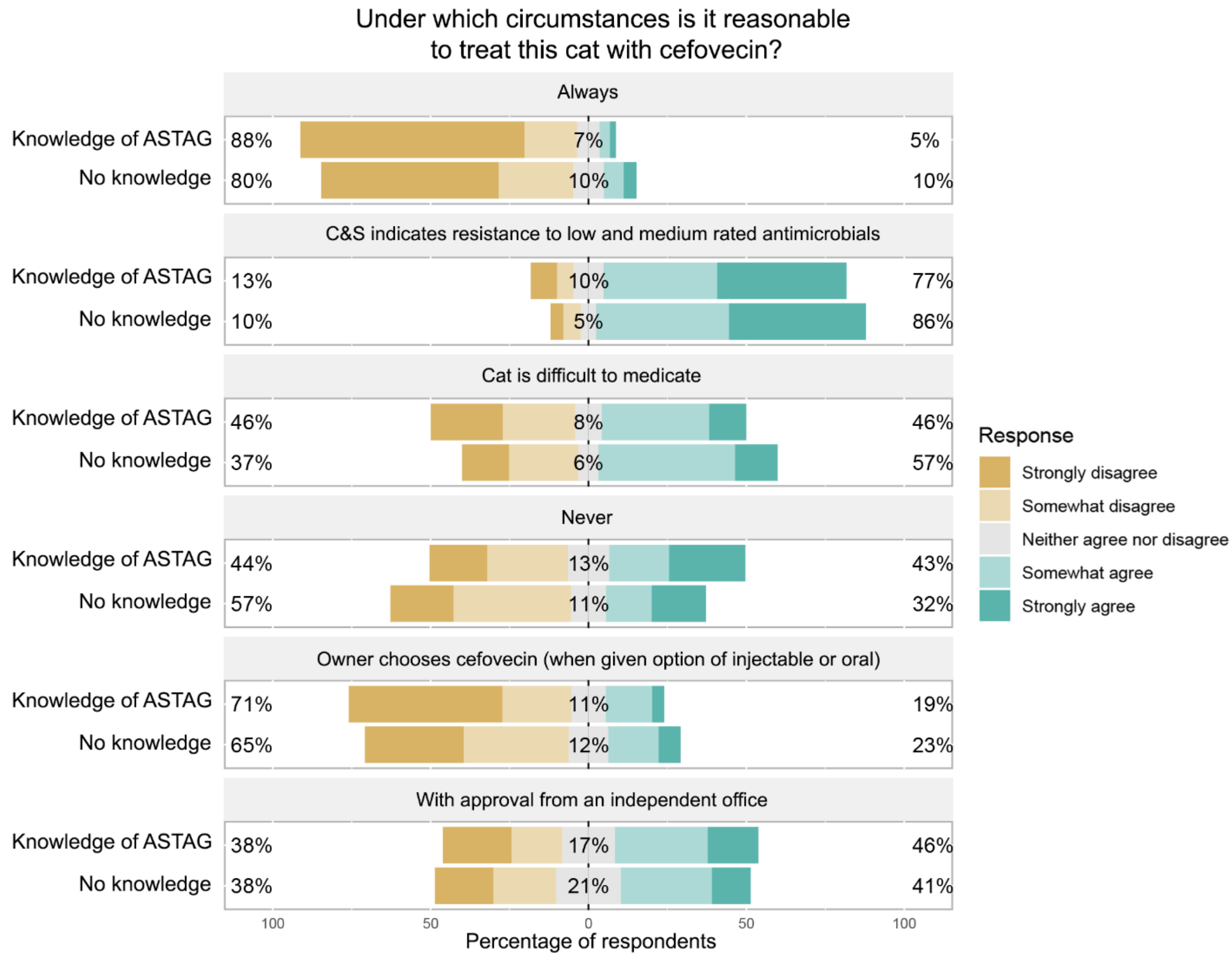

Figure 4 Responses of participants about the reasonableness of use of cefovecin in the different circumstances, with responses segregated based on the respondents' knowledge of the ASTAG rating system.

A greater proportion of clinical veterinarians who started practice after the release of cefovecin onto the Australian market in 2008 agreed that its use for a cat that was difficult to medicate was reasonable (61%) compared to veterinarians who started practice before the release of cefovecin (50%), although this difference was not statistically significant (RR 0.78; CI, 0.58-1.05; p=0.1).

Scenario 2 Horse: *A horse presents with a septic fetlock joint that could be life-threatening. Under which circumstances is it reasonable to inject the joint with amikacin, a high-importance rated aminoglycoside?*

In this scenario, a culture and susceptibility testing result indicating resistance to a medium-importance antimicrobial (gentamicin) was also the situation in which the greatest proportion of respondents agreed that use was reasonable (Figure 5). A higher proportion of respondents with knowledge of the ASTAG rating system thought use was reasonable if it was approved by an independent office (54% agreed or strongly agreed) compared to 44% of those who had not heard of the ASTAG rating system.

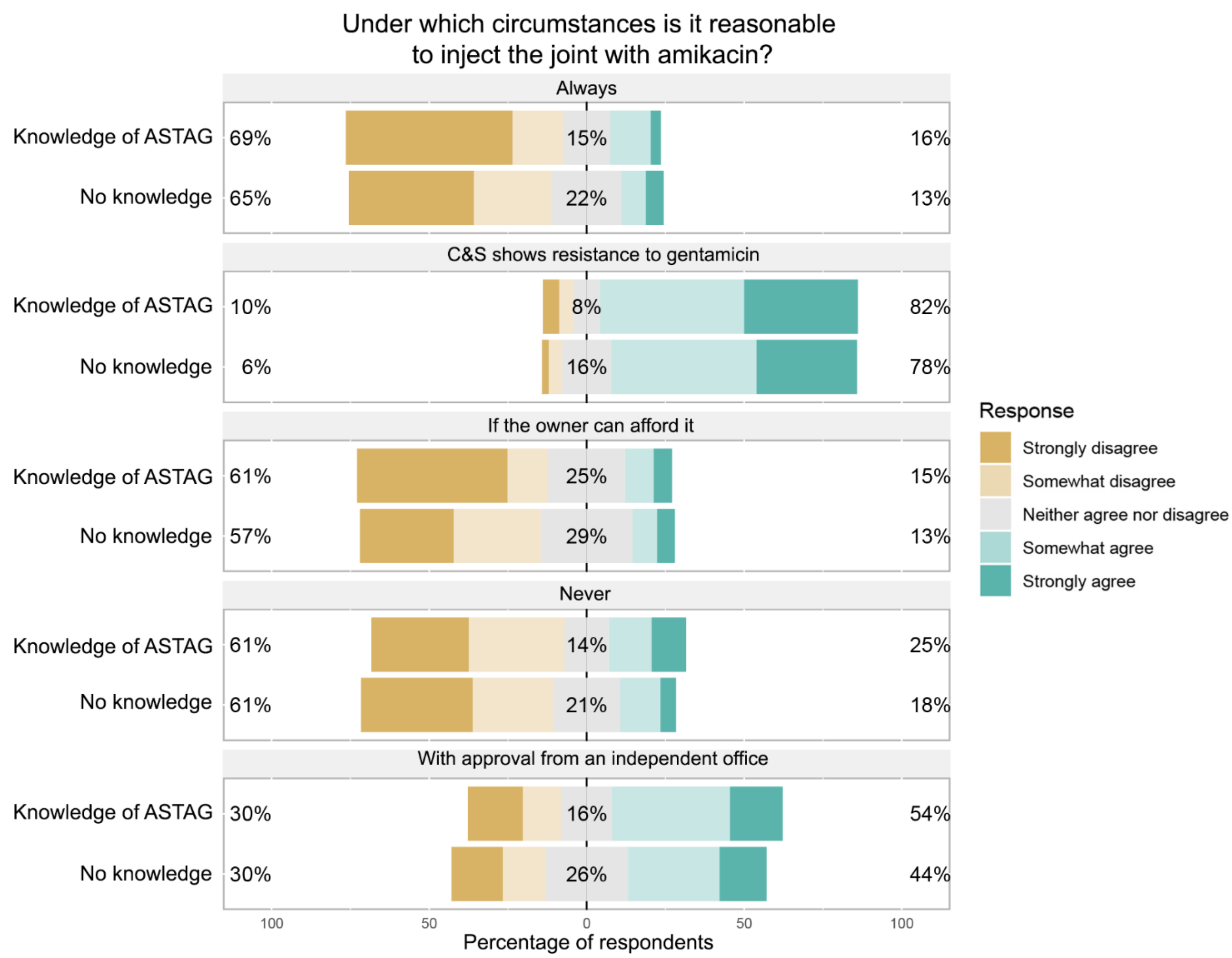

Figure 5 Responses of participants regarding reasonableness of injecting a horse's fetlock with amikacin in different circumstances, with responses segregated based on the respondents' knowledge of the ASTAG rating system.

Respondents were also asked about several other factors that might influence their decision-making about the horse in scenario 2. The horse's insurance status and owner demand were the factors least likely to be felt 'should be taken into account' (Table 2).

Table 2. How would the following situations affect your decision about the horse?

Situation	Should be taken into account (%)	Makes some difference (%)	Makes no difference (%)	Any antimicrobial should be allowed (%)	Unsure (%)
Other treatments have failed	166 (55)	82 (27)	26 (9)	10 (3)	(17) 6
You practice in a region where horses are considered a food-producing species	163 (54)	48 (16)	42 (14)	2 (1)	46 (15)
The prognosis was very poor	132 (44)	79 (26)	63 (21)	6 (2)	21 (7)
If the horse was the leading thoroughbred stallion in Australia	76 (25)	59 (20)	128 (43)	6 (2)	33 (11)
The horse is insured	33 (11)	32 (11)	202 (67)	3 (1)	31 (10)
The owners demand amikacin	16 (5)	37 (12)	218 (72)	2 (1)	28 (9)

Very few respondents thought that 'any antimicrobial should be allowed' under either of the scenarios. The situations most respondents thought 'should be taken into account' or 'makes some difference' were if other treatments had failed (82%, n=248) and if the horse was a food-producing species in that jurisdiction (70.1%, n=211).

Scenario 3 Cow: *A dairy cow presents with pneumonia and you believe antimicrobial therapy is indicated although the infection is not life-threatening. Under which circumstances is it reasonable to treat this cow with ceftiofur (3rd generation cephalosporin), an antimicrobial with a high-importance rating?*

In this scenario, a culture and susceptibility test result indicating resistance to lower rated antimicrobials was also the situation in which the greatest proportion of respondents agreed that use was reasonable (Figure 6). Of the three scenarios, Scenario 3, the only example featuring a food-producing animal, was the scenario in which the highest proportion of veterinarians thought use of ceftiofur was never appropriate. The labelling of ceftiofur (nil milk withholding period and labelled to treat pneumonia in cattle) was not regarded by most respondents as reasonable grounds for its use in this scenario.

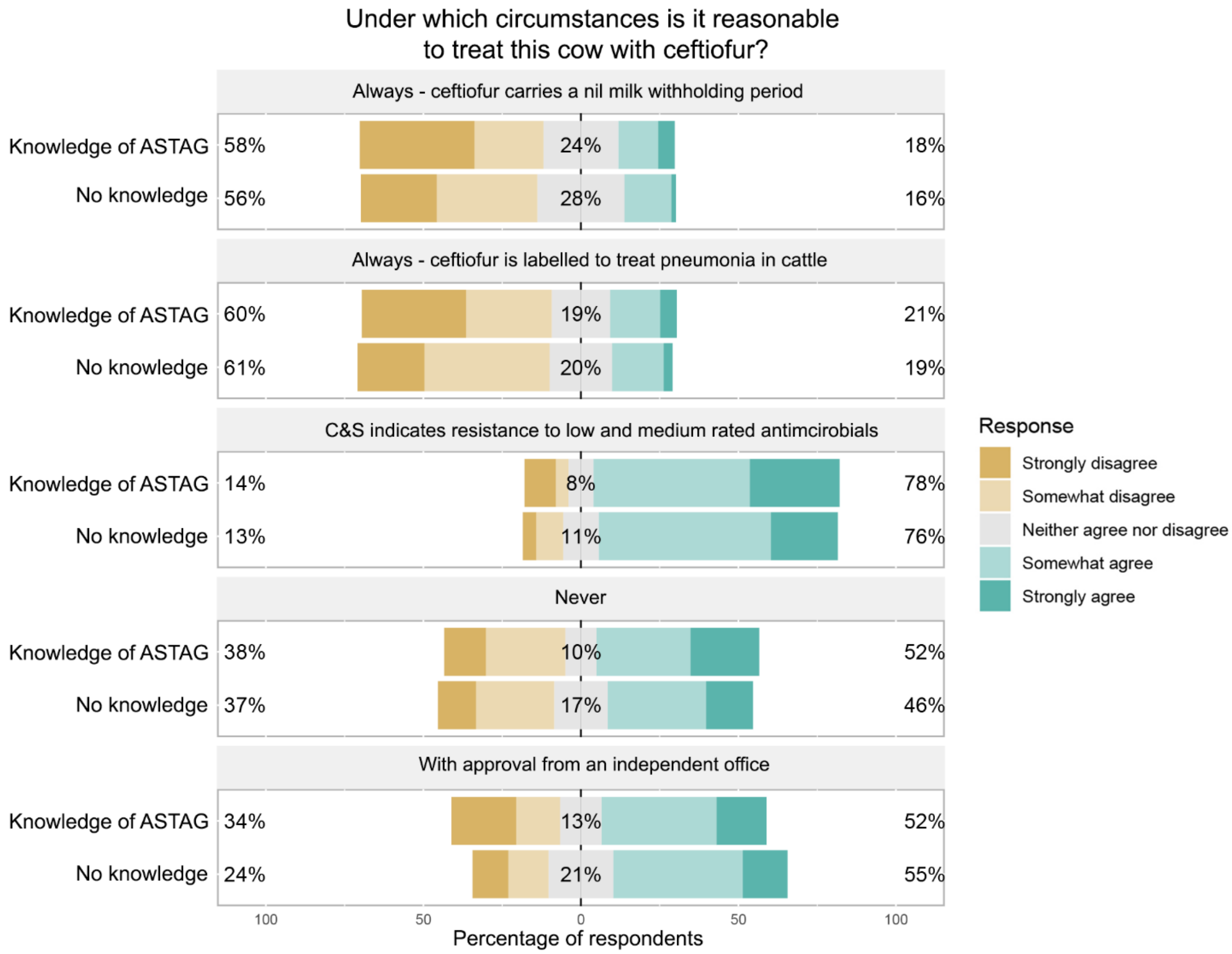

Figure 6 Responses of participants about the reasonableness of treating pneumonia in a cow with ceftiofur, with responses segregated based on the respondents' knowledge of the ASTAG rating system.

Free text responses

The cost of bacterial C&S was cited as an issue for veterinarians. Cost was an important factor when making prescribing decisions before antimicrobial use, e.g.

"…cost of C&S is high for our clients. This also contributes to not 'working up cases properly', or even bothering with the negotiations of this with clients."

However, comments were made in support of using C&S testing first as a way of deciding on or allowing the use of high importance antimicrobials e.g.

"Antimicrobials should be split into 2 categories. "Empirical therapy" and "after C&S". The only restrictions put onto antimicrobials should be that C&S MUST be performed before administering it".

The most common free text comments were about the practicalities of implementing any kind of restrictions requiring an external approval system, particularly given the smaller size of veterinary practices compared to human hospitals and when veterinarians were working after-hours and on weekends or public holidays.

“In the case of a critical patient there is definitely no time to waste waiting for approval, not to mention the added time and strain on all ready overworked vets, especially those on call in the middle of the night”

“…I would be happy with requiring approval in all cases if approval could be reasonably readily got (or denied) within an hour or two, 24 hours a day. If it's going to take longer then I would prefer to be able to use them on the basis of susceptibility testing showing they were the only reasonable option or (perhaps) in critical patients.

“Differences between human and veterinary medicine is the size and integration of the human medical system, which I would anticipate allows for faster approvals of restricted drugs. In veterinary medicine we often see patients presenting with disease courses further along in the disease process and the industry consists of mainly independent small businesses. Applying the same approval requirements would be logistically difficult to achieve in a timely manner for critically ill patients.”

Concerns for animal welfare were also raised, particularly if there would be delays in obtaining approval to use an antimicrobial when there was a perceived need.

“Restrictions on high importance antimicrobials are good in theory, as long as in-practice turnaround times for approval does not compromise ability to treat critically ill animals requiring antimicrobials of high importance.”

Restrictions on prescribing were seen as restricting a veterinarian’s ability to do their work and fulfil other requirements of their role, such as maintaining animal health and welfare.

“In cattle and horse practice, Excede [ceftiofur] has been used a lot as a long-acting antimicrobial which has high practical value for reduced handling of stock with associated welfare benefits. With horses it can be a way to give a Hendra [virus] exclusion case some antibiotic cover to fulfil WH and S [workplace health and safety laws] and welfare obligations.”

“I see strong industry effort to reduce the use and to use them more appropriately, and I believe this is key; not restrictions that could potentially harm the patients we seek to protect and heal (because of human medical industries).”

The need for further education of veterinarians and clear guidance was frequently mentioned as a solution to the issue, either instead of, or as well as, other restrictions.

“Mandatory AMS programs in all vet practices would be a good idea. I think we need to prove that we are using them only in situations where there is a lot of thought put into it - high important antimicrobials are important for a reason”

“Better education of small animal practitioners required. Vets who work with food producing animals are more aware generally.”

“I’m not sure. External approvals create a lot of cost and bureaucracy, but we seem incapable of disciplining ourselves to be scientific in our use of antimicrobials. Maybe looser controls if a practitioner has undergone training and has an antimicrobial stewardship plan in place.”

“Clear guidelines for general practitioners on when use of high importance antibiotics may be valid, and equally, when use is not valid, are important.”

The issue of off-label use of compounded and human products in veterinary medicine was raised and it was highlighted that these products also need to be included if reporting or auditing of any kind is implemented. The use of combination antimicrobial therapy was also mentioned several times.

“This reporting MUST include compounding and human products as these are completely under the radar.”

“Multiple antibiotic combinations need regulating.”

Many comments were made in favour of restrictions of some kind on veterinary prescribing of antimicrobials, particularly high-importance antimicrobials. Many of the comments opposing restrictions raised concerns about the imposition of restrictions on veterinarians who may not be misusing antimicrobials or about limiting the veterinarian’s professional right to prescribe antimicrobials. Some respondents suggested they felt they were being unfairly blamed or targeted.

“I believe the veterinarian, like a human doctor should have the professionalism to decide when they choose to use antibiotics. We are not different to human doctors. I believe I am a professional and I believe I make professional decisions. I do not feel I need to be regulated.”

“It is not a good idea to impose further restrictions on those vets that are already doing the right thing.”

“I am very concerned about this matter, but I am as concerned by the blatant misuse of antimicrobials in human health and their misuse in human and animal medicine overseas in contrast to Australia. More regulation in our highly regulated country will lead to worsening of animal health and welfare outcomes. Education is key, not more regulation.”

“It is important for vets and medicos to work together to lessen our general use of antimicrobials. I resent vets being put to blame for overuse in humans as well.”

“I can't help but feel what we do in a clinic setting will have little overall impact - I think vets in general are judicious…Antibiotic resistance is much more likely to develop from the profligate use and over-the counter access to them in less regulated countries.”

Some of the comments made in favour of restrictions referred to concerns about the prescribing practices of colleagues.

“I think we need a lot more regulations as a lot of my colleagues I work with reach for 3rd generation antibiotics as the first antimicrobial to use on the patient almost 90% of the time.”

“The use of ceftiofur (especially), enrofloxacin and gentamicin in horse practice and especially racehorse track practice is a joke. Common to give Ceftiofur either prophylactically pre-race or even if the horse has minimal symptoms…Needs to be stopped!”

“The off-label use of Ceftiofur to treat scouring calves or calves with pneumonia, for treating endometritis or for treating lame cows are the scenarios that are far more risky (and more common) than use for treating the odd case of pneumonia and are conditions for which there are alternatives.”

Some of the suggestions of respondents for improving AMS in the profession included a phone hotline for advice, having prominent warning labels on high-importance antimicrobials and monitoring the use of antimicrobials by veterinarians using post-prescription auditing, particularly of high users.

Discussion

Most veterinarians are open to some restrictions on antimicrobial prescribing

The results from this survey suggest that the majority of veterinarians agree with more stringent conditions on prescribing antimicrobials, in particular those of high importance. This contrasts with the findings of a survey undertaken in 2016, where veterinarians did not think restrictions would be helpful [96]. This could be a consequence of a change in sentiment over time, in line with increasing awareness of the issue of AMR amongst veterinarians and a focus on this in Australian veterinary schools [198, 199].

Previous research has identified concerns among professionals about a loss of professional autonomy and feelings of resentment about unwarranted blame if prescribing of antimicrobials is restricted [96, 200]. Some of the free text comments in our survey also referred to these themes, however concerns about practicalities and animal welfare were more common. The framing of questions may have influenced the differences between responses to our survey and the survey conducted in 2016. Our question was asked in the context of doctors needing to obtain approval to prescribe high-importance antimicrobials for patients and this not being the case in veterinary practice. This may have appealed to the sense of equality that causes some veterinarians to usually oppose restrictions when questions about restrictions are asked without reference to restrictions on medical prescribing. Given the effect that restrictions on antimicrobial use have had in human medicine, both in Australia and internationally [121, 189, 190], education of veterinarians and veterinary students should focus on the benefits of implementing restrictions. These could include better relationships with clients, improved management through more frequent veterinary consultations and improved clinical care as a result of more accurate diagnoses, as might be the case if diagnostic testing is required prior to prescribing high-importance antimicrobials. Improvements in workplace culture may also be a positive outcome of restrictions if it facilitates discussion amongst colleagues and adoption of more evidence-based practices. When managing 'common pool' resources such as antimicrobials, approaches that foster cooperation and provide a sense of collective ownership of the issue, and the interventions to address it, can be more beneficial than restrictions alone [200].

Most popular restrictions and significance of culture and susceptibility testing

Restricting prescribing of all high-importance antimicrobials was the restriction with the most support, followed by restricting high importance antimicrobials but excluding 3rd generation cephalosporins and fluoroquinolones. As veterinarians, particularly companion animal veterinarians, already prescribe these classes of high-importance antimicrobials, it might be expected that some veterinarians would prefer that they were not restricted in any way.

The most popular restriction was that "Use is only allowed after culture and susceptibility testing confirms the pathogen is resistant to all low- and medium-rated antimicrobials that could be used to treat the case." This was also the situation in which most respondents felt that the use of high-importance antimicrobials was reasonable in all three case-based scenarios. Respondents were divided on whether additional approval was required on top of C&S results. Table 1, shows that 51% of respondents thought additional approval was still required after C&S testing. The imposition of a requirement for further approval after C&S testing also yielded the highest level of disagreement (37%), suggesting that many respondents thought that use of high-importance antimicrobials should be allowed, without any additional approval process, if C&S test results indicated that they were the only effective option.

It is possible that responses may depend on which specific high-importance antibiotic agent is being used, rather than high importance antimicrobials in general, or even particular classes of antibiotics. Our case-based scenarios only referred to two third generation cephalosporins – cefovecin and ceftiofur - and the high-importance aminoglycoside amikacin, and included limited information about the patient presentation and the available options. Some respondents may have made a different choice in a real clinical scenario. Evidence from human medicine has frequently focused on restriction of single classes of antimicrobials or, in some cases, restrictions or new procedures for prescribing a single antimicrobial [201-203]. Similar targeted research in a veterinary setting will be required over time to build on our study as more veterinary practices implement antimicrobial stewardship strategies.

Where restrictions have been introduced into human hospital settings, and where they have been introduced in animal health settings, they have been shown to have a dramatic effect on the quality of prescribing, in terms of compliance with guidelines or appropriateness, as well as effects on reducing levels of AMR [36, 182, 188, 203, 204]. However, the acceptance of restrictions by prescribers is considered a barrier to antimicrobial stewardship [82, 203, 205, 206]. Most success appears to have been achieved when education for healthcare teams is provided alongside the implementation of restrictions. One successful example has been the introduction of pre- or post-prescribing review and feedback, where an infectious diseases physician reviews prescriptions either before they are provided or in the 24-48 hours afterwards and gives face-to-face or written feedback to prescribers about their choices [182, 188, 207-209]. Most Australian veterinary practices do not have readily available access to trained staff who could provide pre- or post-prescribing review or feedback. Therefore, implementation of restrictions combined with other educational support and relevant diagnostic testing (such as C&S testing) is likely to be a more feasible option in terms of time and human resources.

Given the concerns and difficulties veterinarians have reported about costs of testing to clients (and also evident in free-text comments in this study) as well as the practicalities of waiting for C&S results, which can take 2-3 days depending on location, it is interesting that most respondents identified C&S testing as an appropriate restriction on prescribing of high importance antimicrobials and agree with its use in determining the reasonableness of antimicrobial use. If most veterinarians are in favour of using more C&S testing to improve the quality of prescribing and the main barrier is cost, exploring the impacts on antimicrobial prescribing of subsidising or reducing C&S testing costs would be an important target for future AMS interventions and should be explored as part of a one health approach to address AMR [34, 210]. Improving communication with clients about the benefits of using these diagnostic tests could also be beneficial [23, 103, 211].

Respondents appeared to have higher thresholds for reasonable use in the production animal scenario than in the equine and feline scenarios. This may be attributable to the strict legislation already in place in Australia around use of antimicrobials in food-producing animals and the awareness of veterinarians about the risk of residues entering the food chain, and about the importance of infection control, biosecurity, vaccination and other herd health interventions in managing disease in farm animals [36, 198].

Influence of ASTAG awareness and other participant characteristics

Those respondents who were aware of the ASTAG rating system were more likely to respond to the clinical scenarios in a way that was consistent with current Australian-specific veterinary antimicrobial use guidelines. This may reflect greater familiarity with prescribing guidelines, more concern about AMR, or a higher level of knowledge about antimicrobial prescribing.

Recent graduates have more recent knowledge and training in antimicrobial stewardship, which was consistent with their higher level of awareness of the ASTAG guidelines. However, this didn't necessarily result in a more appropriate approach to antimicrobial use. The pressures of clinical practice and concerns about what owners want, as well as pressure from colleagues, may have a stronger influence on less experienced veterinarians [23, 83, 206, 212]. Other research has shown that veterinarians and human health practitioners are influenced by what they have been taught and the pressures of daily practice, including the behaviour of colleagues, particularly those with more experience or seniority [206, 213, 214]. Similar factors may have influenced recent graduate veterinarians in this survey, impacting the appropriateness of their choices in spite of their more up-to-date knowledge. For example, 21% of recent graduates agreed that use of amikacin use was reasonable in Scenario 2 if owners could afford it, compared to only 14% of all respondents. Given that this was their response to a survey question, rather than a clinical case with the pressures that might be felt in practice, it is particularly interesting that recent graduates responded differently. The reasons for this should be explored further.

One of the case-based scenarios provoked a higher level of uncertain responses from recent graduates (graduated 2016-2019) - whether use of cefovecin was reasonable in a cat that was difficult to medicate, with 14% neither agreeing nor disagreeing, compared with an uncertain response rate of only 7% amongst practitioners who graduated prior to 2008, when cefovecin was first registered for use in Australia. Having restrictions in place could be helpful for recent graduates in such situations, particularly if restrictions are implemented in concert with further education and use of guidelines. This might be expected to facilitate a sense of collective ownership of the problem and solutions, rather than an expectation that it is more appropriate to defer to what other veterinarians in the practice are doing even if this is not guideline-compliant [200]. Free-text comments on this theme stated,

"Other than reserving some antimicrobials to human use only, there should be clear guidelines that we can point clients to when they get frustrated."

"I think high importance antimicrobials are often used because inexperienced practitioners lack confidence in themselves."

While experienced clinical veterinarians are less impacted by financial concerns and client demands (real or perceived), they may also be more likely to rely on their past experience rather than on guidelines [23, 83, 102]. This was seen in a survey of Australian dairy cattle veterinarians, where clinical experience was the most influential factor affecting prescribing choices, followed by product label recommendations [215]. In that same survey of dairy cattle veterinarians, the likelihood of choosing a first-line treatment for mastitis dry cow therapy decreased with the number of years of experience.

