

Minerva Access is the Institutional Repository of The University of Melbourne

Author/s:

Scarborough, Riati Olivia

Title:

Antimicrobial use and stewardship in companion animals

Date:

2025

Persistent Link:

<https://hdl.handle.net/11343/368543>

Terms and Conditions:

Terms and Conditions: Copyright in works deposited in Minerva Access is retained by the copyright owner. The work may not be altered without permission from the copyright owner. Readers may only download, print and save electronic copies of whole works for their own personal non-commercial use. Any use that exceeds these limits requires permission from the copyright owner. Attribution is essential when quoting or paraphrasing from these works.

Antimicrobial use and stewardship in companion animals

Riati Olivia Scarborough

ORCID: 0000-0002-7021-0893

This thesis is submitted in total fulfilment for the degree of
Doctor of Philosophy in Veterinary Medicine
October 2025

Melbourne Veterinary School, Faculty of Science

Abstract

This body of research investigates the reasons for suboptimal antimicrobial use in Australian companion animals and ways to encourage veterinarians to make better antimicrobial choices.

There are two categories of suboptimal antimicrobial use: unnecessary use and suboptimal choice of antimicrobial drug, regimen or both. Both phenomena have been identified in Australian companion animal practice. However, the reasons for these behaviours have not previously been explored in this cohort of veterinarians.

In Australia, and many other countries, dog and cat bacterial infections are most often treated with one of two broad-spectrum antimicrobials: medium-importance amoxicillin-clavulanate and high-importance, third-generation cephalosporin, cefovecin. However, Australian treatment guidelines for many common infections recommend lower-importance antimicrobials, such as amoxicillin.

Quantitative analysis was undertaken on antimicrobial susceptibility results from thousands of dogs and cats from Victoria, Australia. For urinary tract pathogens, the guideline-recommended drugs amoxicillin and trimethoprim-sulfamethoxazole were highly effective; only 4% required amoxicillin-clavulanate and 0% required cefovecin. A second quantitative study showed that clavulanate was useful in only around 10% of urinary and other infections. Together, these studies demonstrated that veterinarians' antimicrobial choices were mostly not microbiological.

In-depth interviews with 22 veterinarians revealed many of the non-microbiological reasons for non-compliance with guidelines. Veterinarians reported a sense of safety when using broader-spectrum antimicrobials such as amoxicillin-clavulanate, and with longer durations of therapy. When the veterinarian had doubts about compliance with oral medication, which was particularly common in cats, they chose cefovecin, a third-generation injectable cephalosporin that lasts 14 days, largely because it guaranteed that the animal would 'finish the course'. This, they believed, was critical to reduce the risk of antimicrobial resistance. These interviews also showed that frequently used antimicrobials in a practice become more frequently used, because they are always on the shelf, in a self-perpetuating cycle.

The interviews also explored why veterinarians sometimes gave antimicrobials, even when they did not believe these would help the animal. This behaviour was primarily driven by two fears: fear of clinical deterioration (if they had missed the signs of a developing bacterial infection) and fear of client dissatisfaction, particularly in pet owners who expected to receive antimicrobials.

A cross-sectional survey of more than 500 Australian pet owners demonstrated that this expectation is real; 25% of surveyed pet owners had at some point expected antimicrobials from the veterinarian and 15% admitted to explicitly requesting antimicrobials. This survey also found that pet owners responded better to antimicrobial stewardship messages relating directly to their pet than messages about public health; the majority were unaware of inter-species transfer of bacteria.

Together, these studies showed that veterinarians' preference for amoxicillin-clavulanate and cefovecin is due to inaccurate perceptions, social influences and structural challenges. This work also highlighted several important and novel targets for future veterinary AMS interventions, including challenging beliefs about finishing the course and training veterinarians to communicate AMS messages more effectively with pet owners.

This thesis is dedicated to the pets, past and present, who fill our hearts with a love unlike any other.

Declaration

This thesis comprises only the original work toward the Doctor of Philosophy, except where indicated in the preface.

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

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

Preface

All human research work presented in this thesis (chapters 4, 5 and 6) was approved by a Human Research Ethics Committee at the University of Melbourne and conducted according to those approvals. Approval details are included in the relevant chapters.