The impact of post-graduate qualifications on agreement with restrictions may have differed between those veterinarians that were in clinical and non-clinical roles for several reasons. Those in clinical practice with post-graduate qualifications are likely to be specialists and have significant experience in their field. This can lead to reliance on past experience and a greater trust in one's own knowledge, rather than feeling that restrictions are required to improve the quality of prescribing [206].

Non-clinical veterinarians were generally more in favour of restrictions, which may be related to their separation from the daily challenges of clinical practice that influence prescribing choices. The pressures and practicalities of clinical practice and treating ill animals may also explain why clinical veterinarians were more inclined to support use of high-importance antimicrobials after a failure of treatment with low- and medium-rated antimicrobials and why there was significantly more support amongst clinicians for use of high-importance antimicrobials in critically ill animals. Respondents in specialist referral practice are likely to be seeing more severe and more complex cases, and thus might be expected to believe that use in critically ill animals should not be subject to restriction.

Unlike in human healthcare, practice in rural or metropolitan areas did not seem to influence prescribing significantly in our survey, a finding consistent with other veterinary research [23]. This could be because the difference between rural and metropolitan veterinary practice is less distinct because veterinary clinics in regional locations are often better equipped and have greater in-house diagnostic capacity than smaller metropolitan practices, which can be more reliant on specialist, referral and emergency centres for advanced testing and complex case management.

Issues about feasibility of implementing restrictions

While the responses to some survey questions indicated that respondents did not place as much weight on factors such as owner demand or the insurance status of patients (Table 2), the free-text responses highlighted numerous issues around feasibility of implementation of restrictions. These included time pressures on prescribers, concerns about patient deterioration and animal welfare without antimicrobial use, concerns about client perceptions or direct requests for antimicrobials, and costs associated with additional testing. Communication techniques for use by veterinarians when not prescribing antimicrobials have been developed, but have not yet been evaluated [211]. Other issues around feasibility are likely to require increased education for veterinarians and other associated personnel, and development of systems that do not result in additional time pressures for veterinarians, but instead enable them to obtain permission or the support for appropriate use of high-importance antimicrobials easily when required.

Our survey responses suggest that adopting a non-punitive approach to AMS interventions, including any kinds of restrictions, could help raise awareness of the importance of AMS while also fulfilling needs for increased education about appropriate antimicrobial use and allaying concerns about the practicalities of an approval system. It is clear from the responses to this survey that C&S testing needs to be a key factor in any approval process. However, previous work has highlighted that disease investigation can be difficult in private veterinary practice because there is no or minimal incentive for clients to fund investigations that are primarily in the public interest [216]. To ensure equitable and increased access, public funding for approval systems and for diagnostic testing is justified, given the one health benefits of addressing AMR [217]. Allocating funding for subsidised veterinary C&S testing may be more cost effective in the long term, as it could preserve the efficacy of antimicrobials for human treatment, particularly that of high-importance antimicrobials.

Future research should focus on the practicalities of implementing restrictions and the outcomes of other AMS interventions, such as education programs and subsidised C&S testing. Australia's National Antimicrobial Resistance Strategy states that "Integrated Surveillance and Response to Resistance and Usage" is one of its objectives, and financial support for veterinary AMS at a federal level through subsidised C&S testing would be very much in keeping with this objective [34, 132, 218]. This is particularly the case if such a scheme could be used to increase surveillance for AMR in animals.

Other Challenges

A proportion of veterinarians (19%) use a traffic light system for indicating antimicrobial importance in their workplace and 49% were familiar with the ASTAG rating system. This is already a small improvement from a study conducted in 2017, which found that 15% of survey respondents had antimicrobial prescribing policies or AMS policies in their practices. Guidelines were used by 28% of respondents to this 2017 survey. Global initiatives such as Antibiotic/Antimicrobial Awareness Week started in 2015 and understanding about antimicrobial stewardship amongst veterinarians may have become more common over the past five to ten years, in line with an exponential increase in publications on this topic and the release of Australia's first National Antimicrobial Resistance Strategy in 2015 [13-15]. Ongoing research to track improvements in awareness about AMR and AMS, and guideline use, amongst veterinarians would be beneficial to measure success of any AMS initiatives. Practical education on how to implement a traffic light system in the workplace has been introduced to some veterinary practices in recent years and a further focus on this in education for veterinarians, particularly those in senior or management roles in the practice, may help more veterinarians implement this in daily practice. Recent graduates, who have higher awareness of the traffic light system, may also be more likely to use it in practice if it is already an established part of the practices in which they work rather than recent graduates needing to be responsible for implementation.

The off-label use of high importance antimicrobials was highlighted as a concern numerous times in free text comments in our survey, particularly in relation to dairy cattle and equine practice. Concerns about use of compounded antimicrobials and their bioavailability were also raised. Any restrictions must encompass off-label use, but it is important to realise that off-label use can actually be more appropriate than following product labels in some cases, particularly in relation to dose rates [50, 51]. Label warnings on high-importance antimicrobials was suggested and could be an important first step. The label for the third generation cephalosporin, cefovecin, already states, 'FOR USE ONLY in dogs and cats where indicated by antibiotic susceptibility testing according to principles of prudent use' [219], but 10% of respondents who were unaware of the ASTAG rating system regarded the use of this antimicrobial for a cat bite abscess without culture and susceptibility to always be reasonable, and 57% of these respondents also thought it was reasonable if the cat was difficult to medicate orally. Widespread use of cefovecin without culture and susceptibility testing has been reported in other studies in Australia and overseas [49, 220, 221]. While label restraints are important, current evidence suggests they do not seem to have much impact on prescribing by companion animal veterinarians.

Materials and Methods

The source population for the survey was veterinarians in Australia in 2019/2020. At that time, there were between 12,769 and 13,993 registered veterinarians in Australia, however the survey was also open to veterinarians working in a non-clinical setting, such as industry, government or academia, who may not currently be registered with their state veterinary surgeons board [196, 197]. Respondents self-selected and were invited to participate through email, veterinary organisation newsletters and social media from June 2019 until December 2020. The survey was solely distributed online using the Qualtrics online survey tool. The full survey is available in the supplementary materials. Survey content covered questions about restrictions on veterinary prescribing of high importance antimicrobials, use of antimicrobial importance rating systems and three case scenarios assessing reasonableness of use of high-importance antimicrobials.

To be confident the proportion of veterinarians who had heard of the ASTAG rating system was within 7% of a true prevalence of 50%, a total of 194 completed surveys were required. Sample size calculations were carried out with finite population correction, assuming a 50% prevalence, because this provided the largest sample size estimate for a constant margin of error. Sample size calculations were made using the samplingbook package in R and sample.size.prop function. Statistical analysis and production of data and plots was performed using RStudio Version 1.4.1103 2009-2021 RStudio, PBC.

Short comments in the free text response options were collated and analysed for emerging themes using qualitative analysis techniques.

Conclusions

This study has highlighted the need for further targeted research to provide guidance about how restrictions on the use of high-importance antimicrobials should be implemented in veterinary practice. Supporting veterinarians through practical policies and AMS interventions is key if the efficacy of antimicrobials is to be preserved for the treatment of both humans and animals. Education and a non-punitive approach must be integral to any restrictions placed on prescribing of antimicrobials by veterinarians, who are, in general, open to restrictions and improving the quality of their prescribing. The use and regulation of antimicrobials in veterinary medicine to combat AMR cannot be separated from the manifold challenges facing veterinarians now and into the future. This includes the effects of emerging infectious diseases, including the COVID-19 pandemic, climate change impacts, and workforce challenges. Strategies that are holistic and provide a sense of ownership and empowerment are likely to be the most successful.

Chapter 3 Published Paper

Reaching consensus amongst international experts on the use of high importance-rated antimicrobials in animals – a Delphi study

Anna Sri[1,2], Kirsten E Bailey[1,2], Ri Scarborough[1,2], James R Gilkerson[1,2], Karin Thursky[2], Glenn F Browning[1,2], Laura Y Hardefeldt[1,2].

[1] Asia-Pacific Centre for Animal Health, Melbourne Veterinary School, Faculty of Science, University of Melbourne, Parkville, VIC 3010, Australia

[2] National Centre for Antimicrobial Stewardship, Department of Infectious Diseases Melbourne Medical School and Melbourne Veterinary School, University of Melbourne VIC 3010, Australia,

* Correspondence: aesri@student.unimelb.edu.au

Abstract

In Australia, antimicrobials are given an importance rating by the Australian Strategic and Technical Advisory Group on antimicrobial resistance. High importance antimicrobials are those essential for the treatment or prevention of infections in humans, where there are few or no treatment alternatives. In this study we consulted with experts from across human and animal health using the Delphi consensus-building process to establish the circumstances under which antimicrobials with high importance to human health could be used in animals in Australia. We used three rounds of online surveys. Group responses were provided to participants in each subsequent round to facilitate convergence of opinion. Consensus was defined as 80% or more of respondents selecting the same option for a question. By the end of the third round, consensus was achieved on eight items. This included the use of high importance antimicrobials being appropriate if culture and susceptibility testing indicated the organism was resistant to low- and medium-rated antimicrobials that could be used to treat the case. If any high-importance antimicrobials are prescribed for animals there was also agreement that a clear indication for this use and justification for antimicrobial choice must be recorded in the medical history, along with the dose rate, route of administration, the duration and the time point for review of the condition and associated antimicrobial therapy.
Appropriateness of use of high importance antimicrobials in critically ill animals where culture and susceptibility results are not available is still undefined. Further work is also required to establish which particular organisation should be notified of the use of high importance antimicrobials not registered for use in animals. The Delphi process was valuable in facilitating consensus amongst international experts from a broad range of health backgrounds and experience.

Keywords: antimicrobial resistance; high-priority critically important; antimicrobial stewardship; rating systems; one health

Introduction

The Delphi consensus method is a group facilitation process used to provide expert guidance about the best course of action to take when faced with a problem or issue for which there is no clear solution [146]. The Delphi process involves administration of rounds of surveys and provision of anonymous feedback to participants with the aim of identifying areas where consensus can be reached. It is useful when participants are geographically dispersed and anonymity is desired to control for individuals whose opinions could dominate or disproportionately influence others [222]. The process has been used in numerous contexts to broaden knowledge and advance practice, particularly in relation to guideline development and establishing relevant metrics, for example, for measuring appropriateness of prescribing [223-225]. It is particularly useful where higher quality evidence may not be available [226] or when current evidence may be contradictory but some agreement on the way forward would be beneficial [222].

Currently, such a situation exists in the field of antimicrobial stewardship, particularly about the future consequences of current actions. There is widespread acknowledgement that antimicrobial use in animals needs to be recognised as a contributor towards antimicrobial resistance (AMR) [36, 118, 227], but also that veterinarians' access to antimicrobials is essential to treat infectious disease and maintain good animal welfare [11, 26]. In Australia, antimicrobials are assigned an importance rating by the Australian Strategic and Technical Advisory Group on antimicrobial resistance (ASTAG)[8]. The ASTAG rating system is based upon, and considers, the World Health Organization's Critically Important Antimicrobials list. However, ASTAG has rated some antibiotics differently, depending on the local situation in Australia, where the prevalence of resistance and disease in humans and animals differs from other parts of the world [47, 228]. High importance antibacterials are those "essential for the treatment or prevention of infections in humans where there are few or no treatment alternatives for infections". Use of these drugs in animals is contentious as it could contribute towards the development of antimicrobial resistance that may impact the effective treatment of human infections.

The aim of this study was to define the circumstances under which antimicrobials of high importance in human health could be used in animals. Achieving consensus amongst medical and veterinary experts on key elements of antimicrobial use and stewardship will facilitate progress by enabling a unified approach to the use and management of this shared resource. It will also demonstrate that all sectors can work together to promote antimicrobial stewardship and slow the progression of antimicrobial resistance. For the purposes of this study, antimicrobial stewardship was defined both specifically, as activities that reduce the development of AMR in a clinical setting [60], and also more broadly, as a concept or multifaceted approach that has the ultimate goal of reducing pressure on the development of AMR [58, 61].

Materials and Methods

Potential participants were identified through the researchers' professional networks and by searching for published authors in the field of AMS. Our research group includes veterinarians and physicians with expertise in infectious disease, microbiology, antimicrobial resistance, antimicrobial stewardship, and public health.

Questions were formulated based on identified gaps in previous research [7, 118], with the aim of establishing the circumstances under which antimicrobials of high importance in human health could be used in animals (or if such circumstances ever exist). Issues such as insufficient detail in medical records to assess appropriateness of use were also explored. Reference to previous research also identified areas where there was already significant agreement, such as about the use of culture and susceptibility testing [229]. Questions covered a variety of topics, including establishing the area and years of expertise of the participants, importance rating systems, as well as questions about different situations in which use should be restricted – areas currently lacking sufficient Australian-specific research. Ample opportunity was provided for free-text comments and explanation of the participant's reasoning, and these informed the wording of questions in subsequent rounds and the provision of additional information. Questions were presented back to the group in later rounds after adjustments to the focus or wording based on feedback from earlier rounds. The full text of each survey can be found in Appendix II.

English-speaking experts in the field of AMR or AMS from across the globe were invited to participate by email. Expertise was defined as: having published in the field of AMR or AMS; membership of a working group, committee or other organisation addressing AMR, AMS or a related discipline; or working in a relevant field (e.g. infectious disease, microbiology, AMS, AMR, IPC, medicine, surgery, or public health). Many of the participants had published work that members of the research group were aware of and were thus acknowledged as 'experts' in their field. The participants' level of expertise and involvement in AMS was also established in the first survey round. Three survey rounds were undertaken online between November 2021 and May 2022.

Consensus was pre-defined as 80% or more of respondents selecting either the same option or a similar option. This level of consensus was chosen as it represented a considerable majority of participants, ensuring acceptance of these results amongst human and animal health experts, particularly when advocating for changes in policy or usual practice. Of note is that there was a trend towards consensus and stability of results throughout the rounds, which has been reported as being important in addition to absolute percentage of consensus [230]. Research on defining appropriate levels of consensus for Delphi studies is limited [224, 230]. The Delphi process involved reporting results from each survey round in the subsequent round and asking experts to evaluate their responses based on the provision of additional clarification or information and on the responses of the group as a whole. In subsequent rounds, options such as 'agree' and 'strongly agree' or 'disagree' and 'strongly disagree' were consolidated to simplify choices, encouraging convergence of opinion. Questions and topics were excluded if no option was within 15-20% of consensus or the comments suggested a need for extensive discussion or engagement to achieve agreement, beyond what could be achieved solely through additional survey rounds.

Results and Discussion

Surveys were distributed to 119 experts across human and veterinary medicine. The response rate to the surveys was 38% for Round 1, with 45 experts responding (although one response was only partially completed). Forty-eight percent of respondents (n=21) prescribed antibiotics in their current role (Table 1), 86% of whom were veterinarians (n=18). Eighteen (41%) of the experts who were the lead of an antimicrobial stewardship team, or who had executive oversight over an antimicrobial stewardship team (n=25, 57%), were also veterinarians. Most participants (n=38, 86%) had been working in antimicrobial stewardship or antimicrobial resistance for over 5 years, and fourteen respondents (32%) had over twenty years of experience in these fields. For the second and third rounds, the survey was sent to anyone who had responded to a previous round and response rates were 53% (24/45) and 56% (25/45) respectively. Seventy-five percent of respondents that took part in Round 2 also took part in Round 3 (18/24). The Australian and international experts had a diverse range of occupations and areas of expertise (Table 1)

Table 1. Participant Characteristics

	Round 1	Round 3
Characteristic	**n (%)**	**n (%)**
Total number of participants	44/119	25/45
Prescriber		Not asked
Yes	21 (48)	
No	23 (52)	
Lead or oversight of AMS team		Not asked
Yes	25 (57)	
No	19 (43)	
Occupation		
Academic	1 (2.3)	4 (16)
Epidemiologist	1 (2.3)	1 (4)
Veterinarian and academic	1 (2.3)	6 (24)
Veterinarian and microbiologist	3 (6.8)	-
Veterinarian	23 (52)	8 (32)
Veterinarian and consultant	1 (2.3)	-

Physician/surgeon	2 (4.5)	-
Physician/surgeon and microbiologist	1 (2.3)	1 (4)
Pharmacist	2 (4.5)	1 (4)
Medical or veterinary microbiologist	5 (11)	2 (8)
Government employee	1 (2.3)	1 (4)
Employed in industry/pharmaceutical sector	3 (6.8)	-
Other	-	1 (4)
Species worked with predominantly (for veterinarians only)		Not asked
Dog and cats	8 (18)	
Horses	2 (4.5)	
Dogs, cats, horses	2 (4.5)	
Dogs, cats, horses, exotics	1 (2.3)	
Dairy cattle	4 (9.1)	
Poultry	2 (4.5)	
Pigs	2 (4.5)	
Sheep	1 (2.3)	
Other	1 (2.3)	
All Species	7 (16)	
None	14 (32)	
Area of Expertise*		Not asked
Infectious diseases	27 (61)	
Microbiology	19 (43)	
Antimicrobial stewardship	32 (73)	
Antimicrobial resistance	26 (59)	
Infection prevention and control	19 (43)	
Medicine	13 (30)	
Dermatology	1 (2.3)	
Surgery	3 (6.8)	
General practice	8 (18)	
Epidemiology	2 (4.5)	
Zoonoses, food safety	1 (2.3)	
Regulation of veterinary medicines	2 (4.5)	

Years working in antimicrobial stewardship or antimicrobial resistance		Not asked
< 5	6 (14)	
5-10	16 (36)	
11-19	8 (18)	
>20	14 (32)	
Country		
Australia	27 (61)	14 (58)
Brazil	1 (2.3)	-
Canada	3 (6.8)	1 (4.2)
Denmark	1 (2.3)	1 (4.2)
Netherlands	1 (2.3)	1 (4.2)
New Zealand	1 (2.3)	1 (4.2)
Sweden	1 (2.3)	-
United Kingdom	5 (11)	3 (13)
United States	4 (9.1)	3 (13)
Not answered	-	1 (4.2)

NB: Participant characteristic data was not collected in round 2 to minimise survey length

In Round 1, most participants (n=28, 64%) indicated they used a country-specific antimicrobial importance rating system in their practice. This correlated with responses to a subsequent question, which asked participants for their view about which rating systems veterinarians *should* use, with 73% (32/44) of respondents selecting country-specific ratings. However, the reasoning behind these responses suggested there were varying levels of understanding and definitions used for rating systems, guidelines and practice-specific antimicrobial use policies. Therefore, participants in Round 2 were provided with a flow chart (Figure 1) to more clearly define these terms and how they related to each other. This resulted in consensus in Round 2, where 96% of respondents (n=23) agreed '*The country-specific rating system should take precedence over any other rating system (e.g. WHO rating system) when veterinarians make decisions about antimicrobial prescribing choices*'. There was also consensus (n=20, 83% agreement) that '*Veterinarians should be able to create local practice-specific antimicrobial use protocols, but should not be able to create their own practice-specific antimicrobial importance rating systems*'. This consensus item was important as it removed the capacity for veterinarians to justify inappropriate use based on a less robust importance rating system.

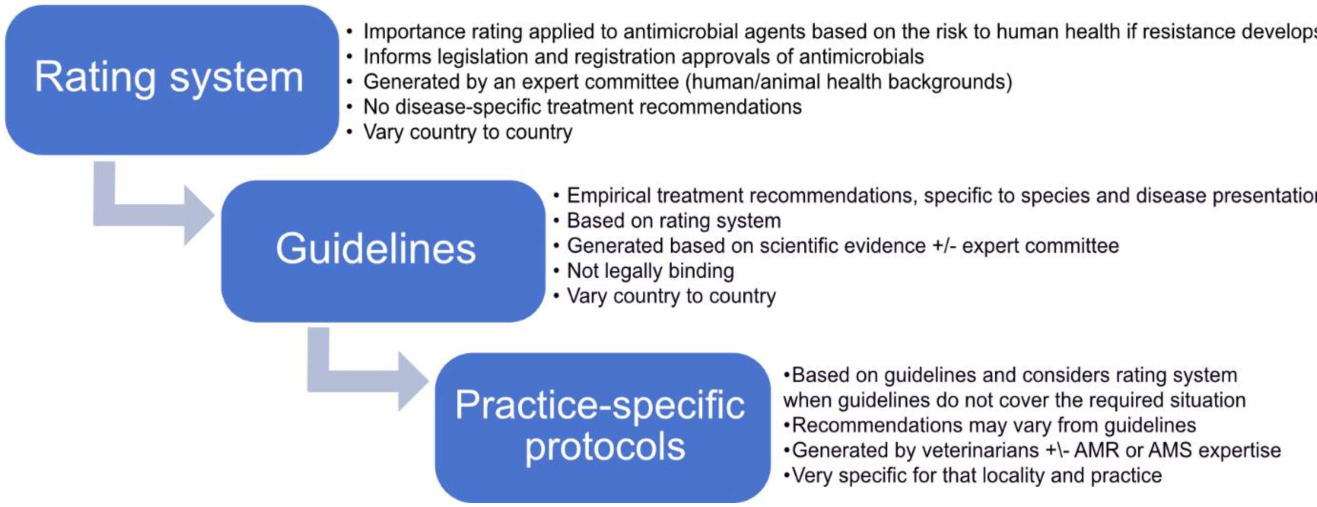

Figure 1. Definitions provided to participants in Delphi survey Round 2.

Restricting antimicrobial use can reduce selection for antimicrobial resistance [118]. While education is an essential part of any AMS plan, controlling antimicrobial use in human and animal populations through restrictions or system-level interventions may have more impact than raising public or practitioner awareness [231]. The low levels of resistance to fluoroquinolones in Australia, which is associated with a long history of prohibiting the use of this class of antimicrobials in food-producing animals, seems to support the beneficial effect of restricting antimicrobial use [36].

Participants were asked to identify antimicrobials to which they thought restrictions on use should apply. Seven possible options were provided: all antimicrobials, all antimicrobials with a medium- or high-importance rating, all antimicrobials with a high importance rating, all antimicrobials with a high-importance rating except for third generation cephalosporins and fluoroquinolones, all antimicrobials with a high-importance rating except for fluoroquinolones, all antimicrobials with a high-importance rating except for third generation cephalosporins, or no antimicrobials should be restricted. There were diverse views on this topic. A higher proportion of people selected 'All antimicrobials with a high-importance rating" in the second round (n=17, 71%) after viewing the results of Round 1 (n=21, 48%). Less popular options were also removed for Round 2, but consensus could still not be reached.In Round 1, participants were asked how strongly they agreed or disagreed with a range of possible restrictions. In Round 2 only the most popular restriction conditions were retained, and response options provided were limited to agree or disagree (Figure 2).

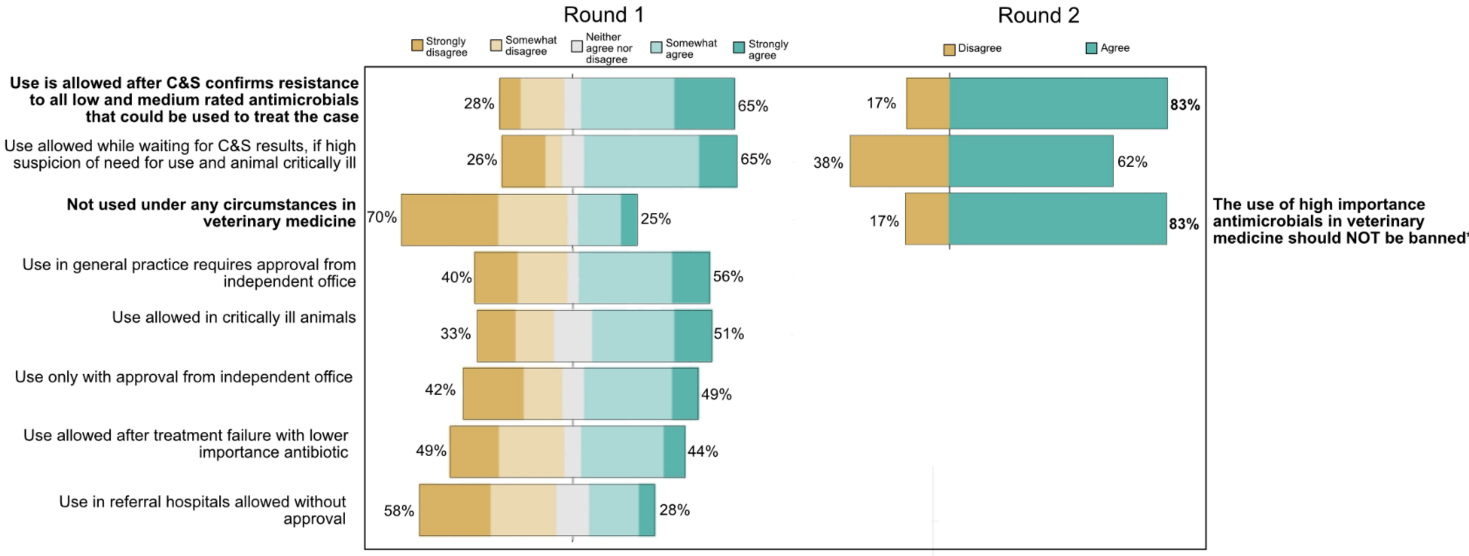

Figure 2. Participants' responses to the question 'If there were restrictions placed on veterinary prescribing of high-importance antimicrobials, which of the following do you think is appropriate? Consensus was reached on the items in bold. The item marked with an asterisk was adapted for Round 2.

Agreement was reached that, "*Use of high importance antimicrobials is allowed after culture and susceptibility testing confirms that the pathogen is resistant to all low- and medium-rated antimicrobials that could be used to treat the case*" (n=20, 83%). This option also consistently received high levels of support in a previous survey of Australian veterinarians, but concerns around costs and timeliness of results were raised [229]. A participant in our study also mentioned the "*widespread confusion with regards to how to interpret susceptibility data and what it really means*" and that this could be leading to incorrect prescribing decisions. This suggests further research, as well as educational, policy and financial support, is required to address concerns related to the costs of culture and susceptibility testing, its accessibility and the waiting times for results, particularly for regional and remote areas, and to ensure the correct prescribing actions are taken by veterinarians on receiving culture and susceptibility testing results [229, 232, 233].

While there was support for the option to allow use of high importance antimicrobials for critically ill patients (Figure 2), the practicalities of defining the subjective terms 'critically ill' and 'high suspicion of need' and reaching consensus within the limitations of the remaining survey round, led to deletion of this option from round 3. It is important to note that welfare concerns were raised by a number of participants, particularly for critically ill patients (see comments 2a and 2b in Appendix III), consistent with previous research findings [229, 231]. The appropriate approach in this scenario will need to be explored further during any implementation of these consensus stewardship measures to ensure there are no unintended consequences [11].

Participants were asked whether antimicrobials with high importance in human medicine that are registered for use in veterinary medicine (such as third generation cephalosporins and fluoroquinolones) should be treated differently to those only registered for use in humans. The majority of participants answered 'yes' (n=26, 59%) with 14% (n=6) 'unsure' and 27% (n=12) answering 'no'. The results and free text comments led to a refined statement, which achieved consensus (n=20, 83%), *"Any use of high importance antimicrobials that are not registered for use in animals, e.g. vancomycin, amikacin or imipenem, must be reported to a central authority."* Surveillance of and understanding about the use of high importance antimicrobials not registered for use in animals is lacking. This makes assessing the quality of this prescribing difficult and also leads to gaps in our knowledge. In their reasoning for supporting this restriction condition, a number of participants highlighted the value of reporting use, including for educational purposes, identifying gaps for future research, and making prescribers more accountable (see example quotes 4a, 4b, 4c, 4d and 4e in Appendix III).

Consensus was not established about which central authority should receive these reports. Based on the free text responses from the previous round, explanatory text was provided to participants (see Supplementary materials). An option to report to a "*newly created independent federal body to address antimicrobial resistance using a One Health framework (e.g. Centre for Disease Control type of organisation or a One Health central authority)*" was provided in the subsequent survey round and was the most popular option. However, this option was still only selected by 36% (n=5) of respondents, followed by the State Department of Health (21%, n=3) and the State Department of Agriculture (21%, n=3). There was little support for reporting to the office of the Chief Veterinary Officer (OCVO) (14%, n=2), the Australian Strategic and Technical Advisory Group (ASTAG) on AMR (0%, n=0), or the Australian Pesticides and Veterinary Medicines Authority (0%, n=0).