As detailed in the relevant chapters, an AI tool was used to create transcripts of the interviews conducted with veterinarians, which were then manually corrected. No AI was used to generate text. No third-party human assistance was used in preparing this thesis.

Included publications

Chapter 2

Title: **Use of Local Antibigram Data and Antimicrobial Importance Ratings to Select Optimal Empirical Therapies for Urinary Tract Infections in Dogs and Cats**

Journal: Antibiotics

Publication date: 18 December 2020

Authors: Ri Scarborough, Kirsten Bailey, Bradley Galgut, Adam Williamson, Laura Hardefeldt, James Gilkerson, Glenn Browning

Contributions:

- Ri Scarborough: conceptualisation, methodology, formal analysis, visualisation, writing – original draft, review and editing
- Kirsten Bailey: conceptualisation, methodology, visualisation, writing – review and editing
- Bradley Galgut: data extraction and curation, methodology
- Adam Williamson: data curation, assistance with analysis
- Laura Hardefeldt: conceptualisation, methodology, visualisation, writing – review and editing
- James Gilkerson: methodology, writing – review and editing
- Glenn Browning: methodology, writing – review and editing

Published supplementary materials relating to this manuscript are in Appendix 1.

Chapter 3

Title: **Clavulanate and cephalosporins: what is the cost of convenience?**

Journal: Australian Veterinary Practitioner

Publication date: 19 December 2023

Authors & Contributions:

- Ri Scarborough: conceptualisation, methodology, formal analysis of all C&S data, visualisation, writing – original draft, review and editing. Note: Prescribing data presented in the combined results and discussion are from research conducted by other members of the research team, and are referenced accordingly.
- Glenn Browning: writing – review and editing
- Laura Hardefeldt: writing – review and editing
- Bradley Galgut: data extraction and curation, writing – review and editing
- Marc Marenda: writing - original draft, review and editing
- Kirsten Bailey: writing – review and editing

Chapter 4

Title: **Pet Owners and Antibiotics: Knowledge, Opinions, Expectations, and Communication Preferences**

Journal: Antibiotics

Publication date: 29 October 2021

Authors & Contributions:

- Ri Scarborough: conceptualisation, methodology, participant recruitment, data collection and cleaning, formal analysis, visualisation, writing – original draft, review and editing
- Laura Hardefeldt: conceptualisation, methodology, writing – review and editing
- Glenn Browning: methodology, writing – review and editing
- Kirsten Bailey: conceptualisation, methodology, visualisation, writing – review and editing

Published supplementary materials relating to this manuscript are in Appendix 2.

Chapter 5

Title: **‘Brave enough’: a qualitative study of veterinary decisions to withhold or delay antimicrobial treatment in pets**

Journal: Antibiotics

Publication date: 8 March 2023

Authors & Contributions:

- Ri Scarborough: conceptualisation, methodology, participant recruitment, data collection and cleaning, formal analysis, visualisation, writing – original draft, review and editing
- Anna Sri: formal analysis, writing – review and editing
- Glenn Browning: methodology, participant recruitment, writing – review and editing
- Laura Hardefeldt: methodology, writing – review and editing
- Kirsten Bailey: methodology, writing – review and editing

Published supplementary materials relating to this manuscript are in Appendix 3.

Chapter 6

Title: **Seeking simplicity, navigating complexity: How veterinarians select an antimicrobial drug, dose, and duration for companion animals**

Journal: Journal of Veterinary Internal Medicine

Publication date: 20 September 2024

Authors:

Authors & Contributions:

- Ri Scarborough: conceptualisation, methodology, participant recruitment, data collection and cleaning, formal analysis, visualisation, writing – original draft, review and editing
- Anna Sri: formal analysis, writing – review and editing
- Glenn Browning: methodology, participant recruitment, writing – review and editing
- Laura Hardefeldt: methodology, writing – review and editing

- Kirsten Bailey: methodology, writing – review and editing

Published supplementary materials relating to this manuscript are in Appendix 4.