There was no consensus about who should provide independent approval to use a restricted antimicrobial, but the greatest support was for a practice stewardship champion (43%) or a veterinary microbiologist (41%). Participants stated that whoever provided approval for use would need to be objective and independent, have a broad range of knowledge and skills (including, but not limited to, microbiology, pathophysiology, public health, and AMS), and potentially this approval would be best sought from a team of experts (see quotes 3a, 3b, 3c and 3d in Appendix III).

There was consensus that clarified details about reporting and medical records. Previous research has found veterinary medical records are often insufficiently complete to make a judgement about the quality of prescribing and that this is an area that could be improved [78]. For example, medical records frequently lack information about the duration of antimicrobial use, the dose rate prescribed, and the indication for use [49, 221, 234].

Reducing the use of high-importance antimicrobials in both companion animals and food-producing animals was important or very important to most participants (88% and 92%, respectively; Table 2). The need to reduce antimicrobial use has received less focus in companion animal medicine than in food-producing animal medicine, in both research and regulation, but it is an emerging area of concern. Many people are very close with their companion animals and the risk of transfer of resistant bacteria or antimicrobial resistance genes from animals to humans, or *vice versa*, has been identified [115, 153]. Currently in Australia there are fewer restrictions on the use of high-importance antimicrobials in companion animals, including horses. As a result, use of high-importance antimicrobials in these species is much more common than in food-producing animals [50, 78, 173, 234].

Several participants indicated they would have preferred to answer some questions differently for companion animals and food-producing animals. While there are differences between these differing animal populations in the risks associated with the development of antimicrobial resistance, we decided not to differentiate between them in most questions about use in domestic animals, given the increasing emergence of antimicrobial resistance in companion animals in Australia [150]. Continually focusing only on the role of food-producing animals in disseminating or amplifying AMR may delay and detract from antimicrobial stewardship practices in the companion animal health sector because use in this sector is perceived to be a less important driver of AMR.

Table 2. Importance of reducing high-importance antimicrobial use

Question	**Responses (%)**				
	Very Important	Important	Moderately Important	Slightly Important	Not Important
How important do you think it is to reduce high-importance antimicrobial use in companion animals?	15 (60)	7 (28)	3 (12)	0 (0)	0 (0)
How important do you think it is to reduce high-importance antimicrobial use in food-producing animals?	18 (72)	5 (20)	2 (8)	0 (0)	0 (0)

Consensus Statements

In total, consensus was reached amongst participants on eight items relating to rating systems and the use of high importance antimicrobials.

1. Reducing the use of high-importance antimicrobials in companion animals and food-producing animals is important.
2. The country-specific rating system should take precedence over any other rating system (e.g. WHO-rating system) when veterinarians make decisions about antimicrobial prescribing choices.
3. When using international prescribing guidelines, these should be adapted to account for the country-specific rating system. e.g. International Society for

Companion Animal Infectious Diseases (ISCAID), British Equine Veterinary Association (BEVA).

4. Veterinarians should be able to create local practice-specific antimicrobial use protocols but should not be able to create their own practice-specific antimicrobial importance rating systems.
5. Use of high-importance antimicrobials is allowed after culture and susceptibility testing confirms the pathogen is resistant to all low- and medium-rated antimicrobials that could be used to treat the case.
6. The use of high-importance antimicrobials in veterinary medicine should NOT be banned.
7. Any use of high-importance antimicrobials not registered for use in animals must be reported to a central authority. Examples include vancomycin, amikacin or imipenem.
    a. The purpose of the reporting should be for record keeping over time for surveillance of antimicrobial use and for auditing or investigating high or frequent users to assist users in finding ways to reduce unnecessary use (non-punitive).
    b. The species the antimicrobial has been prescribed for should be reported along with any other justification, such as supporting diagnostic tests, the reasons other lower importance antimicrobials could not be used, and whether culture and susceptibility testing has been used previously to support the use of the high-importance antimicrobial.
8. If any high-importance antimicrobials are prescribed for animals, a clear indication for use and justification for antimicrobial choice must be recorded in the medical history, along with the dose rate, route of administration, the duration and the time point for review of the condition and associated antimicrobial therapy.

Participants in this study were provided with the opportunity to include free-text comments to explain their reasoning. The option for participants to provide this clarification counteracted some of the concerns that can arise with the Delphi process, such as insufficient opportunity to explore participants' underlying assumptions [235]. In our case, the ability to identify areas of concern facilitated the provision of further information on numerous occasions, ultimately leading to development of consensus.

Some of the free text comments demonstrated a lack of knowledge about how rating systems are determined and developed, even among experts. There is a need for more education about the process for generating rating systems to facilitate compliance, as, even among experts, levels of understanding differed (see free text comments 1a, 1b, 1c, and 1d in Appendix III). Some current divergence within or between professions and sectors may result from varying levels of comprehension, misunderstandings, and different definitions, rather than from completely contrasting viewpoints. On a small number of occasions, participant's responses to the survey question contradicted the reasoning provided in the free text comments. In these cases, the capacity for in-person clarification and discussion would have been beneficial.

This study builds on the results of a previous study of Australian veterinarians [229] that showed veterinarians mostly agreed with restrictions on the use of high importance antimicrobials in animals, particularly on the need for evidence of AMR from culture and susceptibility testing for use of high-importance antimicrobials to be considered reasonable [229]. The situation in Australia is markedly different from countries where antimicrobials are widely available without a prescription [34]. While veterinarians, like medical doctors, are wary of too much involvement, particularly of bureaucrats and non-veterinarians, in their practice and decision-making [96], a balance needs to be found between restricting use for future benefit and enabling the timely and effective treatment of animals when they need it [118].

The rates of participation of human health professionals in this study were lower than that of veterinarians. While it is not possible to determine whether there was less interest in a One Health approach among human health experts, participation may have been impacted by the requirement for human health experts at that time to focus on the COVID-19 pandemic response. Other research has shown a decrease in focus on AMS during the COVID-19 pandemic [32].

The reasonable response rate over multiple rounds, as well as the robust reasoning provided by participants in free-text comments, strengthened the validity of the consensus items developed throughout this process. The use of anonymity, which ensured that dominant individual viewpoints did not overshadow group consensus, as well as the engagement of experts with extensive histories working in the field of antimicrobial stewardship supports the validity of our results.

Conclusions

The use of the Delphi process proved effective in seeking consensus about appropriate restrictions on use of antimicrobials in animal health, despite the additional pressures on participants during the COVID-19 pandemic and was enhanced by the inclusion of experts with a wide range of skills and expertise from geographically diverse areas. Consensus on numerous key indicators suggests paths forward to advance antimicrobial stewardship in animal health in Australia. This study provides veterinarians clear guidance in their daily practice about deciding whether a current clinical situation warrants the use of a high-importance antimicrobial. There was clear agreement about the need to justify, record and report any use of high-importance antimicrobials. Suggestions directly relevant to policy development have been made and will require input from both the public and private sectors. It is hoped these consensus items, identified through a robust process involving a variety of international and national experts will be helpful for practicing veterinarians and policymakers alike in management of antimicrobials as a shared resource.

Chapter 4 Antimicrobial resistance of canine staphylococci isolates from a remote First Nations community: Is this an emerging One Health issue?

Anna E. Sri[1,2], Kirsten E Bailey[1,2], Amy Hii[1,2], Joan Malku Dhamarrandji[3], James Bayung Garrawitja[3], Joanne L. Allen [1], Rhys N. Bushell [1], Marc S. Marenda[1], James R Gilkerson[1,2], Glenn F Browning[1,2], Laura Y Hardefeldt[1,2].

[1] Asia-Pacific Centre for Animal Health, Melbourne Veterinary School, Faculty of Science, University of Melbourne, Parkville, VIC 3010, Australia

[2] National Centre for Antimicrobial Stewardship, Department of Infectious Diseases Melbourne Medical School and Melbourne Veterinary School, University of Melbourne VIC 3010, Australia

[3] Yalu Aboriginal Corporation

* Correspondence: a.sri@unimelb.edu.au

Abstract

Little is known about the ecology and resistance profiles of staphylococci on dogs in remote First Nations communities, nor how this might differ compared to isolates from other environments, people or animals. To investigate the prevalence, species diversity and rates of antimicrobial resistance of isolates of staphylococci in a dog population from a remote First Nations community in the Northern Territory, Australia, eighty-three dogs were sampled over two sampling periods in 2021 and 2022, using a house-to-house sampling methodology, rather than only sampling dogs that are presented for veterinary attention.

Methicillin-resistant *Staphylococcus pseudintermedius* was not detected in samples collected from this population of dogs, neither was methicillin-resistant *Staphylococcus aureus*. Nine species of staphylococci were identified, in addition to the recently reclassified Gram positive species *Mammaliicoccus sciuri*. Overall, the prevalence of resistance to antimicrobials, commonly used in dogs, with the exception of penicillin, were low compared to those seen in studies conducted elsewhere. The prevalence of resistance in coagulase negative staphylococci, and the higher minimum inhibitory concentrations detected in *M. sciuri,* highlight the potential for transfer of resistance between these organisms and more common pathogenic species such as *S. pseudintermedius* and *S. aureus*.

In the absence of more specific data, such as antibiograms or culture and susceptibility results, it should be appropriate to follow current antimicrobial prescribing guidelines when treating suspected staphylococcal infections in dogs in this community. To maintain the current low levels of resistance in staphylococci in this canine population, antimicrobial stewardship measures should extend beyond a focus on the behaviours of community members and veterinarians such as hand-washing, aseptic technique, and

antimicrobial selection, to acknowledge and address upstream influencing factors such as access to diagnostic tests, over-crowding, funding and workforce challenges.

Introduction

Resistance to antimicrobials in staphylococci is an emerging area of concern in companion animals, particularly in the coagulase positive staphylococci (CoPS), *Staphylococcus pseudintermedius* and *Staphylococcus aureus* [226, 236, 237]. Coagulase-negative staphylococci (CoNS) have also been recognised as potential pathogens, rather than just normal flora [238, 239], of humans and animals, and their role as a reservoir of transferable genetic resistance elements is also concerning [240-243].

Currently, staphylococcal isolates from Australian companion animals have been found to have markedly lower frequency of resistance than has been reported in isolates from companion animals in other countries [68, 76, 242]. However, active and passive surveillance for resistance in companion animals has been limited in Australia [14, 150]. The lack of long-term surveillance of antimicrobial use (AMU) and resistance, despite being identified as a 'national priority' [7, 72], impedes our ability to target antimicrobial stewardship (AMS) interventions and further extends the gap in knowledge around the ecology of antimicrobial resistance (AMR) in Australian animals and people. These difficulties are further compounded by the low rates of antimicrobial culture and susceptibility testing rates in animal health [49, 68, 83]. Sampling methods that only identify isolates resistant to specific antimicrobials of importance to human health, such as methicillin, by use of selective media, do not provide a true representation of the susceptibility of microbial populations to commonly used antimicrobials and may fail to detect species diversity within the bacterial population.

Australia has a national antimicrobial importance rating system [8] and there are Australian-specific veterinary antimicrobial prescribing guidelines for numerous conditions affecting companion animals, including wounds, abscesses, and bacterial dermatitis [18]. However, these guidelines were developed based on information available from cities and regional areas, rather than those in remote areas. Veterinarians practicing in remote Indigenous communities face additional challenges when attempting to diagnose and treat bacterial infections in animals. These include lack of access to in-house diagnostics, such as cytology and haematology, as well as extremely limited access to laboratory services to perform bacterial culture and susceptibility testing [144]. Many remote communities may also only have access to veterinary services intermittently for short periods of time, which does not allow regular follow-up of cases nor ongoing treatment with close supervision from a veterinarian, as would be considered the usual standard of care in most regional or urban areas of Australia [144, 145].

This study aimed to progress knowledge about the antimicrobial resistance profiles of staphylococci isolated from dogs in a remote Indigenous community and provide a basis for future initiatives to prevent AMR and evaluate AMS initiatives. The baseline data produced could then be used to evaluate the feasibility of sampling from dogs in the community to act as sentinels of emerging AMR issues amongst the canine population, without the reliance on culture and susceptibility data derived from passive surveillance in this and other similar populations. Only two studies have been reported relating to AMR from canine bacterial isolates in remote communities across Australia, one in regional New South Wales and one in the Kimberley region of Western Australia [151, 152, 244]. This is the first study of its kind conducted in the Northern Territory, and employed a house-to-house sampling methodology and a quantitative method to assess antimicrobial susceptibility.

Methods

Sample Population and Context

Dogs were recruited to the study population from a community located on an island in a tropical region of the Northern Territory, Australia. All sampling was undertaken during the dry season. The dog population in the community at the time of sampling was estimated to be around 550-700 dogs, based on local council reports and the numbers of dogs identified during the sampling process. There is significant annual variation in the population of dogs as new puppies are born and dogs die from infectious disease or because of accidents, in addition to the expected attrition attributable to age-related illnesses. Information about dog breed was collected through observation by the researchers. Owners were asked if their dog had received antimicrobials in the last six months and also about their desexing status.

There was no permanent veterinary clinic in this community, and veterinary services were provided on 3-4 occasions per year for periods of a few days to a few weeks. Veterinary and animal care services in the community have been intermittent since 1977, and have varied in the level of service provision and training of the participants involved [168]. The majority of veterinary services in this community were focused on population control (desexing and euthanasia), as well as treatment and prevention of parasites. Anecdotally, administration of antimicrobials to dogs in the community may have increased over the last four years as a result of the detection and treatment of ehrlichiosis in dogs in the community, after this pathogen was first detected in Australia in mid-2020 [245]. However in the absence of a formal method of collecting and monitoring AMU in this community there is no data to support this assertion.

Sample process

Sampling was undertaken on two separate occasions during the dry season, in June 2021 and August 2022. The researchers visited each house in the community and made contact wherever people were at home. Householders were asked to provide consent to sampling of their dog/s. Samples were collected from each animal using separate sterile plain cotton swabs (Cutiplast LP Italiana and Copan Interpath services) moistened just prior to sampling with 0.9% saline. Samples were taken from the oral mucosa, skin of the perineum and from any skin lesions or wounds present (if the dog tolerated the sampling).

Samples from the oral mucosa were well-tolerated, and the majority of dogs did not require any physical restraint as they were guided with treats. Perineal samples were more commonly taken from small dogs and puppies that were used to being held by their owners. Samples were collected and kept in a cooler box, prior to being stored at 4°C until the end of the sampling trip. At the end of the trip, samples were transported in a cooler box with ice packs, from the community to the laboratory, which took up to twenty hours. As far as possible, no re-sampling of dogs was undertaken. This was confirmed by checking with the owners if their dog/s had been involved in the study, checking their name and description against previously sampled dogs, the lot number (address) sampled from and in some cases, scanning their microchip. Microchip scanning was rarely performed as it was identified this was adverse and made some dogs fearful.

Bacterial isolation

Each swab was inoculated onto sheep blood agar (SBA) plate (Thermofisher Scientific) and a mannitol salt agar (MSA) plate (Micromedia), and the plates were then incubated overnight at 37°C. The swabs were then placed in 3 ml of a 6.5% sodium chloride enrichment broth (Oxoid brain heart infusion broth in 2021 and heart infusion broth in 2022) in 5 ml yellow topped sample tubes. The inoculated enrichment broths were incubated at 37°C overnight. The enrichment broth was then used to inoculate sheep blood agar and mannitol salt agar plates, which were incubated overnight at 37°C.

Up to 3 colonies were selected from each MSA plate based on morphological appearance (discrete, opaque colonies, 1-3mm diameter, white-yellow colour) and sub-cultured onto SBA plates. All colonies from the SBA plates with a gross morphology consistent with that of staphylococci were Gram stained and those that were Gram positive cocci and catalase test positive were sub-cultured onto another SBA plate. All suspected staphylococcal isolates were then stored in LB broth containing 20% glycerol. The tube coagulase test and API (analytical profile index) Staph 32 kits (Biomerieux) were used to identify isolates to the species level. Antimicrobial susceptibility testing was performed on isolates confirmed to be *Staphylococcus* species, following the Clinical & Laboratory Standards Institute (CLSI) broth microdilution method, using Sensititre companion animal plates (Thermo Fischer Scientific). Plates were read at 18 and 24 hours using the Sensititre ARIS system for incubation and plate reading.

Results

Eighty-three dogs were sampled (27 in July 2021 and 56 in August 2022). None of the dogs sampled had received antimicrobials in the previous six months, according to their owners. Two of the dogs sampled were desexed the same day that they were sampled and received antimicrobials after sampling, consistent with the treating veterinarian’s protocols. The dogs sampled were mostly mixed breed dogs with an indoor and outdoor lifestyle. Eight dogs sampled were from single dog households. The remaining dogs were from multi-dog households. The majority of dogs were kept as companion animals and seen as family members. Some were used for hunting and to provide security.

A total of 73 staphylococcal isolates were obtained from 43 of the 83 dogs recruited to the study population. Isolates were from the oral cavity, perineum and wound samples (Table 1). Nine staphylococcal species were identified among these isolates (Table 2), as well as the recently reclassified species *Mammaliicoccus sciuri*. One isolate was not identifiable to species level (possibly *S. simulans*). Methicillin-resistance was not detected in any of the twenty-three *S. pseudintermedius* isolates, 95% CI [0.000, 0.143]) or three *S. aureus* isolates 95%, CI [0.000, 0.561]. In five instances more than one staphylococcal species was isolated from the same swab, in four cases this was a CoNS and a CoPS. In one dog *S. hominis subspecies hominis* was isolated from the perineal swab, and *S. pseudintermedius* and *S. warneri* were isolated from the oral swab.

Of the twenty-three *S. pseudintermedius* isolates, only thirteen (57%, 95% CI [34, 76]) were susceptible to penicillin, while more than ninety percent were susceptible to all the other antimicrobials tested (Table 3). A greater proportion of CoNS were susceptible to penicillin (86%, 95% CI [65-97]), but more of these were resistant to cephalosporins (Table 4). The MICs for the M. sciuri isolates were generally higher than those seen for *S. pseudintermedius*, *S. aureus* or other CoNS *Staphylococcus spp*. (Table 5). The proportions of *M. sciuri* susceptible to each antimicrobial cannot be determined without specific breakpoints, which currently are not available for canine *M. sciuri* isolates. A multi-drug resistant *S. pseudintermedius*, resistant to penicillin, trimethoprim/sulphadiazine, tetracyclines and erythromycin, but susceptible to ampicillin, was isolated from one of the wound samples. It was not resistant to any high importance antimicrobials.

Discussion

Antimicrobial resistance in canine staphylococci did not appear to be an emerging One Health issue in this community. The absence of methicillin-resistant *S. pseudintermedius* (MRSP) suggested that there has not been high levels of antimicrobial use or exposure to antimicrobials in the dog population. In general, susceptibility to low importance-rated antimicrobials was high, particularly for CoPS. The prevalence of susceptibility to penicillin amongst the *S. pseudintermedius* isolates obtained in this study was higher than amongst staphylococci isolated from a population of healthy dogs in Victoria (57% compared to 28%) [246]. The only multi-drug resistant *S. pseudintermedius* was isolated from a skin wound in an entire female dog with severe pyoderma. Contributing factors in this animal could have included previous treatment with antimicrobials (although this was not recalled by the owners), persistent infection due to immunosuppression from underlying disease, such as scabies or ehrlichiosis, or pregnancy, introduction by another animal, veterinarian or community member. A chronic infection may also provide the conditions for transfer of resistance elements from other bacterial species, including CoNS.

This study has provided information about the baseline rates of resistance in staphylococci in this population of dogs, in contrast to studies that have evaluated resistance rates of only clinical isolates in other dog populations. It appeared that, despite close contact between people and their dogs in this community, resistant staphylococci have not been transferred readily between healthy animals and people. Other studies in Australia have detected higher rates of resistance amongst isolates from clinical cases [68, 247, 248]. Whether transfer of genetic elements from CoNS occurs, particularly in polymicrobial infections, requires further investigation. Evaluating culture and susceptibility data from a greater number of wounds or severe pyoderma cases could increase understanding about resistance patterns in bacteria isolated from clinical cases compared to these isolates of commensal staphylococci, which had low rates of resistance.

While this study has helped in gaining an understanding of the risk of AMR to human and animal health in this community, in the future, a focus on the health outcomes of the dogs, and appropriate treatment of sick or injured animals, as well as management of healthy dogs is likely to be more cost effective than continued population level active surveillance for AMR amongst healthy dogs. As resistance takes time to develop, robust monitoring of antimicrobial use (AMU) in this animal population in the future could provide a more feasible approach to AMS in this community.

Currently there is a lack of robust AMU data from animal treatment in remote communities and about the appropriateness of AMU (consistent with the lack of regular monitoring of AMU more generally across Australian animal populations). This prevents early action being taken to address this key driver of AMR. Improving capacity for culture and susceptibility testing when encountering animals with suspected bacterial infections would provide better understanding of resistance issues than further sampling of healthy animals and would enable more appropriate and targeted AMU. There may be a significant difference between the resistance profiles of staphylococci isolated from healthy animals and those isolated from clinical cases, particularly in this remote community. Currently we do not have sufficient data to understand whether this is the case, and if it is, why, particularly in an environment with assumed low exposure to antimicrobials amongst animals.

The absence of MRSP in this population was consistent with the results of a comparable study conducted in NSW. The authors of this study hypothesized that this was attributable to low rates of antimicrobial use, as was the case in the dog population in our study [151]. MRSA was not detected in this study and only three dogs carried *S. aureus*, all of which were methicillin-susceptible (MSSA) (3.6%, 95% CI [0.439, 1.000)]. In contrast, other similar studies have reported MRSA carriage rates of 2.6% [151, 152] and MSSA carriage rates of 4.4% [151]. Given that 83 dogs, approximately 10-15% of the community dog population, were sampled in our study, it is likely that, if MRSP or MRSA is present in this population, the detectable prevalence is likely to be less than 4.4% of *S. pseudintermedius* isolates (95% CI 0.00-0.040) and less than 56% of *S. aureus* isolates (95% CI 0.00-0.56).

Further testing, including whole genome sequencing, to examine the *M. sciuri* isolates for the presence of the *mecA* methicillin-resistance gene, as well as other resistance genes, is needed to understand the role of this organism in the ecology of AMR in canine staphylococci. There are also no specific breakpoints available for *M. sciuri*, and it is only rarely associated with clinical disease. Examination of the isolates for genetic determinants of chloramphenicol and fluoroquinolone resistance would also be beneficial, given recent changes in the veterinary breakpoints for susceptibility to chloramphenicol, enrofloxacin, marbofloxacin and pradofloxacin, which have made evaluation of AMR using current commercially available broth microdilution plates difficult.

The mouth was chosen as a primary sampling site because previous studies have found that it was the most reliable site for isolation of staphylococci from dogs [115]. It was simple to take oral swabs from the dogs without restraint using positive reinforcement in the form of treats. This was preferable, as most of the dogs were not used to being restrained. The rate of isolation appeared low compared to some studies [115, 151, 249], but similar to others [250], with staphylococci isolated from 52% (n=43) of dogs, and *S. pseudintermedius* from 13% of dogs (95% CI 0.08-0.22). It is possible that this underrepresents the true prevalence because the difficult logistics of transporting samples to the laboratory may have reduced viability of the staphylococci on the swabs. However, it is evident samples can be collected in this remote setting and still yield results. Veterinarians working in remote settings should not be concerned about taking samples for culture and susceptibility testing provided that samples are packaged appropriately to ensure maintenance of low temperatures [251, 252] and there is good communication with the receiving laboratory. In-house diagnostic tests, such as cytology, may also help improve the appropriateness of antimicrobial prescribing, and can be performed even in remote settings. Cytology may currently be underutilized by veterinarians in remote settings because of time pressures and limited financial resources [253].

Knowledge of the total population size from which samples are being collected would allow more accurate predictions of resistance levels across the animal population. This was the only study that utilised a house to house sampling methodology. Given that this dog population is also geographically isolated on an island, and dogs do not regularly travel off the island and interact with other dog populations or have easy access to receive antimicrobials from private veterinary practices may also have influenced the low resistance rates.

A One Health approach encourages focusing on the underlying drivers of AMU, instead of using antimicrobials as, “quick fixes for productivity, hygiene, and inequality” [254]. This approach is also exemplified in Indigenist Health Humanities research, which contrasts medical responses to health conditions with approaches that modify the circumstances through which health is created, and acknowledges that health is relational rather than dichotomous [106]. Both approaches encourage thinking about the social and cultural factors that produce health conditions such as AMR [106]. Companion animals can be seen as part of wider societal structures and networks. For example, dogs may be more likely to sustain wounds if insufficient housing is available to enable people to keep their dogs safely inside or contained at night. It is also important to acknowledge differences in factors that may contribute to AMR in other urban settings that were not present in this community, such as dog breeds with a predilection for skin fold pyodermas and recurrent skin infections [255]. All dogs sampled in this study were well-suited to the tropical environment, as they were largely doliocephalic or mesocephalic mixed breeds with short or medium coats

The integration of traditional disease and AMR surveillance data, such as those collected in this study, with other data, such as those relating to housing or sanitation infrastructure, as recommended by Wozniak et al. [167], could be further enhanced by qualitative research and community-led approaches. These approaches may be more likely to highlight broader drivers and systemic issues that are overlooked as barriers to AMS and that may influence current rates of AMU and AMR. They also provide opportunity to give voice to aims that are relevant on a local level. Some upstream drivers of AMR may be external to communities, such as systemic racism, inadequate or biased service provision and inadequate funding allocation by government, but ultimately these have a local impact [10, 106, 256]. In conducting this research, a tendency by some human health organisations and research institutions to see AMR impacting humans and animals as different and separate problems was a barrier to wider engagement and use of more holistic research methodologies.

Limitations

Several limitations in this study related to practical aspects of sample collection such as the inability to take more swabs from the dogs due to temperament and time constraints. Initially there was a target to take multiple oral swabs from each dog to increase the likelihood of bacterial isolation, however this was abandoned due to the increased time this added to the collection process and the impact this had on the dogs' compliance with the procedure. Similarly, it was not possible to take perineal swabs from most adult dogs without restraint yet restraining them was deemed to be an unnecessary risk to handlers and unnecessarily stressful to the dogs. Similarly, the inability to reliably scan the dogs for a microchip prevented accurate identification of the dogs. More accurate identification would have confirmed that re-sampling did not occur or at least would have allowed better monitoring for re-sampling events. It also may have allowed some correlation of potential antimicrobial usage with veterinary records, although it was noted at the time of sampling that veterinary records for some dogs sampled were months to years out of date or there were no records available.

There was variable time between collection of the samples and bacterial isolation at the laboratory. Although isolation rates did not appear to vary significantly between enriched and non-enriched samples, consistent recording of the time of sample collection and subsequent isolation of bacteria may have enabled understanding of the length of time that a sample can remain viable for subsequent bacterial isolation at refrigeration temperatures.

The lack of wound samples prevented understanding of resistance patterns from these clinical cases. Similarly the low isolation rates of *S. aureus* meant that the prevalence could not be determined to a high degree of accuracy.

Conclusion

This study has increased understanding about the dynamic and diverse nature of carriage and colonisation with staphylococci in a canine population in a remote Indigenous community and highlighted how much is unknown about the ecology of staphylococci in a One Health sense. A high level of susceptibility was detected to antimicrobials with a low-importance [8] rating . The establishment of additional canine-specific antimicrobial breakpoints in future will allow more accurate evaluation and comparison of resistance patterns. The successful use of this study's methodology may increase the confidence of veterinarians to undertake sampling for culture and susceptibility testing in future or undertake similar smaller trials involving clinical cases. Reference to current antimicrobial prescribing guidelines for empirical treatment is also recommended, given the low levels of resistance detected in staphylococcal isolates in this dog population. This study was carried out with the understanding that AMR is a socio-political problem, not just a health issue. To maintain current low levels of resistance in staphylococci in the canine population more research and actions may need to focus on upstream social, economic, cultural, and legal conditions the underlie health inequalities and have been shown to drive and maintain AMR [106].

Table 1: Distribution of isolates by sampling site

Site	**No. swabs**	**No. dogs from which ≥1 *Staphylococcus* species including *M. sciuri* was obtained (%)**
Oral mucosa	83	43 (55) 95% CI [0.412, 0.622]
Perineal skin	8	1 (13) 95% CI [0.022, 0.471]
Wound	2	1 (50) 95% CI [0.095, 0.905]
Total	**94**	

Table 2: Staphylococcus spp. isolated from community dogs

	Species	No. dogs	No. isolates from each site			Total
			Oral	Perineal	Wound	
Coagulase positive	*S. pseudintermedius*	11	21	0	2	23
	S. aureus	3	3	0	0	3
Coagulase negative	*S. simulans*	1	2	0	0	2
	S. warneri	1	1	0	0	1
	S. hominis subsp hominis	1	0	1	0	1
	*Mammaliicoccus sciuri**	19	23	1	0	24
	S. xylosus	12	15	0	0	15
	S. epidermidis 2	1	1	0	0	1
	S. hyicus	1	1	0	0	1
	S. saprophyticus	2	2	0	0	2
Total		**43****				**73**

*Formerly *Staphylococcus sciuri*

**Some dogs had more than one isolate

Table 3: Minimum inhibitory concentration distributions for all *S. pseudintermedius* isolates (n=23) and proportions susceptible to each antimicrobial tested

Antimicrobial	Minimum Inhibitory Concentration (µg/ml)											
	0.06	0.12	0.25	0.5	1	2	4	8	16	32	% S	95% CI
Penicillin ●	11	2	3	3		1	2	1			57	34-76
Ampicillin ●			21	1	1						91	72-99
Amoxicillin/clavulanate ▲			23								100	85-100
Oxacillin ●			23								100	85-100
Cefazolin ▲						23					100	85-100
Cephalothin ▲						23					100	85-100
Cefovecin ⬢			20	3							100	85-100
Cefpodoxime ⬢						23					100	85-100
Trimethoprim/sulphadiazine ●						22	1				96	78-99
Tetracycline ●			22		1						96	78-99
Doxycycline ●				1							96	78-99
Minocycline ●				22		1					96	78-99
Chloramphenicol[1] ●								23			-	-
Erythromycin ●			13	8			2				91	72-99
Clindamycin ▲				23							100	85-100
Gentamicin ▲							23				100	85-100
Enrofloxacin[1] ⬢			23								-	-
Marbofloxacin[1] ⬢					23						-	-
Pradofloxacin ⬢			23								100	85-100

Shaded areas indicate the ranges of MICs tested. Vertical red bars indicate the breakpoints for susceptibility. In some cases, a thin double vertical red bar indicates a breakpoint for susceptible-dose dependent, where susceptibility depends on the dosage regimen used in the patient.

[1] In some cases, the most recent guidelines, CLSI VET01S ED7:2024, include a susceptible breakpoint below the lowest concentration tested in this study because of the standardised concentration ranges on the Sensititre plates. In these cases, true levels of susceptibility cannot be confirmed.

● = low importance

▲ = medium importance

⬢ = high importance

Table 4: Minimum inhibitory concentration distributions for all coagulase negative staphylococcal isolates* (n=22)

Antimicrobial	Minimum Inhibitory Concentration (µg/ml)											
	0.06	0.12	0.25	0.5	1	2	4	8	16	32	%S	95% CI
Penicillin ●	13	6	1		1	1					86	65-97
Ampicillin ●			20		2						91	71-99
Amoxicillin/clavulanate ▲			20	2							91	71-99
Oxacillin ●			4	17	1						95	77-100
Cefazolin ▲						22					100	85-100
Cephalothin ▲						22					100	85-100
Cefovecin ⬢			2	11	5	4					59	36-79
Cefpodoxime ⬢						19	3				86	65-97
Trimethoprim/sulphadiazine ●						22					100	85-100
Tetracycline ●			22								100	85-100
Doxycycline ●		22									100	85-100
Minocycline ●				22							100	85-100
Chloramphenicol[1] ●								22			-	-
Erythromycin ●			11	8			3				86	65-97
Clindamycin ▲				22							100	85-100
Gentamicin ▲							21	1			95	77-100
Enrofloxacin[1] ⬢			18	4							-	-
Marbofloxacin[1] ⬢					22						-	-
Pradofloxacin ⬢			22								100	85-100

*Excluding *S. sciuri/Mammaliicoccus sciuri* due to the recent reclassification of the organism, and *S. epidermidis 2* due to its failure to grow in the Sensititre plate.

Shaded areas indicate the ranges of MICs tested. Vertical red bars indicate the breakpoint for susceptibility. In some cases, a thin double vertical red bar indicates a breakpoint for susceptible-dose dependent, where susceptibility depends on the dosage regimen used in the patient.

[1] In some cases, the most recent guidelines, CLSI VET01S ED7:2024, include a susceptible breakpoint below the lowest concentration tested in this study because of the standardised concentration ranges on the Sensititre plates. In these cases, true levels of susceptibility cannot be confirmed.

[2]When species specific breakpoints were unavailable, the closest possible breakpoint was used e.g. *S. pseudintermedius* for dogs from Table 2C-1; CLSI VET01S-ED7:2024

● = low importance

▲ = medium importance

⬢ = high importance

Table 5: Minimum inhibitory concentration distributions for all *Mammaliicoccus sciuri* isolates (n=24)

	Minimum Inhibitory Concentration (µg/ml)									
Antimicrobial	**0.06**	**0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**
Penicillin •	13	8	3							
Ampicillin •			24							
Amoxicillin/clavulanate ▲			24							
Oxacillin •			1	2	20	1				
Cefazolin ▲						24				
Cephalothin ▲						24				
Cefovecin ⬢		1	1	1	3	12	6			
Cefpodoxime ⬢						5	19			
Trimethoprim/sulphadiazine •						24				
Tetracycline •			24							
Doxycycline •		24								
Minocycline •				24						
Chloramphenicol •								23	1	
Erythromycin •			22	1			1			
Clindamycin ▲				14	10					
Gentamicin ▲							24			
Enrofloxacin ⬢			9	15						
Marbofloxacin ⬢					24					
Pradofloxacin ⬢			11	13						

Shaded areas indicate the ranges of MICs tested.

• = low importance

▲ = medium importance

⬢ = high importance

Chapter 5 A One Health approach to AMS in remote Indigenous communities

Abstract

A One Health approach encourages transdisciplinarity and equity when attempting to optimise the health of people, animals and the environment. It is helpful to use a One Health approach to explore issues such as antimicrobial resistance (AMR), where a traditionally medicalised focus may otherwise prevent investigation or understanding of lesser known but still relevant influences. In-depth interviews with fourteen participants (nurses, doctors, Aboriginal health workers, veterinarians and antimicrobial stewardship (AMS) pharmacists) were conducted to explore under-investigated topics of AMR and AMS in remote communities as they relate to medical and veterinary practice. We aimed to explore the relationships between factors influencing antimicrobial use and health systems, such as the social determinants of health. Staff shortages and high workload were identified as factors that influenced AMS and the capacity of prescribers to make more appropriate antimicrobial choices. Generally low antimicrobial use in remote community veterinary practice was identified, however veterinary surgical prophylaxis is an area where the quality of prescribing could be improved. Other enablers for AMS include the positive influence of local Aboriginal health practitioners and their equivalents in animal health, openness by participants to improve their practices, and evidence amongst participants of understanding or acknowledgement of upstream drivers of AMR and interest in working collaboratively across disciplines.

Introduction

The threat of antimicrobial resistance (AMR) has been well-described[1, 132]. The impact of AMR also intersects with other inequalities and social determinants of health such that AMR can be seen as a socio-political problem [257, 258]. In remote Indigenous communities in Australia, the likelihood of people contracting resistant infections such as methicillin-resistant *Staphylococcus aureus* (MRSA) or extended spectrum beta-lactamase *E. coli* (ESBL *E. coli*) can be significantly higher than in urban centres around the country [140, 148]. There is a lack of data from remote Indigenous communities on health practitioners' attitudes and practices towards AMR and antimicrobial use and the specific challenges they face when prescribing in remote settings.

This research aims to increase understanding of how antimicrobials are used in remote Indigenous communities and the broader issues influencing decisions about use in people and animals. To understand more about this complex, cross-sectoral issue, we used a One Health approach. One Health incorporates the philosophy of epistemological pluralism, to create space for principles such as social justice and equity to be highlighted, rather than a reductionist approach focusing only on technical aspects of AMR [3, 6, 106, 259, 260]. Principles of One Health are also consistent with some of the aims of Indigenist Health

Humanities and strength-based approaches [106, 261]. These approaches all encourage transdisciplinarity and inclusion of a broad range of stakeholders, increasing the likelihood that diverse perspectives and ideas will be considered. Indigenist Health Humanities highlights ways of knowing that are relational rather than hierarchical. It encourages consideration of the limitations of some knowledge systems and the need to assess the knowledge created from different perspectives [106].

Methods

In-depth semi-structured interviews with animal, human and environmental health practitioners were performed over an 11 month period from July 2023 to June 2024. Practitioners were included if they were currently working, or had worked in the past 10 years, in a remote Indigenous community. Purposive selection was used to identify participants across a wide geographic area and across different professional roles, for example, nurses, doctors, Aboriginal health workers, veterinarians and AMS pharmacists. Recruitment of participants occurred by contacting health services or other relevant organisations, and individuals known to our researchers via phone and email. Semi-structured interviews were used to obtain rich and complex data. An interview guide (Appendix IV) was created and adjusted for relevance according to the role of the participant being interviewed. Questions included, but were not limited to, those about which antimicrobials were regularly prescribed, access and overuse of antimicrobials, links between AMR in people and animals, impact of AMR on the environment or another health sector, adherence to prescriptions, and the influence of relationships on prescribing decisions. Antimicrobial use described in the interviews was recorded and grouped according to the rating system developed by the Australian Strategic and Technical Advisory Group on AMR (ASTAG). The ASTAG rating system classifies antimicrobials as low, medium, or high importance based on the severity of impact if resistance developed to that antimicrobial.

Interviews were conducted online and were recorded via Zoom video conferencing software. Interviews were transcribed by the primary researcher (AES) as part of the data generation and analysis process. Transcripts were coded inductively with a reflexive approach and analysed using thematic analysis and aspects of grounded theory. Information such as place and organisation names that could identify participants were removed from transcripts to preserve anonymity and confidentiality. This allowed participants to speak more freely. As AES had worked in remote communities as a veterinarian, this also helped participants to feel more comfortable knowing that the researcher understood some of the context to their experiences. Some participants were also previously known to AES. AES practiced reflexivity to position themselves in relation to the data generated and described how their personal experiences influenced interpretation of participant responses [262, 263].

Reflection

AES visited and had an ongoing connection to some remote Indigenous communities as a child due to her mother working as a teacher in North-East Arnhem Land for a period of over thirty years. As a teenager and adult, AES worked in education and then later veterinary roles in remote Indigenous communities in North-East Arnhem Land and the Roper Gulf region. Critically, some of this work occurred before and then during the initial years of the Northern Territory intervention during which AES witnessed increased community policing and less support for Aboriginal-controlled community governance. This, along with the consistent activism of strong community leaders, influenced her view of the importance of sovereignty, self-determination and language in maintaining resilience despite the ongoing harms of colonisation. Knowledge of One Health and AMR motivated AES to conduct this research in an attempt to understand and highlight aspects integral to AMS that may be missed by more quantitative and less holistic methods. AES wanted to focus on principles of equity and transdisciplinarity that are generally not emphasised in veterinary research. Her previous AMS research had emphasised the importance of access to diagnostic tests, which from her experience in remote communities AES knew was generally not readily available.

Results

Fourteen interviews were completed. Interviews ranged in duration from 17 to 63 minutes with a mean of thirty-five minutes. Participants included five veterinarians, two nurses, two Aboriginal health workers, three AMS pharmacists and two doctors. Most participants worked, or had previously worked, in remote communities in the Northern Territory or North Queensland. Most of the AMS pharmacists included worked externally to remote communities, but their work supported health services operating in those areas, so their perspectives were included. Data saturation occurred once numerous participants in each role had been interviewed and consistent themes were revealed within professions but also across the range of participants without the introduction of new themes.

The key themes identified from veterinarian interviews included difficulty maintaining sterile instruments and surgical conditions generally as well as lack of access to diagnostic tests due to remoteness and costs. Both animal and human health participants used prophylactic or precautionary prescribing more than they would in a non-remote context due to perceived serious consequences and lack of access to subsequent care if a complication developed or a condition worsened. Workforce issues were raised by nearly all participants including challenges such as high staff turnover, staff shortages, and lack of capacity for future planning and training. Another common theme was the importance of education. Participants mentioned education of human and animal health staff about AMR, education of patients and the wider community including school children about preventative health strategies for themselves and their animals, and also for owners about how to manage common minor conditions in their pets. The role of personal relationships also emerged from the data and interacted with other themes such as education and precautionary prescribing.

Antimicrobials used by participants in human and animal health are listed in Table 1. There was significant overlap between the antimicrobials used for both humans and animals, however no high importance-rated antimicrobials were reported to be frequently used in animal health. In both human and animal health, common reasons for antimicrobial use were skin and soft tissue infections, including wounds. Other common uses mentioned in human health were to treat respiratory infections, urinary tract infections, sexually transmitted infections, otitis externa and media, and sepsis. Veterinary participants described that most antimicrobials used in animal health were for surgical prophylaxis. Other common uses mentioned in veterinary health were to treat generally unwell animals, parvovirus, and ehrlichiosis cases.

The primary driver for antimicrobial use for surgical prophylaxis in veterinary medicine was inadequate sterilisation of surgical instruments. Veterinarians were using sterilisation methods such as boiling, baking, or using disinfectants such as chlorhexidine rather than the standard autoclave technology used in most veterinary practices in Australia. Veterinarians were using other tools to minimise the risk of surgical contamination, such as using drapes, but the lack of autoclave capacity was perceived to increase the risk of surgical site infection.

"If I could sterilise every kit before I use it, then my surgery technique would be as good if I was at home because we do… everything gets scrubbed…everything gets a drape and things get sterile swabs. It's literally just the kits that we don't have ability to cook everything." (Veterinarian, participant 9)

"It'd be nice to have the funding to put an autoclave in each community and then we wouldn't have to worry." (Veterinarian, participant 5)

However, one participant had found that prophylactic antimicrobials were generally not required for their surgeries even without autoclave sterilisation.

"I don't give any antibiotics for surgery at all... the methods that I'm using for my surgeries, I feel quite confident with infection rates and things like that… it's got to be pretty bad for me to send it with antibiotics post-op." (Veterinarian, participant 1)

Treatment of superficial wounds with topical treatment and wound flushing was also described by veterinarians, with all positive experiences including for deep wounds. This therapy is consistent with the recommendations of current Australian veterinary antimicrobial prescribing guidelines[18].

"We've got our first aid cabinets in each community which have got wound flush packs with chlorhexidine [an antiseptic and disinfectant] and antibiotics and metacam [pain

relief medication] and stuff. Then we will just hand out a wound flush pack and not hand out any antibiotics at all. So yeah, if it's a fresh wound, then we try to just treat it with chlorhex rather than adding in the antibiotic." (Veterinarian, participant 5)

Another issue faced by veterinarians was lack of access to diagnostic tests, particularly culture and susceptibility testing, due to remoteness and costs.
I've never done it to be honest because I guess then there's the thing of, ideal world you'd want to do culture and sensitivity on every single thing, for the cost, who's going to pay for that? Cause in community it's [government] and council funded money. I'm not paying for a $300 culture and sensitivity for my own interest and the council's not going to pay for that for anyone. (Veterinarian, participant 1)

"I think it would have been feasible through the local health centre, the main challenge tends to be that there's such high staff turnover that if you do establish a relationship with people working there that would allow you to throw in a sample with anything that they're sending off, maybe those people won't be there in a months' time and then you're back to square one of trying to talk them around to allowing you to do that stuff during which time an animal is harboring a potentially nasty antimicrobially resistant infection."
(Veterinarian, participant 2)

In human medicine, samples were regularly taken for culture and susceptibility and in some cases were used to change the course of antimicrobials given to that patient if resistance was detected, but these results could also be used to inform development of antibiograms and understand resistance patterns more generally. None of the participants reported that they used culture and susceptibility testing to change the antimicrobial prescribed to a lower importance rated antimicrobial if the initial empirical treatment was of higher importance.

Prophylactic prescription of antimicrobials was practiced in both human and animal health, perhaps to a greater extent due to the remote locations and perceived consequences of not treating. This also intersected with workforce issues– not being able to be present for follow up care, and clinical confidence to withhold antimicrobials.
"Definitely the first few years I was in community, I mean even just the first few years as a vet, I think you just give it some amoxyclav [amoxicillin clavulanic acid] because what if that gets infected and that owner comes in and complains to my boss that 'I came in, and that young vet didn't give me antibiotics.' Whereas now I'm like, 'It'll be fine, go away'."
(Veterinarian, participant 1)

"I have that sort of moral dilemma of whether or not I'm gonna give it to the animal, it's more based on whether the animal would get sick and I'm not going to be here to be able to see it because I leave this afternoon and there's no vet for another three months."
(Veterinarian, participant 4)

For both human and animal health practitioners, considering whether a course of antimicrobials could be completed by the patient or administered to the client's animal influenced whether these were prescribed. There was consideration of numerous factors including social determinants of health when making these prescribing decisions.

"I don't know if it differs to non-remote communities, but certainly compliance and adherence to medication overall is often an issue. I guess culturally, sometimes you know, it's about health literacy, making sure that people understand why they need to take this medication and why they need to take it every day and sometimes multiple times a day. So conferring that understanding, which sometimes may or may not occur with some of our clients because their literacy is low. English literacy is low already, so certainly that presents an issue with understanding, first off, so I think that kind of plays in a bit with some of that also, I guess culturally, sometimes there are other issues in someone's life, and I feel like the social determinants of health kind of play into that as well. Like, if someone's homeless or doesn't have, you know, security, where are they gonna put their medications, if their medications need refrigeration, they don't have a fridge, so you know, medication security is an issue as well. So I think there's a few different factors at play that may impact someone's adherence that sometimes may not be looked at." (AMS pharmacist, participant 13)

Sometimes the dog's not there, or sometimes the owner is asleep for the morning so it doesn't get the morning dose. And there are obviously cultural things that take precedence understandably so one owner might be there one day and the next day they've gone over to another community for ceremony and that sort of thing. There's a lot less predictability in where they might be, where the dog might be, so that is more what stops me from prescribing courses of antibiotics and I guess I'm conscious of tablets not being used and being left there and being used in a different capacity, being picked up by little kids and eaten or if it's just used in a way that they shouldn't be because they're a tablet so I suppose from a compliance point of view not getting into the dog is one thing but I guess misuse, not necessarily in a naughty way, just accidental and obviously having antibiotics lying around and going into the bin and going out to the landfill and that sort of thing isn't particularly ideal either. If I think that an owner isn't going to be compliant I don't think that's necessarily because of the communication error that could be resolved by talking to somebody else that is local to translate that, yeah. I think if that was the case I would be relying on those resources that we do have to communicate that if I thought that that was the main problem." (Veterinarian, participant 4)

Views around overuse of antimicrobials were mixed. Some participants thought the risk of consequences or lack of access to other safeguards justified more frequent use of antimicrobials than in urban practice.

"Any sore throat, even if it's COVID, gets LA bicillin injection [long-acting penicillin] and potentially also tablets like phenoxymethylpenicillin to treat for possible strep" (Doctor, participant 6)

"In our population in remote communities, I think that the risk of rheumatic fever and post strep GN [glomerulonephritis] is incredibly high for those kids with absolutely disastrous potential outcomes. And so I don't think that there's overuse, but I do recognise that outside of that specific environment, then a lot of the antibiotic indications are not necessarily global indications." (Doctor, participant 6)

Some of the consequences that concerned prescribers were not just medical but had flow-on impacts related to trust and preserving good relationships with community members.

"Recognising that relationships with community members are something that needed to be protected and that if surgical cases didn't go well for something as simple as a post-operative infection, that that could really set the care of all animals in that community back due to mistrust." (Veterinarian, participant 2)

The more well known you are in a community, the more trust typically you will have… But then like it can go both ways, right? Like if you upset somebody or if you are like looking after a patient who dies in hospital…there potentially will be a lot of mistrust, and that extends far and wide. It's not just like this four-person family unit will have mistrust. It's suddenly one hundred people. So yeah, it goes both ways. (Doctor, participant 6)

Another participant thought increasing levels of resistance in human health indicated that current prescribing practices were not appropriate.

"We see high resistance in remote settings and so a very, very black and white example is MRSA. In [location] the overall rate is 53% of all Staph aureus isolates and that's crazy. Much, much higher than anywhere else in Australia. I believe that's predominantly caused by overuse of antibiotics. Our ESBL rate has gone up from about 7% back in 2013 to 23% back in 2022. I was dumbfounded by this 'cause [they're] usually low but within a state of 10 years' time, it's just rocketed, just skyrocketed. So we must have been doing something wrong." (AMS Pharmacist, participant 11)

"I think a huge problem is because people are really far away, right, so when they're a bit sick, when they're sick, when they've got respiratory illnesses, a lot of the time, the easiest way is just to give them a shot of ceftriaxone and then send them home. And then keep doing it until if it's not improving then they'll send them to the hospital. If they're improving, then they'll just finish the course. I can understand the mentality, but I cannot accept it because this is really, really poor use of medication and this is something that we're trying to address as well." (AMS Pharmacist, participant 11)

Although views were highly variable, human health practitioners with the exception of Aboriginal Health Workers, did not consider the impact of AMR or zoonotic and zooanthroponotic disease transmission as much as veterinarians did, or when they did, only considered animal to human transmission.

“We keep getting told no, there’s no link between the dogs and people having scabies. You can’t help feel that something’s not right. So whether it's… yeah I don’t know. Again, I would seek clarification if there’s a cross going over, cross-over from dogs to people. The other one we had recently, in the last few months, was fungal infection, kerion, which is a scalp one, tinea capitis, and apparently dogs are associated with passing that on. But we’ve only had one confirmed case – one or two.”(Nurse, participant 3)

“When I was working remote, I think you don't really think about it [AMR] so much, more trying to think about the individual patient.” (Doctor, participant 14)

“I haven't had that sort of discussion with people before [about the impact of AMR on animals and the environment]. And the fact that I've never, not really, had that discussion with people before certainly illustrates that it's not high on my uh, it's not in the forefront of my thoughts. And yeah, it hasn't come up much in conversation, so maybe not in others as well, yeah.” (AMS Pharmacist, participant 10)

However, many participants mentioned upstream factors that would impact on the development of AMR or influence how they prescribed such as housing, education, and environmental factors such as heat and humidity.

“It's like overcrowding sometimes. Problem like you know, people staying in one house – too many people, and that's why people get like scabies and skin infections. And I go there and give education about how to look after your skin or come to the clinic like for checkup, and that's part of my work.” (Aboriginal Health Worker, participant 12)

“I think the housing and the fridges is …that's actually quite a big one...pretty much everything [medication], after you reconstitute it, is generally kept in the fridge…and then sometimes…you're having to reconstitute multiple times and depending on the course and the duration and things. It's not necessarily straightforward for some families who are not all that health literate. (Doctor, participant 14)

Aboriginal Health Workers were very aware of the impact of animals and the environment on human health and emphasised the need to care for animals.

“I always think about it. I have to tell to not do this, or so we have to, like, clean the houses, all that stuff, leave the dog outside, not inside, not in your kitchen area or in the bed. This kind of story we have to educate them over and over. (Aboriginal Health Worker, participant 8)

People love animals. But they need to look after the animals like doing the washing or seeing the vet like to give like a medicine or worm tablet for the dog or you know skin… give ivermectin. Also I talk to the people about how to like look after pets, you know animals, pets, dogs but sometimes people they don't like dogs because they scratch a lot *on the mattress or blanket and the children you know come and sleep on the mattress and sometimes they feel itchy." (Aboriginal Health Worker, participant 12)*

Staff shortages and high workload were regularly mentioned by participants. Workforce issues influenced how some participants prescribed antimicrobials. Concerns included the time period before healthcare services would be available again and the high expectations on staff.

"We might only go out there once a week or once a fortnight, so if I had someone presenting with skin sores I would rather treat them then, than wait two weeks to see if they resolve on their own." (Nurse, participant 3)

"A lot of the communities are working a lot on agency nurses. There's not many people staying permanent in community, the nursing and the doctors… the same as [remote community location] they haven't got a permanent doctor. It's just locums. Sometimes you work without a doctor…and that's quite a big…becomes a bit weary as well." (Nurse, participant 7)

Planning and future training were also impacted. Barriers for new staff joining included training and onboarding requirements and a lack of time made available for this.

"So we have been giving…delivering talks, but I think again it's not just one problem. We're trying to deal with multiple issues, for starters staffing issue, like the workforce is so transient and you know who you get, you know who you get today might not be the person you get tomorrow. You also have the doctors versus nurses versus Aboriginal health workers and also it's so sparsely, you know, it's so spread out so when you run education sessions, you're never ever going to capture everyone. The talks that you give to doctors have to be pitched differently to the talks that you give to nurses. It's just difficult." (AMS pharmacist, participant 11)

"You kind of go down the path of training them and then they just don't turn up to work. I get approached by people on a weekly basis all the time saying that they wanna come and work for us but when it comes to the nitty gritty of, OK, you've gotta go and fill in forms and you gotta do the paperwork and you gotta do this and that…they're just not there… It's all just kind of a bit frustrating and unreliable." (Veterinarian, participant 5)

"I think yes, it's hard for them. If they come to doing the course in Darwin, like training and all these courses." (Aboriginal Health Worker, participant 12)

Nearly all participants mentioned education programs as a way of addressing AMR and infectious diseases.

"Why don't we do more in that space [bush medicine, home remedies], if your dog is sick, these are things you can do. If that doesn't work, the vet can help you, and like education and getting into the schools and doing that kind of thing." (Veterinarian, participant 1)

Mostly… I spoke about, not about the tablets or medication, it's all about like education, how to look after yourself. You have like you know, how to look after the house, outside the house or inside the house, make sure it's clean… Sometimes I like hand over the posters about healthy homes and like stickers – clean the house, make sure that people come and see posters about healthy homes. And also like I give education about scabies or crusted scabies, Strep A, germ bacteria, hygiene. Yeah, all those kind of stuff here." (Aboriginal Health Worker, participant 12)

In some cases, there were concerns about carrying out education programs because an appropriate action or solution was not currently easily accessible to community members (in this case vaccination to prevent canine parvovirus).

"We're currently in decisions and we've just had a parvo outbreak in [remote community location] two weeks ago, which is currently in [remote community location] as well and has made it into [town] with private animals. We can't run an education programme on it without being willing to back that up with vaccinating. So then it's the argument on are we going to offer vaccination. So we'll see. Time will tell." (Veterinarian, participant 5)

There were varying levels of importance placed on working with local staff. In some cases, the focus was on completing urgent tasks rather than local employment or training.

"I found I spent more time running around trying to find the person that was meant to be helping me than actually doing any work or doing the stuff they were meant to be helping me with. So I kind of gave up a little bit." (Veterinarian, participant 5)

Despite this, some participants consistently expressed how important it was to have local people working in healthcare.

"Yeah, have a lot of respect for them, love working with them. It just brings a better feel to the clinic there. So much more knowledge. They just know who's where, so helpful. It's a lot harder without them." (Nurse, participant 7)

"It's great to work with them. They're an amazing resource and you know a lot more trusted in the communities than often we were. As we just fly in and fly out for one day a week. So yeah, they were really amazing to work with. (Doctor, participant 14)

If you didn't have that connection with the local workers, it would be more difficult. It would be harder. It would literally go back to just picking up dogs, desexing them and letting them go again. (Veterinarian, participant 9)

Aboriginal health practitioners stressed the importance of their role and also the influence of role models in encouraging people to become health practitioners was also mentioned.

"If people come, they come to us to see nurse or doctor and as an Aboriginal Health Practitioner, we have to be there as well. So we can explain in our language. Understand what the antibiotic is for – don't have miscommunication with nurse or doctor. So it's important to have an AHP [Aboriginal health practitioner] there, to be present." (Aboriginal Health Worker, participant 8)

Because my mother she was a health worker. Like she was my role-model." (Aboriginal Health Worker, participant 8)

Participants stated that a transitory workforce made it more difficult to build trust and relationships with community members.

"I think those relationships are certainly really important and it's tricky when we have revolving…and the same with our health centre nursing staff as well, there's a lot of locum workers." (AMS pharmacist, participant 13)

Participants who had spent a longer time in communities reported better relationships and interactions.