Research activity during candidature

Published manuscripts (first author)

1. **Scarborough**, R., Bailey, K., Galgut, B., Williamson, A., Hardefeldt, L., Gilkerson, J. and Browning, G., 2020. Use of local antibiogram data and antimicrobial importance ratings to select optimal empirical therapies for urinary tract infections in dogs and cats. *Antibiotics*, 9(12), p.924.
2. **Scarborough**, R., Hardefeldt, L., Browning, G. and Bailey, K., 2021. Pet owners and antibiotics: knowledge, opinions, expectations, and communication preferences. *Antibiotics*, 10(11), p.1326.
3. **Scarborough**, R. O., Sri, A. E., Browning, G. F., Hardefeldt, L. Y., & Bailey, K. E., 2023. 'Brave enough': a qualitative study of veterinary decisions to withhold or delay antimicrobial treatment in pets. *Antibiotics*, 12(3), 540.
4. **Scarborough**, R., Browning, G.F., Hardefeldt L.Y., Galgut, B.I., Marenda, M.S., Bailey, K.E., 2023. Clavulanate and cephalosporins: what is the cost of convenience? *Australian Veterinary Practitioner*, 53(5), 209.
5. **Scarborough**, R. O., Bailey, K. E., Sri, A. E., Browning, G. F., & Hardefeldt, L. Y. , 2024. Seeking simplicity, navigating complexity: How veterinarians select an antimicrobial drug, dose, and duration for companion animals. *Journal of Veterinary Internal Medicine*, 38(6), 3215-3234.

Published manuscripts (co-author)

- Maharaj, A.D., Holland, J.F., **Scarborough**, R.O., Evans, S.M., Ioannou, L.J., Brown, W., Croagh, D.G., Pilgrim, C.H., Kench, J.G., Lipton, L.R. and Leong, T., 2019. The Upper Gastrointestinal Cancer Registry (UGICR): a clinical quality registry to monitor and improve care in upper gastrointestinal cancers. *BMJ open*, 9(9), p.e031434.
- Hardefeldt, L., Hur, B., Verspoor, K., Baldwin, T., Bailey, K.E., **Scarborough**, R., Richards, S., Billman-Jacobe, H., Browning, G.F. and Gilkerson, J., 2020. Use of cefovecin in dogs and cats attending first-opinion veterinary practices in Australia. *Veterinary Record*, 187(11), pp.e95-e95.
- Soh, S.E., Morello, R., Ayton, D., Ahern, S., **Scarborough**, R., Zammit, C., Brand, M., Stirling, R.G. and Zalcborg, J., 2021. Measurement properties of the 12-item Short Form Health Survey version 2 in Australians with lung cancer: a Rasch analysis. *Health and quality of life outcomes*, 19(1), p.157.
- Thursky, K.A., Hardefeldt, L.Y., Rajkhowa, A., Ierano, C., Bishop, J., Hawes, L., Biezen, R., Saha, S.K., Dowson, L., Bailey, K.E. and **Scarborough**, R., 2021. Antimicrobial stewardship in Australia: the role of qualitative research in programme development. *JAC-Antimicrobial Resistance*, 3(4), p.dlab166.
- Hardefeldt, L.Y., Hur, B., Richards, S., **Scarborough**, R., Browning, G.F., Billman-Jacobe, H., Gilkerson, J.R., Ierardo, J., Awad, M., Chay, R. and Bailey, K.E., 2022. Antimicrobial

stewardship in companion animal practice: an implementation trial in 135 general practice veterinary clinics. *JAC-Antimicrobial Resistance*, 4(1), p.dlac015.

- Hur, B., Verspoor, K.M., Baldwin, T., Hardefeldt, L.Y., Pfeiffer, C., Mansfield, C., **Scarborough**, R. and Gilkerson, J.R., 2024. Using natural language processing and patient journey clustering for temporal phenotyping of antimicrobial therapies for cat bite abscesses. *Preventive Veterinary Medicine*, 223, p.106112.
- Richards, S., Bailey, K.E., **Scarborough**, R., Gilkerson, J.R., Browning, G.F., Hur, B., Ierardo, J., Awad, M., Chay, R. and Hardefeldt, L.Y., 2024. Cross-sectional evaluation of a large-scale antimicrobial stewardship trial in Australian companion animal practices. *Veterinary Record*, 194(4).
- Sri, A., Bailey, K.E., **Scarborough**, R., Gilkerson, J.R., Thursky, K., Browning, G.F. and Hardefeldt, L.Y., 2024. Reaching consensus amongst international experts on the use of high importance-rated antimicrobials in animals—a Delphi study. *One Health*, 19, p.100883.
- Hii, A.W., Gilkerson, J.R., Bailey, K.E., **Scarborough**, R., Sri, A.E., Awad, M., Etheridge, L. and Hardefeldt, L.Y., 2025. Outcomes from an intervention study implementing fee-free culture and susceptibility urine testing in dogs and cats. *Veterinary Record*, p.e5500.

Scientific conference presentations and posters

2020

- Australia and New Zealand College of Veterinary Scientists (ANZCVS) Science Week 2020:
 - *Are we treating dog and cat UTIs well?* (oral presentation)
- National Centre for Antimicrobial Stewardship (NCAS) Antimicrobial Awareness Week 2020:
 - *Fears, finances, formulations and fractious felines: influences on antibiotic prescribing in Australian cat and dog practice* (oral presentation)

2021

- Australian Veterinary Antimicrobial Stewardship (AVAMS) Conference:
 - *Could we be treating dog and cat UTIs better?* (oral presentation)
- American College of Veterinary Internal Medicine (ACVIM) Forum:
 - *Urinary Tract Infections in Dogs and Cats: How can we optimize empirical antibiotic therapy?* (ePoster and recorded oral presentation)

2022

- Australian Veterinary Association (AVA) Conference:
 - *Communication is key: How to decline or delay antimicrobial use (and keep people happy)*

2023

- Australian Veterinary Antimicrobial Stewardship (AVAMS) Conference, Gold Coast:
 - *Moving beyond fears: How Australian companion animal vets can be supported to appropriately withhold antimicrobials* (oral presentation)

- *Enablers of AMS for Australian production animal, equine and companion animal veterinarians* (poster)
- European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Copenhagen:
 - *Are veterinarians overusing clavulanate in pets?* (poster)
- International Conference on One Health Antimicrobial Resistance (ICOHAR), Copenhagen
 - *Brave Enough: Veterinary decisions to withhold antimicrobial therapy in pets* (poster)
 - *Balancing effectiveness and AMR risk: A novel method to select rational empirical antimicrobial therapy* (poster)
 - *Are veterinarians overusing clavulanate in pets?* (poster)
- Australian Veterinary Association (AVA) Conference, Adelaide:
 - *Stop bringing guns to a knife fight! Optimise your treatment of dog and cat UTIs* (invited oral presentation, with Amy Hii)
 - *Brave enough: Veterinary decisions to withhold antimicrobial therapy in pets* (poster) - Third prize winner
- Australia and New Zealand College of Veterinary Scientists (ANZCVS) Science Week, Gold Coast:
 - Effectiveness versus risk: a novel method for selecting empirical antimicrobials (oral presentation) – conference abstract 1st prize
 - Brave Enough: Deciding to withhold antimicrobial treatment in companion animals (oral presentation)

2024

- Australian Veterinary Association (AVA) Conference, Melbourne:
 - *Are vets overusing clavulanate in pets* (poster) – first prize winner

2025

- Australian Veterinary Association (AVA) conference, Sydney:
 - *Harnessing the power of VetCompass for research* (oral presentation)
 - *From paddocks to pampered pooches: How Australian veterinarians are implementing antimicrobial stewardship* (poster)
- Australia and New Zealand College of Veterinary Scientists (ANZCVS) Science Week, Gold Coast:
 - *Science or something else? How veterinarians choose antibiotic treatment regimens* (oral presentation)
- Veterinary Antimicrobial Stewardship Summit Asia-Pacific (VASSAP), Melbourne – *How veterinary laboratories can support better antimicrobial use* (oral presentation)

Teaching and outreach activities

2020

- National Centre for Antimicrobial Stewardship (NCAS) Antimicrobial Awareness Week: *Fears, finances, formulations and fractious felines: influences on antibiotic prescribing in Australian cat and dog practice* (oral presentation)
- National Centre for Antimicrobial Stewardship (NCAS) Journal Club, July: *Improving antibiotic use in veterinary practice* (oral presentation)