"We've built that over years and we're at a point where people understand about antibiotics and understand about looking after their dogs and what the vet does and that kind of thing." (Veterinarian, participant 1)

I think that's part of the reason why it's important to…if it's suitable for people to stay for a long time because the more trust you develop, the better. It just takes time. (Doctor, participant 6)

Some practitioners had a desire for self-improvement and also improved standard of care. They expressed frustration at the lack of buy-in from other sectors and that some health practitioners were not trying to improve their own practice, instead blaming external conditions.

"It's not a problem that can be resolved with just one plan, like, you know with one strategy. You need to have everyone on board. I actually thought that you know we are in a pretty bad situation… bad enough to instigate, you know, more buy-in from people, but apparently not. So I don't know." (AMS pharmacist, participant 11)

"It's like "oh well, you know, it's community, it's dirty, we're going to give antibiotics". And I'm like, "but you're dirty!" [laughs] You know better, you have access to education, you could do better" (Veterinarian, participant 1)

Discussion

This study highlights the challenges faced by veterinarians without access to infrastructure and equipment such as clean surgery rooms and autoclaves, and other drivers of antimicrobial use and infectious disease such as housing shortages and overcrowding. These findings were expected from the personal experiences of the primary researcher (AES) working in remote Indigenous communities and from the results of other studies [144, 256]. Previously identified barriers to animal health in Indigenous communities, including remoteness, accessibility and funding limitations [264], were also identified by participants in this study in relation to the use of antimicrobials. However, the use of this qualitative One Health approach highlighted themes not often discussed in veterinary science yet which impact on the development of AMR and implementation of AMS strategies. Some of these include the impact of workforce issues, the influence of relationships and trust with community members, and, particularly in veterinary practice, reliance on informal relationships and strategies to enable treatment of animals or diagnostic testing. Using qualitative semi-structured interviews to gain deeper understandings of AMR and AMS has proven beneficial in previous research with pet owners[211, 233]. We found it provided a safe environment to discuss the issues in a relaxed environment without time pressure.

The issue of workforce has been discussed in the context of AMS [233] but the focus has been on interactions with colleagues and clinical experience. In this case staff shortages, as well as high rates of turnover and overwork generally, may be a significant and potentially overlooked factor in the fight against AMR. Our participants highlighted that providing education and training about AMS to other staff was difficult given staff turnover. Due to having limited time in the communities, there was more motivation to prescribe antimicrobials to prevent infections when no health practitioners would be available to provide follow up care. Given the cost of AMR into the future, funding workforce sustainability could be an investment in AMS. Enablers for AMS include the positive influence of local Aboriginal health workers in human health and their equivalents in animal health, a strong interest by participants to improve their practices or receive more knowledge about aspects of AMR, and evidence amongst all participants of at least some understanding or acknowledgement of upstream drivers of AMR. Transdisciplinarity and collaboration between sectors is critical when dealing with issues such as housing and environmental health [140]. Our results suggest this needs to go further to include animal health and a focus on increased engagement and employment of local people, along with sufficient resourcing.

Direct questions about racism or discrimination were not asked, although there was recognition by one participant that negative experiences by locals and media reports about a particular hospital may have influenced how community members sought healthcare. There was little self-reflection by non-Indigenous participants about how race and discrimination may impact access to antimicrobials or interactions between health practitioners and local people, particularly as adherence to medications and late presentation were mentioned frequently [108]. There have also been recent media and organisational reports about the impact of racism on healthcare in Australia and internationally including as part of “Black Lives Matter” campaigns [265-267]. Participants may not have felt comfortable to raise issues of racism themselves or did not feel it was relevant in AMS research. Whether it was unsaid because it was not occurring, participants weren’t comfortable to raise it, or because participants were unfamiliar with systemic racism and microaggressions such that they did not recognise them cannot be determined. Epidemiology and health research has been described as, “A discipline so neutral it cannot, or rather will not, account for state-sanctioned violence, oppression, and dispossession in ways that could describe, explain, predict, and control inequity”

[106]. Participants did, on occasion, refer to unspecified cultural factors in impacting health-seeking behaviour but did not explore or define this further. Participants may be using this term to describe barriers caused by racism or other discrimination without explicitly naming them, however this still allows the perpetuation of racist outcomes [268].

There is potential for improvement in animal health through veterinarians sharing knowledge and advocating for improved standards. For example, to local councils who are generally responsible for funding animal health programs and providing infrastructure. Exploring the strategies and outcomes of veterinarians not routinely using antimicrobials for surgical prophylaxis may build confidence among other veterinarians to improve their antimicrobial prescribing for surgical cases. A proactive response from the animal health sector also enables more collaboration with the human health and environmental health sector in understanding the barriers and enablers in each section and working together collaboratively where possible. Many community health programs already incorporate aspects of One Health such as prevention of zoonotic diseases and improving access to WASH facilities. Some participants described being involved in such programs incorporating input from other health sectors.

Numerous researchers have mentioned the importance of involving and working with local staff on animal health programs [144, 145]. Our research also identified the difficulties that health practitioners, especially veterinarians, had in increasing the skill level of the local workforce in managing animal health in the absence of a veterinarian in the community. The time taken to strengthen workforce capacity while focusing on tasks perceived as more urgent such as surgery was mentioned by numerous participants and has been identified previously [145]. In the context of AMS education, this may be further exacerbated by the complex nature of AMR and its impacts, which are not often well-understood by the general public [211]. An evaluation of short-term benefits in conducting animal health programs versus the long-term benefits of increasing local capacity would be beneficial.

While many participants mentioned education as a solution to health challenges, we must remember that we don't necessarily 'educate' our way out of health issues in mainstream communities. Behaviour change often requires more than education alone, demonstrated in AMS interventions such as colour-coding antimicrobials and moving HIAs to less accessible parts of the pharmacy [232] as well as in programs for other chronic health behaviour change interventions [269]. Lessons from the COVID-19 pandemic show that social determinants of health had a significant impact on public health that could not be mitigated by provision of education alone [270, 271]. If people do not have reliable access to fundamental needs such as clean water, food and housing, education about handwashing or avoiding over-crowding may not be helpful [272]. Participant responses suggest that there is a tendency for health practitioners to focus on the 'solution' of education, rather than addressing upstream factors, potentially due to the perceived enormity and persistence of current inequalities and associated challenges.

There has been limited qualitative One Health-focused research in the field of AMS in Australia, particularly as it relates to remote communities. Active inclusion of Indigenous viewpoints is recommended by others [264] and our study benefited from their perspectives, with 3 out of 14 participants identifying as Indigenous). There is potential to increase the involvement of more Indigenous participants, however care must be taken ensure a One Health approach does not solely address pre-identified health problems without centring the needs of the communities, whose priorities may differ from those of non-Indigenous academics [106]. If research does occur, participatory and co-designed approaches to ensure activities are conducted in alignment with community priorities and needs should be the minimum standard[273]. Focusing on existing strengths, successes, and enabling factors may help avoid burdening Indigenous health practitioners, community leaders and traditional owners with additional responsibilities related to research [259]. For example, providing additional support for Aboriginal Health Workers to engage in research or targeted training in areas of interest to them[274, 275], and providing financial and mentorship support to young people wanting to train as Aboriginal Health workers or practitioners.

Conclusion

This research highlights the current strengths in remote communities in relation to AMR prevention, as well as the drivers of AMR and their interconnection with upstream factors. This research can guide discussions on how remote communities would like to engage with AMR and existing AMS approaches, such as use of prescribing guidelines and educational materials. AMS efforts must move beyond focusing on individual behaviours of community members, veterinarians, or other health professionals to address upstream social, economic, cultural, legal, linguistic, and political conditions that underlie health inequalities and drive and maintain AMR.

Table 1: Antimicrobials mentioned by practitioners that they usually used or had in stock

Antimicrobials Used in Human Health	Antimicrobials Used in Animal Health	Importance rating
Narrow spectrum penicillins Benzylpenicillin (pen g) Phenoxymethylpenicillin (pen v)	**Narrow spectrum penicillins** Benacillin (procaine penicillin, benzathine penicillin, procaine hydrochloride) Duplocillin (procaine penicillin and benzathine penicillin)	Low
Moderate-spectrum penicillins Amoxicillin	**Moderate-spectrum penicillins** Amoxicillin	Low
Antistaphylococcal penicillins Flucloxacillin - medium		Medium
ß-lactamase inhibitor combinations Amoxicillin/Clavulanic Acid	**ß-lactamase inhibitor combinations** Amoxicillin/Clavulanic Acid	Medium
Sulfonamides Sulfamethoxazole/ trimethoprim (co-trimoxazole) (Bactrim)	**Sulfonamides** Trimethoprim sulfadoxine	Medium
Nitroimidazoles	**Nitroimidazoles**	Medium

Metronidazole	Metronidazole	
Macrolides Azithromycin		Low
1st Generation Cephalosporins Cefazolin (sometimes with probenecid to extend duration)	**1st Generation Cephalosporins** Cephalexin tablets	Medium
3rd Generation Cephalosporins Ceftriaxone	**3rd Generation Cephalosporins** Cefovecin (rarely used)	High
Tetracyclines Doxycycline	**Tetracyclines** Doxycycline Oxytetracycline (alamycin)	Low
Glycopeptides Vancomycin (especially if suspect MRSA and for sepsis pack)		High
Carbapenems Meropenem (for sepsis)		High

Chapter 6 General discussion

There is a tendency for One Health research in Australia to focus on identifying gaps rather than undertaking specific actions or interventions to fill these gaps. The research findings detailed in Chapters 2-5 provide practical steps and data to increase the AMR and AMS knowledge-base in Australia. The particular focus on topics that have not been specifically investigated previously (HIAs) or where data collection and practical tailored advice is lacking (remote Indigenous communities) provides a unique contribution to the field. The explicit linking of research at a higher level about appropriate use and restrictions relating to HIAs with the practical aspects and challenges of veterinary work, particularly in remote areas is also novel. This was done to prioritise some of the less tangible aspects of One Health research such as equity, collaboration and transdisciplinarity. These principles are not usually the focus of One Health research in veterinary science, which tends to prioritise research around more explicit connections between human and animal health such as zoonoses. The use of mixed-methods and a wide scope also increases the accessibility and relevance of these research findings to diverse stakeholders.

Restriction and regulation of AMU including HIAs

While misuse of antimicrobials must be addressed, animal welfare, food safety and the ability of veterinarians to practice is compromised if the ability to use certain antimicrobials is suddenly restricted. The Delphi methodology for addressing complex issues has been used for similar health care and policy issues in the past where there is no "source" of truth, and was successfully adapted for this thesis allowing a move towards proactive evidence-based policy [75, 137]. Results from the Delphi study (Chapter 3) may also be translatable to veterinary practice internationally and help to position Australia as a proactive leader in the field of AMS by encouraging other countries to take similar early precautionary actions. The development of practical consensus items also builds on one of the enablers of AMS in veterinary practices, which is a preparedness amongst Australian veterinarians to change prescribing practices [18].

Australian veterinarians have shown themselves to be open to AMS interventions especially in relation to HIAs (Chapter 2). This was somewhat unexpected based on previous work that was less supportive of restrictions [67, 138]. There was strong support for culture and susceptibility testing (C&S) results to define appropriate use, but this poses challenges due to the costs and time involved (Chapter 2) [139]. In some cases, actually collecting a sample for C&S can be difficult or inaccessible due to the disease presentation e.g. discospondylitis or severe patient illness making sedation or anaesthesia for sample collection risky. If C&S uptake is prioritised and recommended in future, further education for veterinarians about appropriate and safe sample collection would be helpful as well as further guideline development for empirical treatment for conditions where initial sample collection may be difficult due to patient, client or veterinary capacity challenges.

Further exploration of factors impacting AMS in the context of remote Indigenous communities provides additional evidence for more upstream support and resourcing of AMS particularly for animal health (Chapter 5). Both in remote communities and urban and regional veterinary practice, veterinarians have described time and financial challenges that impact their ability to prescribe appropriately (Chapter 2 and Chapter 5). A nuanced approach to antimicrobial restrictions must be taken to prevent animal welfare issues and associated stress for the people involved [11]. For veterinarians that don't have access to C&S due to client financial limitations, significant distance from a laboratory or other sample transport issues, the consenus items around medical records and justification of use are immediately implementable by veterinarians in practice (Chapter 3). This could help balance the use of antimicrobials with interventions to enable better understanding and surveillance of AMU (Chapter 3).

Issues of overwork were raised by veterinarians and other health professionals during qualitative interviews (Chapter 5). Solutions for the workforce challenges facing the global veterinary profession are likely to be complex and to take time to resolve. Inappropriate antimicrobial prescribing should not be used as a 'quick fix' for inadequate staffing or over-scheduling. Workforce issues may become ethical issues when they impact on the serious issue of AMR [6, 140, 141]. Failure of organisations and workplaces to address these upstream workplace influences could have long-term consequences for AMR.

Using a modified Delphi process was valuable in facilitating consensus amongst international experts from a broad range of health backgrounds and experiences. The consensus items provide numerous opportunities to implement practical, high-impact policy to support AMS at the national level. Flow-on effects may address current gaps in veterinary AMS at the level of the prescriber. For example, there is a need for more focused education for veterinarians around prescribing, yet it is sometimes difficult due to a lack of specific data to define the problem [18] (Chapter 2). Implementing reporting of HIAs used in animals but not registered for such use could result in greater awareness of the importance of these antimicrobials by the prescribing veterinarians. It also allows better monitoring of antimicrobial use on a national level and subsequently greater opportunity to tailor educational AMS resources to target any inappropriate use.

A novel finding from this process was that, even among experts, there were varying levels of understanding of the definitions and purposes of rating systems, guidelines and practice-specific antimicrobial use policies. Moving forward, researchers and policymakers should be consistent in the use of such terminology to prevent misunderstandings and the delay of AMS progress. Some confusion can also occur when there are differences in understanding within sectors. A One Health approach requires clear communication to foster transdisciplinarity and multisectoral collaboration.

The development of consenus items between human and animal health experts promotes understanding and ownership of solutions and moves away from blaming sectors for their contribution to AMR [142]. Culture and susceptibility testing (C&S) was identified as a key factor in categorising the veterinary use of HIAs as appropriate. However, previous research has highlighted that disease investigation can be difficult in private veterinary practice because there is no or minimal incentive for clients to fund investigations that are primarily in the public interest [143]. Given that reducing the use of high-importance antimicrobials in companion animals and food-producing animals was identified as important by the majority of experts surveyed during the Delphi process, investigation of cost-sharing arrangements between sectors to preserve the efficacy of HIAs would be worthwhile. Arrangements of this kind would be particularly beneficial for veterinarians working in low-socioeconomic areas including remote Indigenous communities where cost is a barrier to performing diagnostic tests (Chapter 5). Consideration should be given to the costs of C&S, as well as costs involved in obtaining samples (including sedation or anaesthesia), as well more complex procedures (e.g. bronchoalveolar lavage, arthrocentesis) that are needed to collect appropriate samples for many conditions. Cost-sharing between sectors promotes the One Health principle of equity and may also result in more efficient data collection and the development of integrated surveillance systems, which have previously been identified as critical for AMS as well as emergency disease events [41].

Currently, there are many inconsistencies and complexities in the prescribing environment encountered by the Australian veterinary profession particularly as legislation varies across states [276]. This presents a challenge for practicing coordinated and effective antimicrobial stewardship activities [23]. Relevant federal legislation is regulated by the APVMA, whereas relevant state-based legislation may be found in human health acts or those relating to agriculture and the environment [16]. Improving consistency around governance and reporting requirements could improve AMS in the Australian veterinary context [10].

Since the Delphi process was undertaken, an interim Centre for Disease Control, which supports a One Health approach was created in Australia in January 2024 [277]. At present no specific work on AMR is described or promoted and the organisation is dependent on legislation being passed at a federal level prior to becoming formalized into an independent organisation (possibly in January 2026). As such, it is unclear whether this would be a suitable organisation to establish integrated surveillance systems for AMU and AMR or to be the organisation notified of the use of high importance antimicrobials not registered for use in animals. Such an organisation may be well placed if appropriate expertise, resourcing and focus was provided to address AMR.

Practical lessons from a pilot surveillance study of dogs in a remote Indigenous community

Due to the COVID-19 pandemic and associated travel and resource delays, the research detailed in Chapter 4 was scaled down. Fewer dogs were sampled than originally planned. It also did not incorporate sampling from dogs‘ owners as was originally conceptualised, nor did it occur concurrently with data collection about WASH and housing facilities. Nevertheless, knowledge about antimicrobial resistance profiles of staphylococci from dogs in a remote Indigenous community has improved. Results showed lower levels of resistance than may have been expected based on other studies in similar contexts [151, 152]. This highlights the potentially low level of generalisability of such surveillance studies and the need to interpret resistance data in the context of local AMU data wherever possible. Access to AMU and AMR data from other sectors would also improve the interpretation of these results. It is unclear why higher rates of MRSA were identified in some other communities [151, 152]. This could be due to higher AMU in those areas, or due to low sample sizes such that the differences may actually not be significant. It is also difficult to compare results from similar studies that do not report the total population of dogs from which samples were taken or studies which only utilise convenience sampling.

This study was the first in Australia to demonstrate a house-to-house sampling methodology for AMR surveillance in dogs in a remote Indigenous community. Conducting this study as originally planned would have enabled greater understanding about transfer of AMR between people and animals as well as the impact of WASH and housing facilities on AMR in that context. However the practicalities and ethics of undertaking such studies need to be evaluated in line with community priorities, which may be why such studies are not frequently undertaken, particularly in the context of many remote communities facing multiple health challenges [44, 144]. However, this methodology proved valuable in understanding the wider context in which the dogs lived as well as building relationships with community members through responding to requests or identifying dogs that needed additional veterinary care.

In-depth interviews with veterinarians (Chapter 5) indicated that a barrier to undertaking more frequent C&S was remoteness and time to the laboratory – this study (Chapter 4) demonstrates that these concerns may be less significant if a cool chain can be maintained. Samples maintained viability despite transport times of up to 20 hours and collection up to seven days prior to reaching the laboratory. This knowledge may increase the accessibility of C&S to veterinarians working in this context who may be more confident to submit samples. The interpretation of resistance data from healthy animals should also be done with caution because resistance rates may vary in comparison to clinical isolates. However, low levels of resistance detected in this study suggest that high importance antimicrobials have not been frequently used in this dog population. Veterinarians can also feel confident in following current prescribing guidelines given the lack of resistance present and in the absence of data from clinical isolates suggesting otherwise.

Building on needs identified in Chapter 2 and 3, future areas of research could include how to increase clinical confidence and diagnostic accuracy in the absence of availability of C&S. For the treatment of companion animals, possibilities include increasing capacity for in-house cytology, gram stains, and evaluation of blood smears. These results could be recorded and reported in medical records as part of justification for antimicrobial use and would enable better monitoring and evaluation of AMS strategies and an understanding of AMU in remote community settings. Antimicrobial resistance in canine staphylococci did not appear to be an emerging One Health issue in this community. This suggests that future resource allocation may be best utilised by sampling clinical animals when required and investing in essential infrastructure to reduce the need for surgical prophylaxis e.g. autoclaves and clean surgery and recovery areas, which was identified as a barrier to AMS in Chapter 5.

Use of antimicrobials in remote Indigenous communities in relation to One Health, Indigenist Health Humanities, and social determinants of health

In recent years, qualitative methods have been used to better understand AMS including in veterinary science [139, 145-148]. Incorporating aspects of Indigenist Health Humanities and a One Health approach further opens space for deep discussion about barriers and enablers for AMS and drivers of AMR. In addressing a super-wicked problem such as AMR this methodology provides insights that may otherwise be overlooked. It allows space for humility and seeing participants as experts in their own lives [44, 149]. A tendency to focus on disease prevalence, resistance rates and other medicalized aspects of AMR may overshadow the interaction of social determinants of health with AMS. In recognising AMR as a socio-political and ethical issue and exploring AMS at this upstream systemic level, new insights and areas of future focus can be identified [6, 44, 62, 136, 141, 149]. Developing systemic solutions may be differentiated from individualised behaviour-change approaches that are more common in a clinic or hospital setting [150]. However systemic approaches can also work synergistically with individualised approaches to improve equity.

In our research, veterinarians described using prophylactic antimicrobials when performing surgery because they were not confident about the environments in which they were undertaking surgery and did not have the ability to sterilise instruments to a level they were used to. An individualised AMS approach may involve educating the veterinarian about guideline recommendations around prophylactic surgery or providing examples from other veterinarians working in similar settings who are not using surgical prophylaxis for routine cases. Combining this with an upstream approach may incorporate addressing the reasons why an autoclave is not available in the community such as funding, maintenance and storage issues. Another approach may include identifying a more appropriate indoor premise for veterinarians that otherwise perform surgery in dusty outdoor settings or sheds. This could require advocacy at the individual level as well as a collaborative upstream approach educating stakeholders such as local government or businesses about the importance of a hygienic environment when performing surgery to prevent unnecessary antimicrobial use.

Colleagues and workplace culture have an influence on AMS [139]. Being short of time can make dispensing antimicrobials a more feasible option compared to further (often costly) diagnostics or extensive patient or client communication (Chapter 2)[18]. Fear of patient deterioration is interwoven with these concerns. The addition of systemic factors such as high rates of chronic disease, or overcrowded housing, further compound the pressure to prescribe (Chapter 5). From an ethical standpoint, it is not reasonable to hold health practitioners working in remote communities to high standards of AMS without also providing the means and support to address systemic factors, which make AMS even more difficult than in other urban or regional areas.

During initial participant interviews (Chapter 5), veterinarians relied or said they would rely on informal arrangements or pre-existing relationships with staff in other sectors or veterinarians outside of the community to achieve some tasks. These included sending samples for C&S, maintaining inventory at times of sudden shortage and providing treatment for animals when no veterinary staff were in the community. This highlights the resourcefulness of these veterinary participants. Some participants including Aboriginal Health Workers had also engaged with veterinarians to run education programs together focusing on ‘healthy homes’ and ‘healthy pets’.

By overcoming differences between disciplines and using social links to fill gaps in existing care, these participants show a willingness to engage in collaborative humility [149]. Collaborative humility has been described as a solution to fragmentation that can occur when attempting to use a One Health approach to address AMR. Similarly, participants who took part in the Delphi process (Chapter 3) voluntarily contributed their time to engage in a process with other health professionals – some from other sectors or countries - who they may never have met, with the aim of progressing AMS. Identification of these collaborations provides a basis for formalising processes and better addressing challenges to AMS including those that prompted the initial interactions such as lack of formal arrangements for sample transport.

Interview participants (Chapter 5) showed varying levels of engagement and understanding of the topic of One Health and social determinants of health. Some participants were very insightful and passionate while others made comments, which suggested they had not thought deeply about the upstream systemic drivers for their actions or those of their patients or clients. Increased education of health practitioners about the principles underlying One Health and evidence of the social determinants of health could encourage more self-reflection from participants about their position in relation to systemic challenges to AMS [44]. It is after all, difficult to address problems that are not clearly known or identified.

Comments on methodology and limitations

The veterinary survey (Chapter 2) was limited by the number of respondents, which although was sufficient to allow estimation of proportions, did not have a sufficient number of participants to allow meaningful comparisons between groups. Distributing this survey completely online due to disruptions caused by the COVID-19 pandemic may have impacted the number of participants. Previous surveys of veterinary professionals have also been distributed at veterinary conferences which enables an increased number of respondents [52, 53]. However, respondents did appear to be representative of veterinarians in Australia.

Similarly for the Delphi (Chapter 3), there were insufficient participants in some sub-groups such as physicians and human health participants overall to enable comparisons between groups or sub-groups, particularly when there was a tendency for some participants not to answer each question. Some questions, particularly questions about reporting to a central authority, had a high number of non-responders. This impacts the ability to make inferences about these questions but potentially does indicate that participants are not sure about this issue and further work would be beneficial to identify which central authority is trusted by veterinarians and health professionals to collect data on AMU. There were significant insights provided in the free-text comments that were helpful in guiding the reframing of questions for future survey rounds. If there were more survey rounds or a mechanism to enable discussion between the researchers and Delphi participants, such as an online forum, these insights could have been explored further. However, the risks of some individuals dominating the conversation would then need to be managed. The response rates for the Delphi survey rounds were reasonable and similar or slightly lower than those reported in other studies (sometimes response rates have been reported as a proportion of respondents from the round immediately prior rather than as proportion of all those that took place in the study or who were initially invited (for round 1 response rates) [116, 223]. As the experts contacted initially for round 1 were not expecting to participate, generally had not received prior notice of the process and in some cases did not know the researchers, this may have lowered the response rate [278].

In general, there was generally more enthusiasm from veterinarians to participate in the Delphi process (Chapter 3) and the semi-structured interviews (Chapter 5) compared to human health practitioners or experts. More practical assistance was also given by veterinarians rather than human health organisations for the sampling undertaken in Chapter 4. This highlights a challenge when undertaking One Health research to ensure collaboration and involvement across sectors is equitable. As described in Chapter 3, participation of human health participants in the Delphi process may have been impacted by the requirement for these experts to focus on the COVID-19 pandemic response at that time. As described in Chapter 4, limitations for sample collection from dogs were mostly practical. Ideally more samples would have been collected but that was not possible due to time and cost constraints, particularly in the context of travelling between states and high risk remote Aboriginal communities during the COVID-19 pandemic.

Conclusion

There is still significant work to be done in progressing AMS in Australian veterinary practice. This thesis has made an important contribution to extending the scope of veterinary AMS. A focus on equity and justice so that sectors are not left behind is relatively novel for veterinary science in Australia. Contributions towards data gaps have been made. Examples of One Health collaboration are provided and have identified areas for future focus and policy implementation that have the potential to make a significant difference through relatively easy to implement practical changes. A greater understanding of the veterinary use of HIAs and how this use could be addressed in future has been identified. Veterinarians and researchers should be encouraged to use a One Health approach focusing on transdisciplinarity and collaborative humility when addressing the issue of AMS.

Bibliography

1. O'Neill, J., *Tackling drug-resistant infections globally: final report and recommendations - The review on antimicrobial resistance*. 2016, Government of the United Kingdom: London, United Kingdom.
2. Centre for Disease Control, *Antibiotic resistance threats in the United States 2019*. 2019, Centre for Disease Control: Atlanta, United States of America.
3. Millar, M., *Can antibiotic use be both just and sustainable... or only more or less so?* Journal of Medical Ethics, 2011. **37**(3): p. 153-157.
4. World Health Organization. *WHO Coronavirus (COVID-19) Dashboard*. 2021 [cited 2021 19 September]; Available from: https://covid19.who.int/.
5. Drive-AB. *Driving reinvestment in research and development and responsible antibiotic use*. 2014 [cited 2021 19 September]; Available from: http://drive-ab.eu/about/.
6. Littmann, J. and A.M. Viens, *The ethical significance of antimicrobial resistance.* Public Health Ethics, 2015.
7. Hardefeldt, L.Y., *Antimicrobial stewardship in Australian veterinary practices*, in *Melbourne Veterinary School*. 2018, University of Melbourne.
8. Australian Strategic and Technical Advisory Group on Antimicrobial Resistance, *Importance ratings and summary of antibacterial uses in humans in Australia*. 2018, Australian Government: Canberra, Australia.
9. Islam, M.M., *Social determinants of health and related inequalities: confusion and implications.* Frontiers in Public Health, 2019. **7**: p. 11.
10. Daulaire, N., et al., *Universal access to effective antibiotics is essential for tackling antibiotic resistance.* Journal of Law, Medicine & Ethics, 2015. **43**(S3): p. 17-21.
11. Scott Weese, J., et al., *Governance processes and challenges for reservation of antimicrobials exclusively for human use and restriction of antimicrobial use in animals.* Journal of Law, Medicine & Ethics (JLME) 2022. **50**(S2): p. 55-63.
12. Adisasmito, W.B., et al., *One Health: A new definition for a sustainable and healthy future.* PLOS Pathogens, 2022. **18**(6): p. e1010537.
13. Sweileh, W.M. *Bibliometric analysis of peer-reviewed literature on antimicrobial stewardship from 1990 to 2019*. Globalization and health, 2021. **17**, 1 DOI: 10.1186/s12992-020-00651-7.
14. Department of Health, *Final progress report – Australia's first national antimicrobial resistance strategy 2015-2019*. 2021, Government of Australia: Canberra, Australia.
15. Commonwealth of Australia, *Australia's National Antimicrobial Resistance Strategy – 2020 and Beyond*, Department of Health, Editor. 2019, Government of Australia: Canberra, Australia.
16. Australian Pesticides and Veterinary Medicines Authority, *Antibiotic resistance in animals*. 2017, Australian Government: Canberra, Australia.
17. Australian Pesticides and Veterinary Medicines Authority, *Macrolide antibiotics (kitasamycin, oleandomycin and tylosin): proposed regulatory decisions*. 2017, Australian Government: Canberra, Australia.
18. University of Melbourne. *Australian veterinary prescribing guidelines*. 2020 [cited 2025 28 February]; Available from: https://vetantibiotics.science.unimelb.edu.au/.
19. Gray, P., et al., *Antimicrobial prescribing guidelines for poultry.* Australian Veterinary Journal, 2021. **99**(6): p. 181-235.
20. Cutler, R., et al., *Antimicrobial prescribing guidelines for pigs.* 2020. **98**(4): p. 105-134.