- SVS Veterinary Laboratories staff meeting: *Improving antibiotic use in veterinary practice* (oral presentation)
- Vet Expo Melbourne: Can we treat UTIs better? *Using pooled culture and susceptibility data to make smarter empirical choices* (oral presentation)
- University of Melbourne DVM2 workshop: Antimicrobial Stewardship in veterinary practice

2021

- Karingal Veterinary Clinic Staff meeting: *Treating UTIs in dogs and cats* (oral presentation)
- University of Melbourne DVM2 workshop: *Antimicrobial Stewardship in veterinary practice*
- National Centre for Antimicrobial Stewardship (NCAS) Antimicrobial Awareness week:
 - *How veterinary laboratories can contribute to antimicrobial stewardship* (oral presentation)
 - *Know your audience – evidence-based ways to talk to pet owners about responsible antibiotic use* (oral presentation)

2022

- Podcast recording: The Vet Vault – *Antibiotic Mythbusting* with Dr Ri Scarborough
- Slovakian Small Animal Veterinary Association Seminar: *Communication is key: How to decline or delay antimicrobial use ... and keep owners happy!* (recorded webinar)
- Healix Veterinary Laboratories client education seminars:
 - *I've got the C&S results. What next?* (oral presentation)
 - *The antibiotic prescribing mistakes you're probably making* (oral presentation)
- University of Melbourne DVM2 workshop: *Antimicrobial Stewardship in veterinary practice*

2023

- AusVet seminar: *Introduction to qualitative research for veterinarians* (oral presentation)
- Wangaratta Veterinary Clinic Staff meeting: *Treating UTIs in dogs and cats* (oral presentation)
- Podcast recording with Laura Hardefeldt and Kirsten Bailey for the AMR Vet Collective (USyd/CSU resource website): *Common mistakes in antibiotic prescribing and how to avoid them*
- University of Melbourne DVM2 workshop: *Antimicrobial Stewardship in veterinary practice*
- National Centre for Antimicrobial Stewardship (NCAS) Antimicrobial Awareness Week Consumer Forum 'Antibiotics and You' – *Antibiotic use in Pets* (oral presentation)

2024

- Wangaratta Veterinary Clinic: Traffic light labelling of antibiotics on new pharmacy shelves
- Fleming Fund Fellow seminar: *Introduction to qualitative research for veterinarians* (oral presentation)
- Australian Veterinary Association Certified Veterinary Practitioner course webinars:
 - *I've got the C&S results. What next?*
 - *Mythbusters: Veterinary Antibiotic Edition*
 - *How to decline or delay antimicrobial use... and keep owners happy*
- Melbourne Veterinary School Honours student seminar: *Intro to qualitative research*

- National Centre for Antimicrobial Stewardship (NCAS) Antimicrobial Awareness Week Meeting:
- University of Melbourne DVM2 workshop: *Antimicrobial Stewardship in veterinary practice*

2025

- Fleming Fund Fellow seminar: *Introduction to qualitative research for veterinarians* (oral presentation)
- IDEXX Laboratories staff meeting: *Results of 2024 Australian vet survey on C&S reporting styles*
- VetExpo Melbourne: *Big wins from small changes: Six effective ways to improve antimicrobial use in your practice* (oral presentation)
- UniMelb lecture: (Our Health, Our Planet undergrad breadth subject) *Antimicrobial use in animals*
- University of Melbourne DVM2 workshop: *Antimicrobial Stewardship in veterinary practice*

Acknowledgements

There are some people without whom this doctoral research would have been simply impossible, and many more without whom it would have been far less rewarding. Some people belong to both categories and to them, I extend my deepest thanks.

Nick Scarborough, my partner for 30 years and counting, who loves animals as much as I do, you are the actual best! I could not have done a PhD if you hadn't provided your unwavering support over these last six years, as we have juggled family life, work, bereavements, COVID lockdowns and all the other things that have come along. Thank you. I love and appreciate you with all my heart and I'm sorry this thing has taken a bit longer than I said it would. Hopefully my contribution to the family finances will never again drop to the level of the part-time PhD stipend!

To our wonderful children, **Luci** and **Harvey**, also great animal lovers, thank you for believing in me and being (somewhat?) impressed with my efforts. I realise this must have seemed like a never-ending degree to you – after all, when I started in 2019, you were both in primary school and now you're both practically adults! I hope that one day you both also get to experience the joy of deeply exploring an academic interest that excites you. It is a great privilege.

My Dad, **Hendy Hendrata**, has always said that getting a really good education was the most important thing one could do. Having now completed eight years of undergraduate study plus six years of PhD study – I reckon I've probably ticked that box now! Thanks, Dad, for supporting my studies throughout, even when you worried that quitting the medical degree and becoming a vet instead was the wrong move. I'm still really glad I switched.

Very early in my PhD, I realised I had landed an excellent team of academic supervisors in **Glenn Browning**, **Kirsten Bailey** and **Laura Hardefeldt**. All three were supportive of me taking this work in any direction I wanted, generous with their expertise and constructive with their criticism. From talking to others about their PhD experiences at various universities around the world, I understand this situation to be both rare and precious. So, thank you. Kirsten, you brought your thoughtfulness and meticulous attention to detail to every task. Laura, you gave me confidence that I could successfully execute anything I suggested. Glenn, you continue to be a steady support for all of us, quietly creating opportunities and making things work behind the scenes. I am deeply grateful to the three of you for making this one of the most enriching and enjoyable experiences of my life.

I also thank the Melbourne Veterinary School academics who were in no way obliged to help me with my research, but cheerfully did so regardless, because it is just that kind of place. In particular, **James Gilkerson**, whom I think of as a sort of academic godfather; **Brian Hur**, who was always happy to help with my VetCompass questions; **Vern Bowles**, my supervisory committee chair, who always had a smile and an encouraging word for me; **Anke Wietholter**, for teaching me how to analyse my survey results in SPSS and **Alistair Legione**, for rescuing me out of an 'R hole' with the AST data. I dare not try to individually list all the other MVS academics and students who have helped me in small yet meaningful ways over the last six years, making me feel welcome in building 400, making conference trips more fun, listening to my many presentations and sharing tips and suggestions - please know that I appreciate your support.

For a range of financial and other supports, I am grateful to the Australian Government's Research Training Program scholarship, the Asia-Pacific Centre for Animal Health (APCAH), and the National Centre for Antimicrobial Stewardship (NCAS), especially **Courtney Ierano** and **Kas Thursky**, The University of Melbourne's various scholarships and the generous donors who make

them possible, the Postgrads of Veterinary Science (POVS) group, the Melbourne Veterinary School Early- and Mid-Career Researcher group, the Australian Veterinarian Network Facebook group and Healius Laboratories.

Brad Galgut, one of my vet school friends from the Class of 2003, your contribution to the AST studies in this thesis was invaluable. Not only did you apply for the laboratory permissions and extract the data for me, but you also suggested the master stroke of separating the results by bacterial morphology. This resulted in what I consider to be the most clinically applicable insight of this entire PhD! On the topic of data, I also want to thank my data scientist friend, **Adam Williamson**, who massaged those messy, raw urinary AST results into shape with Python, and then patiently coached me through the data analysis over multiple Zoom calls. I look forward to continuing to work with you.

I am very fortunate to have a lot of other supportive friends and family who have spurred me on, but I need to call out a couple: (Emeritus Professor) **Adrienne Clarke**, the brilliant friend I met walking our dogs – how very apt! - in Royal Park almost 20 years ago. You helped me find my way back to the Melbourne Veterinary School and encouraged me throughout. I might never have begun this journey without your friendship and wise counsel. And **Sally Greenberg**, a dear friend of mine since our undergrad days, who went above and beyond in helping recruit hundreds of pet-owning Medical Mums for my survey and in delivering strategic drops of Haighs milk chocolate bullets. I loved going on long walks along the Yarra River with our dogs and being (gently) ordered to hurry up and finish this PhD! I also want to mention my numerous running buddies: to the members of the **Bory Crouchers**, the **Splinters** and **Code Black Run Club**, thank you for keeping me entertained (and fit!) throughout my studies.