21. Batey, R., et al., *Antimicrobial prescribing guidelines for sheep.* Australian Veterinary Journal, 2024. **102**(4): p. 103-142.
22. House, J.K., et al., *Antimicrobial prescribing guidelines for dairy cattle.* Australian Veterinary Journal, 2024. **102**(4): p. 143-186.
23. Hardefeldt, L.Y., et al., *Barriers to and enablers of implementing antimicrobial stewardship programs in veterinary practices.* Journal of Veterinary Internal Medicine, 2018. **32**(3): p. 1092-1099.
24. Toombs-Ruane, L.J., et al., *Carriage of extended-spectrum-beta-lactamase-and AmpC Beta-lactamase-producing Escherichia coli strains from humans and pets in the same households.* Applied Environmental Microbiology, 2020. **86**(24): p. e01613-20.
25. Watkins, L.F., et al., *Ongoing outbreak of extensively drug-resistant Campylobacter jejuni Infections associated with US pet store puppies, 2016-2020.* JAMA Network Open, 2021. **4**(9): p. e2125203.
26. Allerton, F., et al., *Overview and Evaluation of Existing Guidelines for Rational Antimicrobial Use in Small-Animal Veterinary Practice in Europe.* Antibiotics, 2021. **10**(4): p. 409.
27. Frey, E., *The role of companion animal veterinarians in one-health efforts to combat antimicrobial resistancein.* Journal of the American Veterinary Medical Association, 2018. **253**(11): p. 1396-1404.
28. Woods, M., J.A. McAlister, and J. Geddes-Mcalister, *A One Health approach to overcoming fungal disease and antifungal resistance.* WIREs Mechanisms of Disease, 2023. **15**(4).
29. World Health Organisation, *Global action plan on antimicrobial resistance*. 2015, World Health Organisation: Geneva, Switzerland.
30. Fears, R. and V. Ter Meulen, *What do we need to do to tackle antimicrobial resistance?* The Lancet Global Health, 2014. **2**(1): p. e11-e12.
31. World Health Organisation. *Addressing the crisis in antibiotic development*. 2020 [cited 2021 19th September]; Available from: https://www.who.int/news/item/09-07-2020-addressing-the-crisis-in-antibiotic-development.
32. Rodríguez-Baño, J., et al., *Key considerations on the potential impacts of the COVID-19 pandemic on antimicrobial resistance research and surveillance.* Transactions of The Royal Society of Tropical Medicine and Hygiene, 2021.
33. Kopinathan, A., et al. *The next pandemic: antimicrobial resistance*. 2021 [cited 2021 19th September]; Available from: https://www.science.org.au/curious/policy-features/next-pandemic-antimicrobial-resistance.
34. Collignon, P. and S. McEwen, *One Health—Its importance in helping to better control antimicrobial resistance.* Tropical Medicine and Infectious Disease, 2019. **4**(1): p. 22.
35. Unicomb, L., et al., *Fluoroquinolone resistance in campylobacter absent from isolates, Australia.* Emerging Infectious Disease Journal, 2003. **9**(11): p. 1482.
36. Cheng, A.C., et al., *Control of fluoroquinolone resistance through successful regulation, Australia.* Journal Emerging Infectious Diseases, 2012. **18**(9): p. 1453.
37. Wozniak, T., Nguyen, A., Rollin, A., Brock, J., Bowskill, A., Morgan, B., Good, N., *Antimicrobial resistance (AMR) impact report: How big is Australia's AMR threat?* 2022: Australia.
38. Commonwealth of Australia, *Australian Government response to the 2013 Senate Finance and Public Administration References Committee report: Progress in the implementation of the recommendations of the 1999 Joint Expert Technical Advisory Committee on Antibiotic Resistance*. 2019, Commonwealth of Australia.

39. The Joint Expert Technical Advisory Committee on Antibiotic Resistance, *The use of antibiotics in food-producing animals: antibiotic-resistant bacteria in animals and humans*, Department of Health and Aged Care and Department of Agriculture, Fisheries and Forestry, Editors. 1999, Commonwealth of Australia: Canberra, Australia.
40. Dyke, T.M., *Regulation of veterinary antibiotics in Australia.* Communicable diseases intelligence quarterly report, 2003. **27**: p. S6-8.
41. Department of Agriculture, Water and the Environment. *National Residue Survey*. 2021 [cited 2021 19 September]; Available from: https://www.agriculture.gov.au/ag-farm-food/food/nrs.
42. Department of Agriculture and Water Resources, *Responding to antimicrobial resistance: Australian animal sector national antimicrobial resistance plan 2018*. 2019: Canberra.
43. Department of Agriculture Fisheries and Forestry, *Australia's animal sector antimicrobial resistance action plan 2023 to 2028*. 2023: Canberra.
44. World Organisation for Animal Health, *WOAH List of Antimicrobial Agents of Veterinary Importance*. 2024.
45. World Health Organization, *The selection and use of essential medicines 2023: Executive summary of the report of the 24th WHO Expert Committee on the Selection and Use of Essential Medicines*. 2023: Geneva.
46. World Health Organization, *WHO's List of Medically Important Antimicrobials: a risk management tool for mitigating antimicrobial resistance due to non-human use*. 2024: Geneva.
47. World Health Organisation, *Critically important antimicrobials for human medicine*. 2019: Geneva.
48. Organization, W.H., *Critically important antibacterial agents for human medicine for risk management strategies of non-human use: report of a WHO working group consultation, 15-18 February 2005, Canberra, Australia.* 2005.
49. Hardefeldt, L., et al., *Use of cefovecin in dogs and cats attending first-opinion veterinary practices in Australia.* Veterinary Record, 2020. **187**(11).
50. Hardefeldt, L.Y., K.E. Bailey, and J. Slater, *Overview of the use of antimicrobial drugs for the treatment of bacterial infections in horses.* Equine Veterinary Education, 2020. **33**(11): p. 602-611.
51. Hardefeldt, L.Y., et al., *Antimicrobial labelling in Australia: a threat to antimicrobial stewardship?* Australian Veterinary Journal, 2018. **96**(5): p. 151-154.
52. Hardefeldt, L.Y., et al., *Antimicrobials used for surgical prophylaxis by equine veterinary practitioners in Australia.* Equine Veterinary Journal, 2018. **50**(1): p. 65-72.
53. Hardefeldt, L.Y., et al., *Antimicrobials used for surgical prophylaxis by companion animal veterinarians in Australia.* Veterinary Microbiology, 2017. **203**: p. 301-307.
54. Hardefeldt, L.Y., et al., *Antimicrobials used for surgical prophylaxis by equine veterinary practitioners in Australia.* Equine Vet J, 2017.
55. Hardefeldt, L.Y., et al., *Cross-sectional study of antimicrobials used for surgical prophylaxis by bovine veterinary practitioners in Australia.* Veterinary Record, 2017. **181**(16).
56. Hardefeldt, L.Y., et al., *Antimicrobial dosing for common equine drugs: a content review and practical advice for veterinarians in Australia.* Australian Veterinary Journal, 2019. **97**(4): p. 103-107.
57. Hardefeldt, L.Y., et al., *Appraisal of the Australian veterinary prescribing guidelines for antimicrobial prophylaxis for surgery in dogs and cats.* Australian Veterinary Journal, 2019. **97**(9): p. 316-322.

58. Dyar, O.J., et al., *What is antimicrobial stewardship?* Clinical Microbiology and Infection, 2017. **23**(11): p. 793-798.
59. Hallett, M.F., T. Kjær, and L. Bjørnskov Pedersen, *The Use of Nudge Strategies in Improving Physicians' Prescribing Behavior: A Systematic Review and Meta-analysis.* Med Decis Making, 2024. **44**(8): p. 986-1011.
60. McKenzie, D., M. Rawlins, and C. Del Mar, *Antimicrobial stewardship: what's it all about?* 2013.
61. Doron, S. and L.E. Davidson, *Antimicrobial Stewardship.* Mayo Clinic Proceedings, 2011. **86**(11): p. 1113-1123.
62. AMR Vet Collective. *Prescribing Support*. [cited 2021 23rd September]; Available from: https://www.amrvetcollective.com/home/prescribing-support/.
63. Australian Veterinary Association. *Fighting antimicrobial resistance*. 2021 [cited 2021 23rd September]; Available from: https://www.ava.com.au/library-resources/other-resources/fighting-antimicrobial-resistance/.
64. Osset-Trénor, P., A. Pascual-Ahuir, and M. Proft, *Fungal Drug Response and Antimicrobial Resistance.* Journal of Fungi, 2023. **9**(5): p. 565.
65. Hume, J., et al., *Cytomegalovirus in children undergoing haematopoietic stem cell transplantation: a diagnostic and therapeutic approach to antiviral resistance.* Frontiers in Pediatrics, 2023. **11**.
66. Holmes, E.C., et al., *Understanding the Impact of Resistance to Influenza Antivirals.* Clinical Microbiology Reviews, 2021. **34**(2).
67. Norris, J.M., et al., *Development of a veterinary antimicrobial stewardship online training program for Australian veterinarians: a national collaborative effort.* Australian Veterinary Journal, 2019. **97**(8): p. 290-291.
68. Scarborough, R., et al., *Use of local antibiogram data and antimicrobial importance ratings to select optimal empirical therapies for urinary tract infections in dogs and cats.* Antibiotics, 2020. **9**(12): p. 924.
69. Coombe, J., *Antimicrobial stewardship in Australian livestock industries*. 2021.
70. Prescott, J.F., et al., *The publication of studies involving the use of human critically important antimicrobial agents in veterinary species.* 2021.
71. Hardefeldt, L.Y., et al., *Population wide assessment of antimicrobial use in companion animals using a novel data source - a cohort study using pet insurance data.* Veterinary Microbiology, 2018. **225**: p. 34-39.
72. Shaban, R.Z., et al., *Surveillance and reporting of antimicrobial resistance and antibiotic usage in animals and agriculture in Australia*, Department of Agriculture, Editor. 2014, Commonwealth of Australia: Canberra, Australia.
73. Kawarizadeh A, G.J., Mitchell K, Bailey K, Marenda MS, Chicken C., *Prevalence and antimicrobial resistance patterns of Klebsiella pneumoniae reproductive isolates from mares*, in *Australian Veterinary Antimicrobial Stewardship Conference*. Gold Coast, QLD.
74. Flood. JA., C., JB., Collins, NM., Russell, CM., Cudmore, LA., *Blood culture isolates and antimicrobial sensitivities from 1621 critically ill neonatal foals (2005-2022)*, in *Bain Fallon Memorial Lectures*. 2023: Tweed Heads, Queensland.
75. Papadogiannakis, E., E. Velonakis, and A. Vatopoulos, *Ever-increasing emergence of multi-drug resistant Staphylococcus pseudintermedius in the dog and its zoonotic potentials.* Journal of the Hellenic Veterinary Medical Society, 2016. **67**(2): p. 109-116.
76. Worthing, K.A., et al., *Clonal diversity and geographic distribution of methicillin-resistant Staphylococcus pseudintermedius from Australian animals: Discovery of novel sequence types.* Veterinary Microbiology, 2018. **213**: p. 58-65.

77. van Duijkeren, E., et al., *Transmission of methicillin-resistant Staphylococcus pseudintermedius between infected dogs and cats and contact pets, humans and the environment in households and veterinary clinics.* Veterinary Microbiology, 2011. **150**(3): p. 338-343.
78. Hur, B.A., et al., *Describing the antimicrobial usage patterns of companion animal veterinary practices; free text analysis of more than 4.4 million consultation records.* PLOS ONE, 2020. **15**(3): p. e0230049.
79. Richards, S., et al., *Cross-sectional evaluation of a large-scale antimicrobial stewardship trial in Australian companion animal practices.* Veterinary Record, 2024. **194**(4).
80. Hardefeldt, L.Y., et al., *Antimicrobial prescribing in dogs and cats in Australia: results of the Australasian infectious disease advisory panel survey.* Journal of Veterinary Internal Medicine, 2017. **31**(4): p. 1100-1107.
81. Sri, A. *Improvements in Australian veterinarians' use of antimicrobial prescribing resources*. in *Australian Veterinary Association Annual Conference 2024* 2024. Melbourne, Australia.
82. Adekanye, U.O., et al., *Knowledge, attitudes and practices of veterinarians towards antimicrobial resistance and stewardship in Nigeria.* Antibiotics, 2020. **9**(8).
83. Mateus, A.L., et al., *Qualitative study of factors associated with antimicrobial usage in seven small animal veterinary practices in the UK.* Prev Vet Med, 2014. **117**(1): p. 68-78.
84. Norris, J.M., et al., *Factors influencing the behaviour and perceptions of Australian veterinarians towards antibiotic use and antimicrobial resistance.* Plos One, 2019. **14**(10).
85. Weese, J.S., et al., *Evaluation of antimicrobial prescriptions in dogs with suspected bacterial urinary tract disease.* **n/a**(n/a).
86. Graham, M.M., M.T. James, and J.J. Spertus, *Decision support tools: realizing the potential to improve quality of care.* Canadian Journal of Cardiology, 2018. **34**(7): p. 821-826.
87. Catho, G., et al., *Study protocol for a multicentre, cluster randomised, superiority trial evaluating the impact of computerised decision support, audit and feedback on antibiotic use: the COMPuterized Antibiotic Stewardship Study (COMPASS).* BMJ Open, 2018. **8**(6): p. e022666.
88. Graham, M.M., M.T. James, and J.A. Spertus, *Decision Support Tools: Realizing the Potential to Improve Quality of Care.* Canadian Journal of Cardiology, 2018. **34**(7): p. 821-826.
89. Leibovici, L., et al., *The TREAT project: decision support and prediction using causal probabilistic networks.* International Journal of Antimicrobial Agents, 2007. **30**: p. 93-102.
90. Central Australian Rural Practitioners Association, *CARPA Standard Treatment Manual 8th Edition*. 2022.
91. Cuningham, W., et al., *Antimicrobial stewardship in remote primary healthcare across northern Australia.* Peerj, 2020. **8**.
92. Hardefeldt, L.Y., et al., *Antimicrobials used for surgical prophylaxis by companion animal veterinarians in Australia.* Vet Microbiol, 2017. **203**: p. 301-307.
93. Hardefeldt, L.Y., et al., *Cross-sectional study of antimicrobials used for surgical prophylaxis by bovine veterinary practitioners in Australia.* Vet Rec, 2017. **181**(16): p. 426.
94. Costelloe, C., et al., *Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis.* BMJ, 2010. **340**(may18 2): p. c2096-c2096.
95. Chatzopoulou, M. and L.J. Reynolds, *Role of antimicrobial restrictions in bacterial resistance control: a systematic literature review.* Journal of Hospital Infection, 2020. **104**(2): p. 125-136.

96. Zhuo, A., et al., *Opportunities and challenges to improving antibiotic prescribing practices through a One Health approach: results of a comparative survey of doctors, dentists and veterinarians in Australia.* BMJ Open, 2018. **8**(3): p. e020439.
97. Hardefeldt, L.Y., et al., *Barriers to and enablers of implementing antimicrobial stewardship programs in veterinary practices.* J Vet Intern Med, 2018. **32**(3): p. 1092-1099.
98. European Parliament, *Motion for a Resolution pursuant to Rule 111(3) of the Rules of Procedure on the Commission delegated regulation of 26 May 2021 supplementing Regulation (EU) 2019/6 of the European Parliament and of the Council by establishing the criteria for the designation of antimicrobials to be reserved for the treatment of certain infections in humans*. 2021.
99. European Parliament, *Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC*. 2018.
100. Government of France, *Ecoantibio 2 The French national plan for the reduction of the risks of antimicrobial resistance in veterinary medicine 2017-2021*, M.o.A.a.F. Sovereignty, Editor. 2017.
101. Prouillac, C., *Use of Antimicrobials in a French Veterinary Teaching Hospital: A Retrospective Study.* Antibiotics (Basel), 2021. **10**(11).
102. King, C., et al., *Exploring the behavioural drivers of veterinary surgeon antibiotic prescribing: a qualitative study of companion animal veterinary surgeons in the UK.* BMC Veterinary Research, 2018. **14**(1): p. 1-9.
103. Matt, S., et al., *Pet owner and vet interactions: exploring the drivers of AMR.* Antimicrobial Resistance and Infection Control, 2018. **7**(1): p. 1-9.
104. Zinsstag, J., et al., *One Health: the theory and practice of integrated health approaches*. 2020: CABI.
105. Steele, S.G., *Operationalising One Health: preparedness and response to zoonoses and emerging infectious diseases in Australia*. 2021.
106. Watego, C., et al., *Black to the Future: Making the Case for Indigenist Health Humanities.* International Journal of Environmental Research and Public Health, 2021. **18**(16): p. 8704.
107. Hillier, S.A., et al., *Examining the concept of One Health for indigenous communities: A systematic review.* One Health, 2021. **12**: p. 100248.
108. Gatwiri, K., D. Rotumah, and E. Rix, *BlackLivesMatter in Healthcare: Racism and Implications for Health Inequity among Aboriginal and Torres Strait Islander Peoples in Australia.* International Journal of Environmental Research and Public Health, 2021. **18**(9).
109. Cinquepalmi, V., et al., *Environmental Contamination by Dog's Faeces: A Public Health Problem?* International Journal of Environmental Research and Public Health, 2013. **10**(1): p. 72-84.
110. Finley, R.L., et al., *The Scourge of Antibiotic Resistance: The Important Role of the Environment.* Clinical Infectious Diseases, 2013. **57**(5): p. 704-710.
111. Keen, P.L. and M.H. Montforts, *Antimicrobial resistance in the environment*. 2011: John Wiley & Sons.
112. Pruden, A., et al., *Management Options for Reducing the Release of Antibiotics and Antibiotic Resistance Genes to the Environment.* Environmental Health Perspectives, 2013. **121**(8): p. 878-885.
113. Iwu, C.D., L. Korsten, and A.I. Okoh, *The incidence of antibiotic resistance within and beyond the agricultural ecosystem: A concern for public health.* MicrobiologyOpen, 2020. **9**(9): p. e1035.

114. Somayaji, R., et al., *Human infections due to Staphylococcus pseudintermedius, an emerging zoonosis of canine origin: report of 24 cases.* Diagnostic Microbiology and Infectious Disease, 2016. **85**(4): p. 471-476.
115. Iverson, S.A., et al., *Anatomical patterns of colonization of pets with staphylococcal species in homes of people with methicillin-resistant Staphylococcus aureus (MRSA) skin or soft tissue infection (SSTI).* Veterinary Microbiology, 2015. **176**(1): p. 202-208.
116. Degeling, C., et al., *A delphi survey and analysis of expert perspectives on one health in Australia.* 2017. **14**(4): p. 783-792.
117. Hannah, A. and E.J.P.s. Baekkeskov, *The promises and pitfalls of polysemic ideas:'One Health'and antimicrobial resistance policy in Australia and the UK.* 2020. **53**: p. 437-452.
118. Tang, K.L., et al., *Restricting the use of antibiotics in food-producing animals and its associations with antibiotic resistance in food-producing animals and human beings: a systematic review and meta-analysis.* The Lancet Planetary Health, 2017. **1**(8): p. 316-327.
119. Joosten, P., et al., *Antimicrobial Usage and Resistance in Companion Animals: A Cross-Sectional Study in Three European Countries.* Antibiotics-Basel, 2020. **9**(2).
120. Leekitcharoenphon, P., et al., *Genomic evolution of antimicrobial resistance in Escherichia coli.* Scientific Reports, 2021. **11**(1): p. 15108.
121. Kurita, G., et al., *Reduced rates of antimicrobial resistance in Staphylococcus intermedius group and Escherichia coli isolated from diseased companion animals in an animal hospital after restriction of antimicrobial use.* Journal of Infection and Chemotherapy, 2019. **25**(7): p. 531-536.
122. Brealey, J.C., et al., *The oral microbiota of wild bears in Sweden reflects the history of antibiotic use by humans.* Current Biology, 2021. **31**: p. 1-9.
123. Nelson, J.M., et al., *Fluoroquinolone-Resistant Campylobacter Species and the Withdrawal of Fluoroquinolones from Use in Poultry: A Public Health Success Story.* Clinical Infectious Diseases, 2007. **44**(7): p. 977-980.
124. Cocker, D., et al., *Healthcare as a driver, reservoir and amplifier of antimicrobial resistance: opportunities for interventions.* Nature Reviews Microbiology, 2024. **22**(10): p. 636-649.
125. Checcucci, A., et al., *Exploring the Animal Waste Resistome: The Spread of Antimicrobial Resistance Genes Through the Use of Livestock Manure.* 2020. **11**.
126. Hendriksen, R.S., et al., *Global monitoring of antimicrobial resistance based on metagenomics analyses of urban sewage.* Nature Communications, 2019. **10**.
127. von Eiff, C., G. Peters, and C. Heilmann, *Pathogenesis of infections due to coagulasenegative staphylococci.* The Lancet Infectious Diseases, 2002. **2**(11): p. 677-685.
128. Gomez-Sanz, E., et al., *Clonally Diverse Methicillin and Multidrug Resistant Coagulase Negative Staphylococci Are Ubiquitous and Pose Transfer Ability Between Pets and Their Owners.* Frontiers in Microbiology, 2019. **10**.
129. Webb, H.E., et al., *Illustrative examples of probable transfer of resistance determinants from food animals to humans: Streptothricins, glycopeptides, and colistin.* 2017. **6**.
130. Santaniello, A., et al., *Systematic Review and Meta-Analysis of the Occurrence of ESKAPE Bacteria Group in Dogs, and the Related Zoonotic Risk in Animal-Assisted Therapy, and in Animal-Assisted Activity in the Health Context.* International Journal of Environmental Research and Public Health, 2020. **17**(9): p. 3278.
131. Alliance to Save Our Antibiotics, *Alliance to Save Our Antibiotics – Written Evidence*. 2020: Online.
132. Laxminarayan, R., et al., *Antibiotic resistance—the need for global solutions.* The Lancet Infectious Diseases, 2013. **13**(12): p. 1057-1098.

133. Wielinga, P.R., et al., *Evidence-based policy for controlling antimicrobial resistance in the food chain in Denmark.* FOOD CONTROL, 2014. **40**: p. 185-192.
134. Mader, R., et al., *Building the European Antimicrobial Resistance Surveillance network in veterinary medicine (EARS-Vet).* Eurosurveillance, 2021. **26**(4).
135. More, S.J., *European perspectives on efforts to reduce antimicrobial usage in food animal production.* Irish Veterinary Journal, 2020. **73**(1).
136. Lagrange, J., et al., *Pilot testing the EARS-Vet surveillance network for antibiotic resistance in bacterial pathogens from animals in the EU/EEA.* 2023. **14 - 2023**.
137. Mader, R., et al., *Defining the scope of the European Antimicrobial Resistance Surveillance network in Veterinary medicine (EARS-Vet): a bottom-up and One Health approach.* Journal of Antimicrobial Chemotherapy, 2022. **77**(3): p. 816-826.
138. Becket, S., Heller, Jane., Langstaff, I., Norris, J.,, *Quantifying antimicrobial usage in Australian companion and production animals: CSIRO Project report*. 2022.
139. Wozniak, T., et al., *Geospatial epidemiology of Staphylococcus aureus in a tropical setting: an enabling digital surveillance platform.* 2020. **10**(1): p. 1-10.
140. Bowen, A.C., et al., *An urgent need for antimicrobial stewardship in Indigenous rural and remote primary health care.* Medical Journal of Australia, 2019. **211**(1): p. 9.
141. Parsonage, B., et al., *Control of Antimicrobial Resistance Requires an Ethical Approach.* 2017. **8**(2124).
142. Garau, J., *Impact of antibiotic restrictions: the ethical perspective.* Clinical Microbiology and Infection, 2006. **12**: p. 16-24.
143. Price, D., *Impact of antibiotic restrictions: the physician's perspective.* Clinical Microbiology and Infection, 2006. **12**: p. 3-9.
144. Bradbury, L. and S. Corlette, *Dog health program in Numbulwar, a remote Aboriginal community in east Arnhem Land.* Australian veterinary journal, 2006. **84**(9): p. 317-320.
145. Brookes, V.J., et al., *One Health promotion and the politics of dog management in remote, northern Australian communities.* Scientific Reports, 2020. **10**(1).
146. Meagher, K.M., et al., *The New Precision Stewards?* Journal of Personalized Medicine, 2022. **12**(8): p. 1308.
147. Brookes, V.J., et al., *Qualitative Research to Design Sustainable Community-Based Surveillance for Rabies in Northern Australia and Papua New Guinea.* Front Vet Sci, 2017. **4**: p. 19.
148. Tong, S.Y.C., et al., *Impact of ethnicity and socio-economic status on Staphylococcus aureus bacteremia incidence and mortality: a heavy burden in Indigenous Australians.* Bmc Infectious Diseases, 2012. **12**.
149. Tong, S.Y.C., et al., *Progressive increase in community-associated methicillin-resistant Staphylococcus aureus in Indigenous populations in northern Australia from 1993 to 2012.* Epidemiology and Infection, 2015. **143**(7): p. 1519-1523.
150. Saputra, S., et al., *Antimicrobial resistance in coagulase-positive staphylococci isolated from companion animals in Australia: A one year study.* PLOS ONE, 2017. **12**(4): p. e0176379.
151. Ma, G.C., et al., *Commensal Staphylococci Including Methicillin-Resistant Staphylococcus aureus from Dogs and Cats in Remote New South Wales, Australia.* Microbial Ecology, 2020. **79**(1): p. 164.
152. Rusdi, B., et al., *Carriage of critically important antimicrobial resistant bacteria and zoonotic parasites amongst camp dogs in remote Western Australian indigenous communities.* Scientific reports, 2018. **8**(1): p. 8725.

153. Worthing, K.A., et al., *Methicillin-resistant staphylococci amongst veterinary personnel, personnel-owned pets, patients and the hospital environment of two small animal veterinary hospitals.* Veterinary Microbiology, 2018. **223**: p. 79-85.
154. Worthing, K.A., et al., *Qac genes and biocide tolerance in clinical veterinary methicillin-resistant and methicillin-susceptible Staphylococcus aureus and Staphylococcus pseudintermedius.* Veterinary Microbiology, 2018. **216**: p. 153-158.
155. Bhooshan, S., V. Negi, and P.K. Khatri, *Staphylococcus pseudintermedius: an undocumented, emerging pathogen in humans.* Gms Hygiene and Infection Control, 2020. **15**.
156. Morris, D.O., et al., *Recommendations for approaches to meticillin-resistant staphylococcal infections of small animals: diagnosis, therapeutic considerations and preventative measures.: Clinical Consensus Guidelines of the World Association for Veterinary Dermatology.* Veterinary Dermatology, 2017. **28**(3): p. 304-+.
157. Somayaji, R., et al., *Exploring Staphylococcus pseudintermedius: an emerging zoonotic pathogen?* Future Microbiology, 2016. **11**(11): p. 1371-1374.
158. Yadav, R., et al., *Prevalence and antibiotyping of Staphylococcus aureus and methicillin-resistant S. aureus (MRSA) in domestic animals in India.* Journal of Global Antimicrobial Resistance, 2018. **15**: p. 222-225.
159. Fessler, A.T., et al., *Methicillin-resistant Staphylococcus aureus (MRSA) and methicillin-resistant Staphylococcus pseudintermedius (MRSP) among employees and in the environment of a small animal hospital.* Veterinary Microbiology, 2018. **221**: p. 153-158.
160. Van Den Bunt, G., et al., *Faecal carriage, risk factors, acquisition and persistence of ESBL-producing Enterobacteriaceae in dogs and cats and co-carriage with humans belonging to the same household.* Journal of Antimicrobial Chemotherapy, 2020. **75**(2): p. 342-350.
161. Bannoehr, J. and L. Guardabassi, *Staphylococcus pseudintermedius in the dog: taxonomy, diagnostics, ecology, epidemiology and pathogenicity.* Veterinary Dermatology, 2012. **23**(4): p. 253-E52.
162. Marmot, M. and R. Wilkinson, *Social determinants of health*. 2005: Oxford.
163. Kim, C., et al., *Health Equity and Antibiotic Prescribing in the United States: A Systematic Scoping Review.* Open Forum Infectious Diseases, 2023. **10**(9).
164. Centers for Disease Control and Prevention. *CDC's Priority to Address Health Equity Issues Across Antibiotic-Resistant Threats*. 2022 [cited 2023 11 September]; Available from: https://www.cdc.gov/drugresistance/solutions-initiative/stories/ar-health-equity.html#:~:text=Many%20risks%20for%20antibiotic%2Dresistant,outcomes%20and%20quality%20of%20life.
165. Broom, A., et al., *Antibiotic optimisation in 'the bush': Local know-how and core-periphery relations.* Health & Place, 2017. **48**: p. 56-62.
166. Steven, et al., *Global Implications of the Emergence of Community-Associated Methicillin-Resistant Staphylococcus aureus in Indigenous Populations.* Clinical Infectious Diseases, 2008. **46**(12): p. 1871-1878.
167. Wozniak, T.M., et al., *Contribution of socio-economic factors in the spread of antimicrobial resistant infections in Australian primary healthcare clinics.* Journal of Global Antimicrobial Resistance, 2022. **30**: p. 294-301.
168. Warambula, D. and R. Brand, *Caring for Your Dog - Animal Care at Galiwin'ku.* Aboriginal and Islander Health Worker Journal, 1979. **3**(2): p. 8-12.
169. Schurer, J.M., et al., *Stabilizing Dog Populations and Improving Animal and Public Health Through a Participatory Approach in Indigenous Communities.* Zoonoses and Public Health, 2015. **62**(6): p. 445-455.

170. Constable, S., R. Dixon, and R.J.A. Dixon, *For the love of dog: the human–dog bond in rural and remote Australian indigenous communities.* 2010. **23**(4): p. 337-349.
171. Raw, C., et al., *A systematic review and meta-analysis of human and zoonotic dog soil-transmitted helminth infections in Australian Indigenous communities.* PLOS Neglected Tropical Diseases, 2022. **16**(10): p. e0010895.
172. Maguire, G.P., et al., *Emerging epidemic of community-acquired methicillin-resistant Staphylococcus aureus infection in the Northern Territory.* Medical Journal of Australia, 1996. **164**(12): p. 721-723.
173. Hardefeldt, L.Y., et al., *Population wide assessment of antimicrobial use in dogs and cats using a novel data source - A cohort study using pet insurance data.* Veterinary Microbiology, 2018. **225**: p. 34-39.
174. Jordan, D., et al., *Antimicrobial use in the Australian pig industry: results of a national survey.* Australian Veterinary Journal, 2009. **87**(6): p. 222-229.
175. Cuningham, W., et al., *Antimicrobial stewardship in remote primary healthcare across northern Australia.* PeerJ, 2020. **8**: p. e9409.
176. Wang, H., et al., *Estimating excess mortality due to the COVID-19 pandemic: a systematic analysis of COVID-19-related mortality, 2020–21.* The Lancet, 2022. **399**(10334): p. 1513-1536.
177. World Health Organization, *Global antimicrobial resistance and use surveillance system (GLASS) report: 2021*. 2021, World Health Organization: Geneva, Switzerland.
178. Australian Pesticides and Veterinary Medicines Authority. *Substances not permitted for use on food-producing animals in Australia*. 2014 [cited 2022 12 January]; Available from: https://apvma.gov.au/node/11626.
179. Jordan, D. *Antimicrobial resistance in food animals – national and international developments*. Flock & Herd Case Notes 2016 [cited 2022 14 June]; Available from: https://www.flockandherd.net.au/other/reader/antimicrobial-resistance.html.
180. Barlow, R.S., et al., *Prevalence and Antimicrobial Resistance of Salmonella and Escherichia coli from Australian Cattle Populations at Slaughter.* Journal of Food Protection, 2015. **78**(5): p. 912-920.
181. Abraham, S., et al., *Salmonella enterica isolated from infections in Australian livestock remain susceptible to critical antimicrobials.* International Journal of Antimicrobial Agents, 2014. **43**(2): p. 126-130.
182. Claeys, K.C., et al., *Fluoroquinolone restriction as an effective antimicrobial stewardship intervention.* Current Infectious Disease Reports, 2018. **20**(5).
183. Jiang, X.P., et al., *Analysis of fecal microbial flora for antibiotic resistance in ceftiofur-treated calves.* Foodborne Pathogens and Disease, 2006. **3**(4): p. 355-365.
184. Dutil, L., et al., *Ceftiofur resistance in Salmonella enterica serovar Heidelberg from chicken meat and humans, Canada.* Emerging Infectious Diseases, 2010. **16**(1): p. 48-54.
185. Sparham, S.J., et al., *Emergence of multidrug resistance in locally-acquired human infections with Salmonella Typhimurium in Australia owing to a new clade harbouring blaCTX-M-9.* International Journal of Antimicrobial Agents, 2017. **50**(1): p. 101-105.
186. Vieira, A.R., et al., *Association between antimicrobial resistance in Escherichia coli isolates from food animals and blood stream isolates from humans in Europe: An ecological study.* Foodborne Pathogens and Disease, 2011. **8**(12): p. 1295-1301.
187. Kieke, A.L., et al., *Use of streptogramin growth promoters in poultry and isolation of streptogramin-resistant Enterococcus faecium from humans.* Journal of Infectious Diseases, 2006. **194**(9): p. 1200-1208.

188. Pitiriga, V., et al., *The impact of antibiotic stewardship programs in combating quinolone resistance: a systematic review and recommendations for more efficient interventions.* Advances in Therapy, 2017. **34**(4): p. 854-865.
189. Aarestrup, F.M., et al., *Effect of abolishment of the use of antimicrobial agents for growth promotion on occurrence of antimicrobial resistance in fecal enterococci from food animals in Denmark.* Antimicrobial Agents and Chemotherapy, 2001. **45**(7): p. 2054-2059.
190. Agersø, Y. and F.M. Aarestrup, *Voluntary ban on cephalosporin use in Danish pig production has effectively reduced extended-spectrum cephalosporinase-producing Escherichia coli in slaughter pigs.* Journal of Antimicrobial Chemotherapy, 2012. **68**(3): p. 569-572.
191. Li, W., et al., *Dramatic decrease in colistin resistance in Escherichia coli from a typical pig farm following restriction of colistin use in China.* International Journal of Antimicrobial Agents, 2019. **53**(5): p. 707-708.
192. Nobrega, D.B., et al., *Prevalence of antimicrobial resistance genes and its association with restricted antimicrobial use in food-producing animals: a systematic review and meta-analysis.* Journal of Antimicrobial Chemotherapy, 2021. **76**(3): p. 561-575.
193. Belay, D.G. and J.D. Jensen, *'The scarlet letters': Information disclosure and self-regulation: Evidence from antibiotic use in Denmark.* Journal of Environmental Economics and Management, 2020. **104**.
194. Maron, D.F., T.J.S. Smith, and K.E. Nachman, *Restrictions on antimicrobial use in food animal production: an international regulatory and economic survey.* Globalization and Health, 2013. **9**(1): p. 48.
195. Rodrigues Da Costa, M. and A. Diana, *A Systematic Review on the Link between Animal Welfare and Antimicrobial Use in Captive Animals.* Animals, 2022. **12**(8): p. 1025.
196. Australian Veterinary Association, *Australian Veterinary Workforce Survey 2018*. 2019, Australian Veterinary Association: Canberra, Australia.
197. Australian Veterinary Association, *Veterinary Workforce Survey 2021 Analysis Report*. 2022, Australian Veterinary Association: Canberra, Australia.
198. Hardefeldt, L., et al., *Veterinary students' knowledge and perceptions about antimicrobial stewardship and biosecurity-a national survey.* Antibiotics, 2018. **7**(2).
199. McClelland, J.W., et al., *Knowledge and perceptions of Australian postgraduate veterinary students prior to formal education of antimicrobial use and antimicrobial resistance.* One Health, 2022. **14**: p. 100366.
200. Tarrant, C., et al., *Optimizing antibiotic prescribing: collective approaches to managing a common-pool resource.* Clinical Microbiology and Infection, 2019. **25**(11): p. 1356-1363.
201. Yarrington, M.E., et al., *Well-being tradeoffs: Effect of loosening overnight restrictions on antimicrobial starts.* Infection Control & Hospital Epidemiology, 2022. **43**(2): p. 255-257.
202. Chin, J., et al., *Restriction-free antimicrobial stewardship initiative targeting fluoroquinolone reduction across a regional health-system.* Infection Prevention in Practice, 2019. **1**(2): p. 100019.
203. Reed, E.E., et al., *Impact of formulary restriction with prior authorization by an antimicrobial stewardship program.* Virulence, 2013. **4**(2): p. 158-162.
204. Moerer, M., R. Merle, and W. Bäumer, *A cross-sectional study of veterinarians in Germany on the impact of the TÄHAV amendment 2018 on antimicrobial use and development of antimicrobial resistance in dogs and cats.* Antibiotics, 2022. **11**(4): p. 484.
205. Avent, M.L., et al., *Antimicrobial stewardship activities: a survey of Queensland hospitals.* Australian Health Review, 2014. **38**(5): p. 557-563.

206. Ierano, C., et al., *Antibiotic prescribing in surgery: a clinically and socially complex problem in Australia.* Infection, Disease & Health, 2020. **25**(4): p. 309-313.
207. Nadrah, K., et al., *Impact of cephalosporin restriction on incidence of infections with extended-spectrum beta-lactamase-producing Klebsiella pneumoniae in an endemic setting.* Journal of Chemotherapy, 2018. **30**(3): p. 150-156.
208. Hamilton, K.W., et al., *Point-of-prescription interventions to improve antimicrobial stewardship.* Clinical Infectious Diseases, 2015. **60**(8): p. 1252-1258.
209. Van Dort, B.A., et al., *The impact of digital interventions on antimicrobial stewardship in hospitals: a qualitative synthesis of systematic reviews.* Journal of Antimicrobial Chemotherapy, 2022.
210. McEwen, S.A. and P.J. Collignon, *Antimicrobial Resistance: a One Health Perspective.* Microbiology Spectrum, 2018. **6**(2): p. UNSP ARBA-0009-2017.
211. Scarborough, R., et al., *Pet Owners and Antibiotics: Knowledge, Opinions, Expectations, and Communication Preferences.* Antibiotics-Basel, 2021. **10**(11).
212. Smith, M., et al., *Pet owner and vet interactions: exploring the drivers of AMR.* Antimicrobial Resistance and Infection Control, 2018. **7**.
213. Doidge, C., et al., *To prescribe or not to prescribe? A factorial survey to explore veterinarians' decision making when prescribing antimicrobials to sheep and beef farmers in the UK.* PLOS ONE, 2019. **14**(4): p. e0213855.
214. Lewis, P.J. and M.P. Tully, *Uncomfortable prescribing decisions in hospitals: the impact of teamwork.* Journal of the Royal Society of Medicine, 2009. **102**(11): p. 481-488.
215. Tree, M., et al., *Antimicrobial use on Australian dairy cattle farms - A survey of veterinarians.* Preventive veterinary medicine, 2022. **202**.
216. Steele, S.G., S.M. Mor, and J.L.M.L. Toribio, *'It's our job': Constraints to investigation of atypical disease events—Opinions of Australian veterinarians.* Zoonoses and Public Health, 2021. **68**(5): p. 493-502.
217. Robinson, T.P., et al., *Antibiotic resistance is the quintessential One Health issue.* Transactions of The Royal Society of Tropical Medicine and Hygiene, 2016. **110**(7): p. 377-380.
218. Djordjevic, S. and B.S. Morgan, *A One Health genomic approach to antimicrobial resistance is essential for generating relevant data for a holistic assessment of the biggest threat to public health.* Microbiology Australia, 2019. **40**: p. 73-76.
219. Australian Pesticides and Veterinary Medicines Authority. *Public Chemical Registration Information System Search - Convenia*. 2022 20 January 20 September]; Available from: https://websvr.infopest.com.au/LabelRouter?LabelType=L&Mode=1&ProductCode=60461 .
220. Hubbuch, A., et al., *Antimicrobial prescriptions in cats in Switzerland before and after the introduction of an online antimicrobial stewardship tool.* BMC Veterinary Research, 2020. **16**(1): p. 229.
221. Burke, S., et al., *Use of cefovecin in a UK population of cats attending first-opinion practices as recorded in electronic health records.* Journal of Feline Medicine and Surgery, 2017. **19**(6): p. 687-692.
222. Taylor, E., *We Agree, Don't We? The Delphi Method for Health Environments Research.* HERD, 2020. **13**(1): p. 11-23.
223. Khanina, A., et al., *Establishing essential metrics for antifungal stewardship in hospitals: the results of an international Delphi survey.* Journal of Antimicrobial Chemotherapy, 2021. **76**(1): p. 253-262.

224. Keeney, S., F. Hasson, and H. McKenna, *Consulting the oracle: ten lessons from using the Delphi technique in nursing research.* 2006. **53**(2): p. 205-212.
225. Richmond, J., et al., *Developing the Australasian Hepatology Association's consensus-based guidelines for the nursing care of patients with liver disease.* Contemporary Nurse, 2014. **48**(1): p. 36-45.
226. Weese, J.S., et al., *ACVIM Consensus Statement on Therapeutic Antimicrobial Use in Animals and Antimicrobial Resistance.* Journal of Veterinary Internal Medicine, 2015. **29**(2): p. 487-498.
227. McEwen, S.A. and P.J. Collignon, *Antimicrobial Resistance: a One Health Perspective*. Antimicrobial Resistance in Bacteria from Livestock and Companion Animals, ed. S. Schwarz, L.M. Cavaco, and J. Shen. 2018. 521-547.
228. Jordan, D., *Antimicrobial ratings: the importance of importance.* 2019. **97**(8): p. 283-284.
229. Sri, A., et al., *Attitudes towards use of high-importance antimicrobials-A cross-sectional study of Australian veterinarians.* Antibiotics, 2022. **11**.
230. Hasson, F., S. Keeney, and H. McKenna, *Research guidelines for the Delphi survey technique.* Journal of Advanced Nursing, 2000. **32**(4): p. 1008-1015.
231. Hawkins, O., et al., *Comparing public attitudes, knowledge, beliefs and behaviours towards antibiotics and antimicrobial resistance in Australia, United Kingdom, and Sweden (2010-2021): A systematic review, meta-analysis, and comparative policy analysis.* PLOS ONE, 2022. **17**(1): p. e0261917.
232. Hardefeldt, L., et al., *Antimicrobial stewardship in companion animal practice: an implementation trial in 135 general practice veterinary clinics.* JAC-Antimicrobial Resistance 2022. **4**(1).
233. Scarborough, R.O., et al., *'Brave Enough': A Qualitative Study of Veterinary Decisions to Withhold or Delay Antimicrobial Treatment in Pets.* Antibiotics, 2023. **12**(3): p. 540.
234. Hur, B., et al., *Evaluating the dose, indication and agreement with guidelines of antimicrobial use in companion animal practice with natural language processing.* JAC-Antimicrobial Resistance, 2021. **4**(1).
235. Linstone, H.A. and M. Turoff, *Delphi: A brief look backward and forward.* Technological Forecasting and Social Change, 2011. **78**(9): p. 1712-1719.
236. Beck, K.M., et al., *Prevalence of meticillin-resistant Staphylococcus pseudintermedius (MRSP) from skin and carriage sites of dogs after treatment of their meticillin-resistant or meticillin-sensitive staphylococcal pyoderma.* 2012. **23**(4): p. 369-e67.
237. Bemis, D.A., et al., *Evaluation of susceptibility test breakpoints used to predict mecA-mediated resistance in Staphylococcus pseudintermedius isolated from dogs.* Journal of Veterinary Diagnostic Investigation, 2009. **21**(1): p. 53-58.
238. Teixeira, I.M., E.D. Ferreira, and B.D. Penna, *Dogs as reservoir of methicillin resistant coagulase negative staphylococci strains - possible neglected risk.* Microbial Pathogenesis, 2019. **135**.
239. Kern, A. and V. Perreten, *Clinical and molecular features of methicillin-resistant, coagulase-negative staphylococci of pets and horses.* J Antimicrob Chemother, 2013. **68**(6): p. 1256-66.
240. Miragaia, M., *Factors contributing to the evolution of mecA-mediated β-lactam resistance in staphylococci: update and new insights from whole genome sequencing (WGS).* Frontiers in microbiology, 2018. **9**: p. 396897.
241. Rossi, C.C., A.L. Andrade-Oliveira, and M. Giambiagi-deMarval, *CRISPR tracking reveals global spreading of antimicrobial resistance genes by Staphylococcus of canine origin.* Veterinary Microbiology, 2019. **232**: p. 65-69.

242. Ocloo, R., et al., *Epidemiology and antimicrobial resistance of staphylococci other than Staphylococcus aureus from domestic animals and livestock in Africa: a systematic review.* Frontiers in Veterinary Science, 2022. **9**.
243. Rossi, C.C., M.F. Pereira, and M. Giambiagi-DeMarval, *Underrated <i>Staphylococcus</i> species and their role in antimicrobial resistance spreading.* GENETICS AND MOLECULAR BIOLOGY, 2020. **43**(1).
244. Ma, G.C., et al., *Molecular characterization of community-associated methicillin-resistant Staphylococcus aureus from pet dogs.* Zoonoses and Public Health, 2020. **67**(3): p. 222-230.
245. Neave, M.J., et al., *Comparative genomic analysis of the first Ehrlichia canis detections in Australia.* Ticks and Tick-Borne Diseases, 2022. **13**(3).
246. Bean, D.C. and S.M. Wigmore, *Carriage rate and antibiotic susceptibility of coagulase-positive staphylococci isolated from healthy dogs in Victoria, Australia.* Australian Veterinary Journal, 2016. **94**(12): p. 456-460.
247. Rynhoud, H., et al., *Molecular Epidemiology of Clinical and Colonizing Methicillin-Resistant Staphylococcus Isolates in Companion Animals.* Frontiers in Veterinary Science, 2021. **8**.
248. Siak, M., et al., *Characterization of meticillin-resistant and meticillin-susceptible isolates of Staphylococcus pseudintermedius from cases of canine pyoderma in Australia.* Journal of Medical Microbiology, 2014. **63**: p. 1228-1233.
249. Schmidt, V.M., et al., *Impact of systemic antimicrobial therapy on mucosal staphylococci in a population of dogs in Northwest England.* 2018. **29**(3): p. 192-e70.
250. Daley, P., et al., *A cross sectional study of animal and human colonization with Methicillin-Resistant Staphylococcus aureus (MRSA) in an Aboriginal community.* BMC Public Health, 2016. **16**(1): p. 1-7.
251. IATA, *Dangerous Goods Regulations*, in *Packing Instruction 650*. 2023: Online. p. 569-571.
252. Labcabs. *Packaging options for all your shipping requirements.* . 2025 [cited 2024 20 February]; Available from: https://labcabs.com.au/useful-info/.
253. Tompson, A.C., et al., *What drives antimicrobial prescribing for companion animals? A mixed-methods study of UK veterinary clinics.* Preventive Veterinary Medicine, 2020. **183**: p. 105117.
254. Tompson, A.C., et al., *Understanding Antibiotic Use in Companion Animals: A Literature Review Identifying Avenues for Future Efforts.* Front Vet Sci, 2021. **8**: p. 719547.
255. Hobi, S., V.R. Barrs, and P.M. Bęczkowski *Dermatological Problems of Brachycephalic Dogs*. Animals, 2023. **13**, DOI: 10.3390/ani13122016.
256. Hall, N.L., *Challenges of WASH in remote Australian Indigenous communities.* Journal of Water, Sanitation and Hygiene for Development, 2019. **9**(3): p. 429-437.
257. Wallace, R.G., et al., *The dawn of Structural One Health: A new science tracking disease emergence along circuits of capital.* Social Science & Medicine, 2015. **129**: p. 68-77.
258. Laurie Denyer, W. and C. Clare, *Quick fix for care, productivity, hygiene and inequality: reframing the entrenched problem of antibiotic overuse.* BMJ Global Health, 2019. **4**(4): p. e001590.
259. Plaisime, M.V., M. Jipguep-Akhtar, and H.M.E. Belcher, *'White People are the default': A qualitative analysis of medical trainees' perceptions of cultural competency, medical culture, and racial bias.* SSM - Qualitative Research in Health, 2023. **4**: p. 100312.
260. Davis, M.D.M., et al., *Fragmentation in One Health policy and practice responses to antimicrobial resistance and the salutary value of collaborative humility.* 2024. **22**(3): p. 230-247.

261. Bullen, J., et al., *From Deficit to Strength-Based Aboriginal Health Research-Moving toward Flourishing.* International journal of environmental research and public health, 2023. **20**(7).
262. Tompson, A.C., L. Manderson, and C.I.R. Chandler, *Understanding antibiotic use: practices, structures and networks.* Jac-Antimicrobial Resistance, 2021. **3**(4).
263. Olmos-Vega, F.M., et al., *A practical guide to reflexivity in qualitative research: AMEE Guide No. 149.* Medical Teacher, 2023. **45**(3): p. 241-251.
264. Riley, T., et al., *One Health in Indigenous Communities: A Critical Review of the Evidence.* International Journal of Environmental Research and Public Health, 2021. **18**(21): p. 11303.
265. Bourke, C., et al., *Perspectives Brief: Confronting racism to improve healthcare for Aboriginal and Torres Strait Islander patients with kidney disease.* 2020.
266. Woodburn, J., *Racism blamed for Aboriginal patients' distrust of NSW public health system*. 2021, ABC News. p. https://www.abc.net.au/news/2021-03-15/cultural-barriers-to-healthcare-in-nsw/13229218.
267. Gara, C., *Black Lives Matter in Medicine: What Must Change?* 2020. p. https://www.hopkinsmedicine.org/news/articles/2020/09/black-lives-matter-in-medicine-what-must-change.
268. van Dijk, T.A., *Discourse and the Denial of Racism.* 1992. **3**(1): p. 87-118.
269. Darcy, M., et al., *Multicomponent approaches to promoting healthy behaviours in people with Type 2 diabetes: an integrative review.* Health Promotion International, 2023. **38**(3).
270. Abrams, E.M. and S.J. Szefler, *COVID-19 and the impact of social determinants of health.* The Lancet Respiratory Medicine, 2020. **8**(7): p. 659-661.
271. Kelaita, P., et al., *Pandemic policing and the construction of publics: an analysis of COVID-19 lockdowns in public housing.* Health Sociology Review, 2023. **32**(3): p. 245-260.
272. Mariner, W.K., *Beyond Lifestyle: Governing the Social Determinants of Health.* American Journal of Law & Medicine, 2016. **42**(2-3): p. 284-309.
273. Laycock, A., et al., *Researching Indigenous Health: a practical guide for researchers*. 2011, Lowitja Institute.
274. Bowen, A.C., et al., *Capacity building to address antimicrobial resistance in remote Australia: The inaugural HOT NORTH Antimicrobial Academy.* Infection Disease & Health, 2024. **29**(3): p. 117-123.
275. NACCHO. *NACCHO Antimicrobial Stewardship Academy*. 2024 [cited 2025 28th February]; Available from: https://www.naccho.org.au/medicines-and-pharmacy/ams-academy/.
276. Bond, M.P.E., *Guidelines for Prescribing, Authorising and Dispensing Veterinary Medicines*. 2005, Australian Veterinary Association Ltd.
277. *Delivering an Australian CDC*. 2024.
278. Steele, S.G., R. Booy, and S.M. Mor, *Establishing research priorities to improve the One Health efficacy of Australian general practitioners and veterinarians with regard to zoonoses: A modified Delphi survey.* One Health, 2018. **6**: p. 7-15.

Appendices

Appendix I Survey questions for veterinarians (Chapter 2)

Use of Antimicrobials with High Importance to Human Medicine by Vets

INFORMATION ABOUT YOU

What type of veterinary work are you currently employed to do?
First opinion/general Emergency
Referral
University - teaching & research University - clinical
Government
Industry/pharmaceutical

Where is your workplace located?
Metropolitan (population >100,000)
Rural

How many veterinarians are employed in your workplace?
○ 1 or 2
○ 3 or 4
○ 5-10
○ 11-20
○ >20

In which state do you practice?
○ ACT ○ NSW ○ NT ○ SA ○ QLD ○ TAS ○ VIC ○ WA

Gender
Male
Female
Non-binary
Rather not say

What is your position in the workplace?
Partner
Associate
Locum/casual Other

What year did you graduate?

Do you hold post-graduate qualifications in veterinary medicine?
Yes
No

What qualifications do you have?
Membership Masters
Certificate
Specialist (Fellowship or Diplomate) Diploma
PhD
Other

Antimicrobials with high importance for human medicine in Australia are classified by the Australian Strategic and Technical Advisory Group on AMR (ASTAG). Here's an example: You can also access the classifications at this link.

Have you heard of this rating system?
Yes
No

Do you use a traffic-light system for antimicrobial importance in your workplace?
Yes
No

In medical general practice, doctors have to get approval to prescribe high-importance antimicrobials to patients. This is not the case in veterinary practice. **Do you agree that veterinarians should be able to prescribe antibiotics with high importance to human medicine without restrictions?**

Strongly agree
Agree
Somewhat agree
Neither agree nor disagree
Somewhat disagree
Disagree
Strongly disagree

Referring to the graphic above, if there were to be restrictions placed on veterinary prescribing of antimicrobials, which antimicrobials should they apply to?
Select on scale Strongly agree Somewhat agree Neither agree nor disagree Somewhat disagree Strongly disagree

All antimicrobials
Antimicrobials with medium and high importance rating
All antimicrobials with high importance rating
All high importance rating antimicrobials except 3rd generation cephalosporins (ceftiofur & cefovecin) and fluoroquinolone (enrofloxacin, marbofloxacin etc)
All high importance rating antimicrobials except 3rd generation cephalosporins (ceftiofur & cefovecin)
All high importance rating antimicrobials except fluoroquinolone (enrofloxacin, marbofloxacin etc)

If there were to be restrictions placed on veterinary prescribing of antimicrobials with high importance rating , which of the following do you think is appropriate?
Select on scale from Strongly agree, Somewhat agree, Neither agree nor disagree, Somewhat disagree, Strongly disagree

These antimicrobials must not be allowed to be used in veterinary medicine under any circumstance
These antimicrobials must never allowed to be used in food-producing animals but can be used in other animals
Use can only proceed with approval from an independent office

Use in referral hospitals is allowed without approval
Use in general practice requires approval from an independent office
Use is only allowed after culture and susceptibility testing confirms that the pathogen is resistant to all low and medium rated antimicrobials that could be used to treat the case
Use is allowed after treatment failure with a lower importance rating antimicrobials
Use is allowed in critically ill animals
Other restrictions

What other restrictions do you think are appropriate? (free text)

Please indicate how strongly you agree with the following statements:
Agree, Unsure, Disagree

Approval is still required prior to high importance drugs being used in veterinary medicine:
If culture and susceptibility testing confirms that the pathogen is resistant to all low and medium rated antimicrobials that could be used to treat the case
If treatment has failed with a lower importance rating antimicrobial
in critically ill animals

Would you like to tell us anything else about the role in veterinary medicine of antimicrobials with high importance to human medicine? (free text)

SOME CASE SCENARIOS

A cat presents with a draining abscess on its face. While the cat is febrile and inappetent and you
believe that antimicrobial therapy is indicated, you do not think that the infection is life-threatening.
Under which circumstances is it reasonable to treat this cat with cefovecin (long-acting 3rd generation cephalosporin), an antimicrobial with a high importance rating?