Although I know they are unlikely to see this thesis, I want to thank all the lovely **vets** who allowed me to interview them for my qualitative studies, some of whom are also my vet school friends. I have so much admiration for the clinical work you do, and I deeply appreciate your time, candour and humour in the interviews. Thank you, too, to the **pet owners** who completed my survey and the ones who kindly allowed me to interview them. You have all inspired in me a passion for qualitative research that will stay with me.

Finally, I wish to thank to the examiners for reading this thesis. The goodwill and collegiality shown by donating your expertise and time to review someone else's work, for the benefit of the scientific record, is one of the many things I admire about academia. Thank you.

Table of Contents

Abstract.....	2
Declaration.....	3
Preface.....	5
Included publications	6
Research activity during candidature	9
Acknowledgements	14
Table of Contents	16
Tables and Figures.....	21
Chapter 1: Literature Review.....	24
<i>Introduction</i>	<i>24</i>
<i>Definition and goals of antimicrobial stewardship</i>	<i>24</i>
<i>Antimicrobial resistance in companion animals</i>	<i>25</i>
Zoonotic risk and anthroponotic risk of antimicrobial resistance.....	26
<i>Other risks associated with antimicrobial use</i>	<i>27</i>
Dysbiosis	27
Toxicity and hypersensitivity	28
<i>Antimicrobial stewardship in companion animals</i>	<i>28</i>
Antimicrobial importance ratings.....	28
Antimicrobial use guidelines	29
<i>Antimicrobial use in companion animal practice.....</i>	<i>30</i>
National data on antimicrobial use in companion animals	30
Suboptimal antimicrobial use in companion animal practice	31
Cat subcutaneous abscesses.....	32
Urinary tract infections.....	33
<i>Factors influencing antimicrobial prescribing decisions</i>	<i>35</i>
Clinical factors influencing antimicrobial prescribing decisions	35
Non-clinical factors influencing antimicrobial prescribing decisions	36
<i>Strategies for improving antimicrobial use in companion animal practice</i>	<i>37</i>
Involuntary approaches.....	38
Voluntary approaches	38
<i>Conclusion</i>	<i>40</i>

<i>Research questions.....</i>	<i>40</i>
<i>References</i>	<i>40</i>
Chapter 2: Use of local antibiogram data and antimicrobial importance ratings to select optimal empirical therapies for urinary tract infections in dogs and cats	54
<i>Abstract.....</i>	<i>54</i>
<i>Introduction</i>	<i>55</i>
<i>Results</i>	<i>56</i>
<i>Discussion.....</i>	<i>66</i>
<i>Materials and Methods</i>	<i>69</i>
<i>Conclusions</i>	<i>71</i>
<i>References</i>	<i>72</i>
Chapter 3: Clavulanate and cephalosporins: what is the cost of convenience?	75
<i>Abstract.....</i>	<i>75</i>
<i>Methods</i>	<i>77</i>
<i>Results and discussion</i>	<i>77</i>
What are veterinarians prescribing?	77
What are the risks associated with overuse of clavulanate and third-generation cephalosporins? ..	78
Urinary tract infections: a case in point	80
Why don't veterinarians follow the guidelines? And what can individuals do about it?	82
<i>References</i>	<i>85</i>
Chapter 4: Pet owners and antibiotics: knowledge, opinions, expectations, and communication preferences	88
<i>Abstract.....</i>	<i>88</i>
<i>Introduction</i>	<i>88</i>
<i>Results</i>	<i>90</i>
Respondents	90
Pet owner expectations of the veterinary consultation, treatment preferences and trust.....	91
Pet owner opinions on antibiotic use; knowledge of microbiology and antibiotic resistance.....	97
<i>Communication preferences</i>	<i>101</i>
<i>when not prescribing antibiotics, and delayed prescribing preferences</i>	<i>101</i>
Reasons to give a course of antibiotic tablets, rather than a single, long-acting injection	102
<i>Discussion.....</i>	<i>104</i>
Pet owner expectations of the veterinary consultation, treatment preferences and trust.....	104
Pet owner opinions on antibiotic use; knowledge of microbiology and antibiotic resistance.....	105