Select from Strongly agree; Somewhat agree; Neither agree nor disagree; Somewhat disagree; Strongly disagree

If the cat is difficult to medicate
If you give the owner options of either oral or injectable antimicrobials and they choose cefovecin
If culture and susceptibility testing
indicates that the pathogen is resistant to all low and medium rated antimicrobials that could be used to treat the case
With approval from an independent office
Always

A horse presents with a septic fetlock joint that could be life-threatening. Under which circumstances is it reasonable to inject the joint with amikacin, a high importance rated aminoglycoside?
Select from Strongly agree; Somewhat agree; Neither agree nor disagree; Somewhat disagree; Strongly disagree

Never
If culture and susceptibility testing
indicates that the pathogen is resistant to gentamicin
If the owner can afford it
With approval from an independent office
Always

How would the following scenarios affect your decision about the above horse:
Select from Makes no difference, Makes some difference, Not sure, Should be taken into account, Any antimicrobial should be allowed

If the horse was the leading
thoroughbred stallion in Australia
The prognosis was very poor
The horse is insured
You practice in a region where horses are considered a food-producing species.
The owners demand amikacin
Other treatments have failed

A dairy cow presents with pneumonia and you believe antimicrobial therapy is indicated although the infection is not life-threatening. Under which circumstances is it reasonable to treat this cow with ceftiofur (3rd generation cephalosporin), an antimicrobial with a high importance rating?
Strongly agree, Somewhat agree, Neither agree nor disagree, Somewhat disagree, Strongly disagree

Never
If culture and susceptibility testing indicates that the pathogen is
resistant to all low and medium rated antimicrobials that could be used to
treat the case
With approval from an independent office
Always, as ceftiofur is labelled to treat pneumonia in cattle
Always, as ceftiofur carries a nil milk with-holding period

Thanks for completing the survey. Do you have anything else you'd like to tell us? (free text)

Appendix II Survey questions for Delphi study (Chapter 3)

Round 1
Q1
"Do you prescribe antibiotics in your current role?"
Yes
No

Q2
"Are you the lead of an antimicrobial stewardship team, or do you have executive oversight over an antimicrobial stewardship team?"
Yes
No

Q3
"What is your occupation (select all that apply)?"
[Checked or Unchecked for each possible response]

Veterinarian
Physician/Surgeon
General practitioner
Pharmacist
Medical or Veterinary Microbiologist
Public Health physician/official
Government employee
Other
Please specify [free text box]

Q4 "What species do you predominately work with? (tick all that apply)"

Dog and cats
Horses
Beef cattle
Dairy cattle
Poultry
Exotics
Pigs
Sheep
Other

Q5 "Please select your area(s) of expertise (select all that apply)"

Infectious diseases
Microbiology
Antimicrobial stewardship
Antimicrobial resistance
Infection prevention and control
Medicine
Surgery

General practice
Public health
Other
Please specify [free text box]

Q6
"How many years have you been working in antimicrobial stewardship or antimicrobial resistance?"
< 5 years
5-10 years
11-19 years
>20 years

Q7 "What country do you primarily practice in?"
Afghanistan
Albania
Algeria
Andorra
Angola
Antigua & Deps
Argentina
Armenia
Australia
Austria
Azerbaijan
Bahamas
Bahrain
Bangladesh
Barbados
Belarus
Belgium
Belize
Benin
Bhutan
Bolivia
Bosnia Herzegovina
Botswana
Brazil
Brunei
Bulgaria
Burkina
Burundi
Cambodia
Cameroon
Canada
Cape Verde
Central African Rep
Chad
Chile
China
Colombia
Comoros
Congo
Costa Rica
Croatia
Cuba
Cyprus
Czech Republic
Denmark
Djibouti
Dominica
Dominican Republic
East Timor
Ecuador
Egypt
El Salvador
Equatorial Guinea
Eritrea
Estonia
Ethiopia
Fiji
Finland
France
Gabon
Gambia
Georgia
Germany
Ghana
Greece
Grenada
Guatemala
Guinea
Guinea-Bissau
Guyana
Haiti
Honduras
Hungary
Iceland
India
Indonesia
Iran
Iraq
Ireland
Israel
Italy
Ivory Coast
Jamaica
Japan
Jordan
Kazakhstan
Kenya
Kiribati
Korea North
Korea South
Kosovo
Kuwait
Kyrgyzstan
Laos
Latvia
Lebanon
Lesotho
Liberia
Libya
Liechtenstein
Lithuania
Luxembourg
Macedonia
Madagascar
Malawi
Malaysia
Maldives
Mali
Malta
Marshall Islands
Mauritania
Mauritius
Mexico
Micronesia
Moldova
Monaco
Mongolia
Montenegro
Morocco
Mozambique
Myanmar
Namibia
Nauru
Nepal
Netherlands
New Zealand
Nicaragua
Niger
Nigeria
Norway
Oman
Pakistan
Palau
Panama
Papua New Guinea
Paraguay
Peru
Philippines
Poland
Portugal
Qatar
Romania
Russian Federation
Rwanda
St Kitts & Nevis
St Lucia
Saint Vincent & the Grenadines
Samoa
San Marino
Sao Tome & Principe
Saudi Arabia
Senegal
Serbia
Seychelles
Sierra Leone
Singapore
Slovakia
Slovenia
Solomon Islands

Somalia
South Africa
South Sudan
Spain
Sri Lanka
Sudan
Suriname
Swaziland
Sweden
Switzerland
Syria
Taiwan
Tajikistan
Tanzania
Thailand
Togo
Tonga
Trinidad & Tobago
Tunisia
Turkey
Turkmenistan
Tuvalu
Uganda
Ukraine
United Arab Emirates
United Kingdom
United States
Uruguay
Uzbekistan
Vanuatu
Vatican City
Venezuela
Vietnam
Yemen
Zambia
Zimbabwe

Q8
"In which state do you primarily work?"
ACT
NSW
NT
SA
QLD
TAS
VIC
WA

Q9 "Which antimicrobial importance rating system do you use in your clinical practice or workplace? (select all that apply)"
Practice/institution specific
Country-specific (e.g. ASTAG, BSAVA Protect Me traffic lights, Canadian categorization)
World Health Organisation
OIE (World Organisation for Animal Health)
Unsure
None
Other
Please specify [free text box]

Q10
"Veterinarians should be able to create practice specific rating systems to suit their situations. *For example, choose to reclassify cefovecin (a third generation cephalosporin) as lower importance."

Strongly agree
Somewhat agree
Neither agree nor disagree
Somewhat disagree
Strongly disagree

Q11 "In your view which rating systems should veterinarians use?"
Country-specific (i.e. ASTAG)
World Health Organisation
OIE (World Organisation for Animal Health)
Other →Please specify [free text box]

Q12
"Is there anything else you'd like to tell us about rating systems for antimicrobial importance in veterinary medicine including anything about the implementation of such systems?"
[free text box]

Q13
"If restrictions were to be placed on veterinary prescribing of antimicrobials, which antimicrobials should they apply to? (select one)"
All antimicrobials
Antimicrobials with medium and high importance rating
All antimicrobials with high importance rating
All high-importance rating antimicrobials except 3rd generation cephalosporins and fluoroquinolones
All high-importance rating antimicrobials except fluoroquinolones
All high-importance rating antimicrobials except 3rd generation cephalosporins
No antimicrobials should be restricted

Q14 "If there were to be restrictions placed on veterinary prescribing of antimicrobials with high importance rating, which of the following do you think is appropriate?"
"These antimicrobials must not be used in veterinary medicine under any circumstance"
Strongly agree
Somewhat agree
Neither agree nor disagree
Somewhat disagree
Strongly disagree

"Use can only proceed with approval from an independent office"
Strongly agree
Somewhat agree
Neither agree nor disagree
Somewhat disagree
Strongly disagree

"Use in referral hospitals is allowed without approval"
Strongly agree
Somewhat agree
Neither agree nor disagree
Somewhat disagree
Strongly disagree

"Use in general practice requires approval from an independent office"
Strongly agree
Somewhat agree
Neither agree nor disagree
Somewhat disagree
Strongly disagree

"Use is allowed while waiting for culture and susceptibility results, if there is a high suspicion of need for use and the animal is critically ill"
Strongly agree
Somewhat agree
Neither agree nor disagree
Somewhat disagree
Strongly disagree

"Use is only allowed after culture and susceptibility testing confirms that the pathogen is resistant to all low and medium rated antimicrobials that could be used to treat the case"
Strongly agree

Somewhat agree
Neither agree nor disagree
Somewhat disagree
Strongly disagree

"Use is allowed after treatment failure with a lower importance antimicrobial"
Strongly agree
Somewhat agree
Neither agree nor disagree
Somewhat disagree
Strongly disagree

"Use is allowed in critically ill animals"
Strongly agree
Somewhat agree
Neither agree nor disagree
Somewhat disagree
Strongly disagree

Q15
"Should antimicrobials with high-importance to human medicine that are registered for use in veterinary medicine be treated differently to those that are not?
Examples of antimicrobials with high-importance that are registered for use in veterinary medicine include; 3rd generation cephalosporins, fluoroquinolones, virginiamycin and macrolides. Human formulations for which no registered veterinary product exist include; amikacin, imipenem and ticarcillin-clavulanate. "

Yes
Unsure
No

Q15
"How should these high-importance to human medicine antimicrobials that are registered for use in veterinary medicine be treated differently?"
[free text box]

Q16
"If independent approval is required to use a restricted antimicrobial, who do you think should provide this approval?"

Practice stewardship champion
Veterinary microbiologist
Corporate regional clinical director (where this role exists)
Office of the state chief veterinary officer
Australian Veterinary Association
University antimicrobial stewardship academics
Veterinary pharmacologist
Other

Q16
"If you selected 'other', please specify"
[free text box]

Q17

"Are there other restrictions you think should be placed on the prescribing of antimicrobials with high importance to human health?"
Yes
No

Q17
"What other restrictions do you think should be placed on antimicrobials with high-importance to human health?"
[free text box]

Round 2
Q1
"In light of the previous results, please state whether you agree with the following statement.
Veterinarians should be able to create local practice-specific antimicrobial use protocols, but should not be able to create their own practice-specific antimicrobial importance rating systems."

Agree
Disagree

"Please provide your reasoning for this choice."
[free text box]

Q2
"Do you agree that practice-specific antimicrobial use protocols are justified in the following situations? - Specific disease presentations not covered by guidelines"

1. Strongly agree
2. Agree
3. Neither agree nor disagree
4. Disagree
5. Strongly disagree

"Do you agree that practice-specific antimicrobial use protocols are justified in the following situations? - When local susceptibility data suggests resistance to first-line antimicrobial treatment"

1. Strongly agree
2. Agree
3. Neither agree nor disagree
4. Disagree
5. Strongly disagree

Q2Reasoning
"Please provide your reasoning for the above choices."
[free text box]

Q3
"Considering the response to the rating system question above and the information provided at the start of this survey, would you agree with the following statement?
The country-specific rating system should take precedence over any other rating system (e.g. WHO rating system) when veterinarians make decisions about antimicrobial prescribing choices."

1. Yes
0. No

"Please provide your reasoning for this choice."
[free text box]

Q4
"When using international prescribing guidelines e.g. International Society for Companion Animal Infectious Diseases (ISCAID), British Equine Veterinary Association (BEVA),
these should be adapted to accountfor the country-specific rating system."

1. Yes
0. No

"Please provide your reasoning for this choice."
[free text box]

Q5
"Considering the results above, if restrictions were to be placed on veterinary prescribing of antimicrobials, which antimicrobials should they apply to? (select one)"

1, All high-importance rating antimicrobials except 3rd generation cephalosporins and fluoroquinolones
2, Antimicrobials with medium and high importance rating
3, All antimicrobials with high importance rating
4, No antimicrobials should be restricted

"Please provide your reasoning for this choice."
[free text box]

Q6
"Considering the results provided, do you agree with the following statements? Use of high importance antimicrobials is allowed after culture and susceptibility testing confirms that the pathogen is resistant to all low and medium rated antimicrobials that could be used to treat the case"

1. Agree
2. Disagree

"Considering the results provided, do you agree with the following statements? - Use of high importance antimicrobials is allowed while waiting for culture and
susceptibility results, if there is a high suspicion of need for use and the animal is critically ill"

1. Agree
2. Disagree

"Considering the results provided, do you agree with the following statements? - The use of high importance antimicrobials in veterinary medicine should NOT be banned."

1. Agree
2. Disagree

"Please provide your reasoning for this choice."
[free text box]

Q7

"Considering the results provided, do you agree with the following statement? Any use of high importance antimicrobials that are not registered for use in animals e.g. vancomycin, amikacin or imipenem, must be reported to a central authority."

1. Yes
0. No

"Please provide your reasoning for this choice."
[free text box]

Q8
"Do you have any other comments or questions about the use of high importance antimicrobials in a veterinary setting?"

Q9
"Do you have any other comments or questions about this consensus-building process?"

Round 3
Q1

"What is your primary occupation? (select one)"

1. Academic
2. Epidemiologist
3. Government Employee
4. Employed in Industry/Pharmaceutical sector
5. Medical or Veterinary Microbiologist
6. Pharmacist
7. Physician/Surgeon
8. Physician/Surgeon and Microbiologist
9. Veterinarian
10. Veterinarian and Academic
11. Epidemiologist (including expertise in diseases in humans and/or animals)
12. Other

Q2Country

"In which country do you primarily work?"
1, Afghanistan
2, Albania
3, Algeria
4, Andorra
5, Angola
6, Antigua & Deps
7, Argentina
8, Armenia
9, Australia
10, Austria
11, Azerbaijan
12, Bahamas
13, Bahrain
14, Bangladesh
15, Barbados
16, Belarus
17, Belgium
18, Belize
19, Benin
20, Bhutan
21, Bolivia
22, Bosnia Herzegovina
23, Botswana
24, Brazil
25, Brunei
26, Bulgaria
27, Burkina
28, Burundi
29, Cambodia
30, Cameroon
31, Canada
32, Cape Verde
33, Central African Rep
34, Chad
35, Chile
36, China
37, Colombia
38, Comoros
39, Congo
41, Costa Rica
42, Croatia
43, Cuba
44, Cyprus
45, Czech Republic
46, Denmark
47, Djibouti
48, Dominica
49, Dominican Republic
50, East Timor
51, Ecuador
52, Egypt
53, El Salvador
54, Equatorial Guinea

55, Eritrea
56, Estonia
57, Ethiopia
58, Fiji
59, Finland
60, France
61, Gabon
62, Gambia
63, Georgia
64, Germany
65, Ghana
66, Greece
67, Grenada
68, Guatemala
69, Guinea
70, Guinea-Bissau
71, Guyana
72, Haiti
73, Honduras
74, Hungary
75, Iceland
76, India
77, Indonesia
78, Iran
79, Iraq
80, Ireland
81, Israel
82, Italy
83, Ivory Coast
84, Jamaica
85, Japan
86, Jordan
87, Kazakhstan
88, Kenya
89, Kiribati
90, Korea North
91, Korea South
92, Kosovo
93, Kuwait
94, Kyrgyzstan
95, Laos
96, Latvia
97, Lebanon
98, Lesotho
99, Liberia
100, Libya
101, Liechtenstein
102, Lithuania
103, Luxembourg
104, Macedonia
105, Madagascar
106, Malawi
107, Malaysia
108, Maldives
109, Mali
110, Malta
111, Marshall Islands
112, Mauritania
113, Mauritius
114, Mexico
115, Micronesia
116, Moldova
117, Monaco
118, Mongolia
119, Montenegro
120, Morocco
121, Mozambique
Myanmar
122, Namibia
123, Nauru
124, Nepal
125, Netherlands
126, New Zealand
127, Nicaragua
128, Niger
129, Nigeria
130, Norway
131, Oman
132, Pakistan
133, Palau
134, Panama
135, Papua New Guinea
136, Paraguay
137, Peru
138, Philippines
139, Poland
140, Portugal
141, Qatar
142, Romania
143, Russian Federation
144, Rwanda
145, St Kitts & Nevis
146, St Lucia
147, Saint Vincent & the Grenadines
148, Samoa
149, San Marino
150, Sao Tome & Principe
151, Saudi Arabia
152, Senegal
153, Serbia
154, Seychelles
155, Sierra Leone
156, Singapore
157, Slovakia
158, Slovenia
159, Solomon Islands
160, Somalia
161, South Africa
162, South Sudan
163, Spain
164, Sri Lanka
165, Sudan
166, Suriname
167, Swaziland
168, Sweden
169, Switzerland
170, Syria
171, Taiwan
172, Tajikistan
173, Tanzania
174, Thailand
175, Togo
176, Tonga
177, Trinidad & Tobago
178, Tunisia
179, Turkey
180, Turkmenistan
181, Tuvalu
182, Uganda
183, Ukraine
184, United Arab Emirates
185, United Kingdom
186, United States
187, Uruguay
188, Uzbekistan
189, Vanuatu
190, Vatican City
191, Venezuela
192, Vietnam
193, Yemen
194, Zambia
195, Zimbabwe

"Over the past two survey rounds, consensus amongst participants has been reached on the following items relating to the use of high importance antimicrobials as rated by the ASTAG (Australian Strategic and Technical Advisory Group on AMR) system.

1. The country-specific rating system should take precedence over any other rating system (e.g. WHO rating system) when veterinarians make decisions about antimicrobial prescribing choices.

2. When using international prescribing guidelines e.g. International Society for Companion Animal Infectious Diseases (ISCAID), British Equine Veterinary Association (BEVA), these should be adapted to account for the country-specific rating system.

3. Veterinarians should be able to create local practice-specific antimicrobial use protocols, but should not be able to create their own practice-specific antimicrobial importance rating systems.

4. Use of high importance antimicrobials is allowed after culture and susceptibility testing confirms that the pathogen is resistant to all low and medium rated antimicrobials that could be used to treat the case.

5. The use of high importance antimicrobials in veterinary medicine should NOT be banned.

6. Any use of high importance antimicrobials that are not registered for use in animals e.g. vancomycin, amikacin or imipenem, must be reported to a central authority.

Q3
How important do you think it is to reduce high importance antimicrobial use in companion animals?"

1, Very Important
2, Important
3, Moderately Important
4, Slightly Important
5, Not Important

Q4
How important do you think it is to reduce high importance antimicrobial use in food-producing animals?
1, Very Important
2, Important
3, Moderately Important
4, Slightly Important
5, Not Important

Q5
"To which central authority in Australia should use in animals of high importance antimicrobials that are not registered for animal use (e.g. vancomycin, amikacin, or imipenem) be reported?

Please read the following information to assist you in answering the question.

The Australian Pesticides and Veterinary Medicines Authority (APVMA) is responsible for registration of all agricultural and veterinary chemical products into the Australian marketplace.

A newly formed One Health independent federal body would work to address issues such as AMR using a one health framework with the goal of improving the coordination of actions related to the health of people, animals and the environment, particularly in relation to disease prevention and control.

State and territory departments of health in Australia are generally responsible for ‘control of use’ legislation to monitor the use of schedule 8 medicines such as ketamine and opioids in veterinary practice as well as schedule 4 medicines and poisons, including antibiotics. Resourcing for these purposes varies across states.

State departments of agriculture have varying roles across the states but generally promote and support the agriculture sector to develop and add value to the economy in partnership with farmers, industry and communities. Focus on companion animal issues varies across the states but these sectors generally do not receive a high level of funding or support.

The Australian Chief Veterinary Officer (ACVO) is the primary representative of, and advisor to, the Australian Government on matters relating to Australia’s animal health status. The objective of the Office of the Australian Chief Veterinary Officer (OCVO) is to mitigate threats to the Australian economy, and the productivity of Australia’s animal-dependent industries. The OCVO provides policy coordination, strategic direction and leadership on animal issues of national significance.

The Australian Strategic and Technical Advisory Group on AMR (ASTAG) is a working group composed of fourteen representatives with expertise in human, animal, plant and environmental health. The current role of ASTAG is to provide expert advice on AMR-related issues, research priorities and implementation approaches to support Australia’s national antimicrobial resistance strategy."

1, Australian Pesticides and Veterinary Medicines Authority (APVMA)
2, A newly created independent federal body to address antimicrobial resistance using a One Health framework e.g. Centre for Disease Control type of organisation or a One Health central authority
3, State Department of Health
4, State Department of Agriculture
5, Office of the Chief Veterinary Officer (OCVO)
6, Australian Strategic and Technical Advisory Group (ASTAG) on AMR working group
7, Other

"If you selected 'other', to which authority do you think use should be reported?"
[free text box]

"Please provide your reasoning for the above choice."
[free text box]

Q6
"Given consensus on item number 6, "Any use of high importance antimicrobials that are not registered for use in animals e.g. vancomycin, amikacin or imipenem, must be reported to a central authority", the purpose of the reporting should be for the following reasons: (Select all that apply)"

Record keeping over time for surveillance of antimicrobial use
Auditing or investigating high or frequent users to assist users in finding ways to reduce unnecessary use (non-punitive)
Acting as a deterrent due to the additional reporting requirements
Other
Please specify [free text box]

"Please provide your reasoning for this choice"
[free text box]

Q7
"Given the consensus on item number 6, “Any use of high importance antimicrobials that are not registered for use in animals e.g. vancomycin, amikacin or imipenem, must be reported to a central authority”, which data should be reported? (Select all that apply)"
1, The species the antimicrobial has been prescribed for in this occurrence
2, Whether culture and susceptibility testing has been used previously to support the use
3, Any other justification for use e.g. supporting diagnostic tests, reasons other lower importance antimicrobials can not be used
4, Other - please specify

"Please specify"
[free text box]

"Please provide your reasoning for this choice"
[free text box]

Q8
"Please state whether you agree or disagree with the following statement:

If any high importance antimicrobials (as rated by the ASTAG rating system) are prescribed to animals, a clear indication for use and justification for antimicrobial choice, must be recorded in the medical history along with the dose rate given, route of administration, the duration and the time point for review of the condition and associated antimicrobial therapy."

1, Agree
2, Disagree
3, Other - please specify

"Please specify"
[free text box]

Q9
"Do you have any other comments or questions about the use of high importance antimicrobials in a veterinary setting?"
[free text box]

Q10Process
"Do you have any other comments or questions about this consensus-building process?"
[free text box]

If you would like your name to be published with these consensus items when results of the consensus process are reported, please click here [hyperlink to new survey] and record your name as you would like it to appear along with any relevant post-nominals e.g. MANZCVS, PhD.

Appendix III Free text quotations (Chapter 3)

Sample of free text responses about rating systems for antimicrobial importance in veterinary medicine

Reference	Quote
1a	There is a real need for unity in this area - having so many ratings systems all disagreeing with each other confuses prescribers and lowers the impact of such effects. Although I have selected WHO here, in reality I am more pointing toward the need for a single, internationally agreed approach adopted by all countries, whether that would or would not be led by WHO.
1b	Ratings systems should be based on an AM's importance to human medicine and risks of AMR development, not on factors such as cost, convenience, etc.
1c	Rating systems in veterinary medicine should align with actual evidence rather than theoretical hysterical hyperbole. In other words, does the evidence justify the classification. (e.g. 1. evidence of actual veterinary/human AMR issues being proven to be the result of specific drug usage in veterinary practice over time).
1d	More harmony, or at least removing inconsistency, between country rating systems would be helpful. Also more accessible explanation or methodology on how importance ratings are decided.

Free-text responses about how high-importance antimicrobials that are registered for use in veterinary medicine be treated differently to those that are not registered use in veterinary medicine

Reference	Quote
2a	Only use when lower importance products are unlikely to be effective or when high risk of poor patient outcome likely if alternative antimicrobial is used. In food producing animals the antimicrobial spectrum and alternatives is sometimes limited relative to the anticipated pathogen. In cases such as a septic neonate waiting for the antimicrobial susceptibility may have dire consequences for the patient.
2b	Use should be on strict guidelines which require substantiation and review by the prescribing veterinarian. For example: Emergency, short-term use of virginiamycin to grazing ruminants should be permitted on animal welfare grounds under specified protocols and/or guidelines for adaptation to grain feeding such as under circumstances of drought or pasture toxicity. However, prescribing for routine use should generally not occur and perhaps treated as professional misconduct.

Free-text responses about who should provide independent approval if it is required to use a restricted antimicrobial

Reference	Quote
3a	It needs to be a system with wide representation, veterinary and human health, not just one type.
3b	Similar to medical general practitioner – qualified and experienced public health veterinarian in CVO office to be contacted prior to antibiotic being prescribed.
3c	A team of experts including pharmacologist, microbiologist, internal medicine and/or surgery specialist, etc.
3d	Too practice and location specific. Must be practical. Ideally it's a veterinarian with expertise in infectious diseases. That might be university stewardship academics but not all those have the clinical expertise that is needed for proper case discussions.

Free-text responses about the purpose of reporting the use of antimicrobials not registered for use in animals

Reference	Quote
4a	High importance antibiotic use should be discouraged, though may play an important role in exceptional cases. Any use would need to be monitored and assessed for appropriateness.
4b	Documentation and surveillance needed to provide oversight, but should not be punitive to individual users.
4c	We need the surveillance to create data if our prescriptions drive resistance levels, and audit and education is better than regulation and punishing
4d	Would be great if this included the animal, indication etc. to identify trends and areas for targeted improvement
4e	I think the most important principle here is accountability for prescribers, and ensuring prescribers think through the rational for, and implications of, their decisions

Appendix IV Interview guide (Chapter 5)

INTERVIEW GUIDE

Introduction

- Welcome, briefly introduce yourself (name, position, organisation)
- Small talk & acclimatization
- **Share Patient Information Sheet and Consent** form, talk interviewee through, answer any questions and let her/him sign digitally or in hardcopy if not already done, collect Consent Form
- Inform interviewee ('Just letting you know that I'm turning on the recorder now') & **turn on the audio recorder**

Opening statement

Thank you very much for taking the time to meet with me and doing this interview as part of our project. During this interview today I would like to learn more about your personal experience with antimicrobial resistance and stewardship and hear about your experiences relating to this while working in a remote Indigenous community. Sometimes I might ask you to give an example or describe your thought process. Feel free to take your time and think about it. Remember, I'm interested in hearing your experiences and opinions, so there are no right or wrong answers.

And also, you don't have to talk about anything you don't want to. You can stop the interview at any time, take a break, or end the interview altogether – just let me know.

The interview will take about 45 minutes. As mentioned before and on the consent form it is recorded. I would like to emphasize that your responses will be de-identified when transcribed so that your identity and details of your property or locations you might mention will not be known.

For the record – have you received the information sheet, signed the consent form and are you willing to proceed with the interview?

Do you have any questions before we begin?

1. General introductory question enquiring how they came to work in the community and for how long they worked there.

[For Veterinary Prescribers]
1v. Can you tell me about which antibiotics you stocked when you were working in the remote communities?

2v. Did you ever use a third generation cephalosporin like cefovecin "convenia" or fluoroquinolone like enrofloxacin "baytril"?

3v. Why did you carry this range of antibiotics?
- price/donated stock
- ease of administration
- efficacy
- familiarity
- drugs already in stock when started
- other

4v. Do you use antibiotics for surgical prophylaxis? How do you choose which cases need surgical prophylaxis? Route, frequency/time of administration.

[For All Prescribers]
1p. Does the way you prescribe antibiotic differ in remote communities compared to other places you've worked? How?

2. For what conditions did you mostly use antibiotics and what influences which antibiotic you choose? Do you use antimicrobial prescribing guidelines (i.e. Therapeutic guidelines for medical practitioners, AVA guidelines)?

2. Is lack of access to antibiotics an issue that affects human or animal welfare? Do you think there is an overuse of antibiotics in this community or other remote communities that you've worked in?

3. Do you think AMR is/was a problem in this community?

Who is it a problem for?
Does it affect how you (or others) prescribe antibiotics?
Can you tell me about the most common diseases you see where AMR is a problem?

4. When you were working in the community did you think much about antibiotic resistance or know much about it?
- the impact on animals
- the impact on people
- the impact on the environment

5. Do you think that there is a link between AMR carriage in animals (ie MRSA in dogs) and AMR in people? Why do you think there is or is not?

Compliance/importance of taking medicines

6. Can you think of any particular tool or resources that could help you when choosing whether to use antibiotics or not or which antibiotic and dose to choose?

1. Can you speak about the impact of relationships in the community and social connections on your prescribing habits?

7. Closing question:
We've covered quite a lot – thank you! Is there anything else you think is relevant or important about the use of antimicrobials in remote Indigenous communities?