Communication preferences	107
Strengths and limitations	108
<i>Materials and Methods</i>	108
<i>Conclusions</i>	110
<i>References</i>	111
 Chapter 5: ‘Brave Enough’: A Qualitative Study of Veterinary Decisions to Withhold or Delay Antimicrobial Treatment in Pets	114
<i>Abstract</i>	114
<i>Introduction</i>	115
<i>Materials and Methods</i>	116
Pre-Interview Survey	116
Interviews	116
<i>Results and Discussion</i>	118
Pre-Interview Survey (Participant Characteristics)	118
Interviews	119
Background Factors	120
Behavioural Beliefs	126
Normative Beliefs	132
Control Beliefs	137
Suggestions for Curbing Unnecessary Antimicrobial Use in Companion Animals	139
Further Discussion	140
<i>Conclusions</i>	141
<i>References</i>	142
 Chapter 6: Seeking simplicity, navigating complexity: How veterinarians select an antimicrobial drug, dose and duration for companion animals	146
<i>Abstract</i>	147
<i>Introduction</i>	148
<i>Methods</i>	148
<i>Results</i>	149
Participant characteristics	149
Case studies	149
Semi-structured interviews	150
Individual case factors	152
Antimicrobial drug factors	154
Owner factors	157
Veterinarian factors	161

Selecting drug and dose	161
Selecting duration of therapy	165
Practice and colleague factors	169
External factors	174
<i>Discussion</i>	176
<i>Conclusion</i>	178
<i>References</i>	178
Chapter 7: General discussion	182
<i>Conclusion</i>	187
<i>References</i>	188
Appendix 1: Supplementary materials for Chapter 2	189
<i>Figure S1: Frequency of samples by dog breed and age</i>	<i>189</i>
<i>Figure S2 a-f: Changes in susceptibility over time for the most common species/genera.....</i>	<i>190</i>
<i>Table S1: Urine sample source by animal species, age and sex</i>	<i>191</i>
<i>Table S2: Multiple resistance patterns in E. coli</i>	<i>192</i>
<i>Table S3: Multiple resistance patterns in Enterococcus faecalis</i>	<i>193</i>
<i>Table S4: Multiple resistance patterns in Staphylococcus pseudintermedius</i>	<i>194</i>
<i>Table S5: Multiple resistance patterns in Proteus mirabilis</i>	<i>195</i>
<i>Document S6: Extract from CDS Manual, 10th Edition, pages 67-79.....</i>	<i>196</i>
Appendix 2: Supplementary materials for Chapter 4	209
<i>Document S1: Pet owner questionnaire</i>	<i>209</i>
<i>Table S1: Demographics of respondents excluded from analysis.....</i>	<i>219</i>
Appendix 3: Supplementary materials for Chapter 5	220
<i>Table S1. Participant's estimates of the contribution made by different sectors to the overall problem of AMR in Australia.</i>	<i>220</i>
<i>Document S2: Interview Guide</i>	<i>221</i>
<i>Document S3: Codebook</i>	<i>225</i>
Appendix 4: Supplementary materials for Chapter 6	226
<i>Document S1: Example of traffic-light AST report</i>	<i>226</i>

Acronyms

AMS = antimicrobial stewardship

AMR = antimicrobial resistance

AMU = antimicrobial use

AST = antimicrobial susceptibility testing

ASTAG = Australian Strategic and Technical Advisory Group on Antimicrobial Resistance

ISCAID = International Society for Companion Animal Infectious Diseases

MCAS = Microbiological culture and antimicrobial susceptibility testing

TMS = trimethoprim-sulfonamide

UTI = urinary tract infection

WHO = World Health Organization

Tables and Figures

Chapter 2: Use of Local Antibigram Data and Antimicrobial Importance Ratings to Select Optimal Empirical Therapies for Urinary Tract Infections in Dogs and Cats

Figure 1: Distribution of samples by patient age and sex in (a) dogs and (b) cats.

Table 1: Organisms cultured for each collection method, and proportion cultured as a pure growth.

Figure 2: Bacterial species cultured, by collection method.

Table 2: Antimicrobial susceptibility and importance ratings for the most prevalent urinary isolates from dogs

Table 3: Antimicrobial susceptibility and importance ratings for the most prevalent urinary isolates from cats

Figure 3: Impact factors of the six routinely tested antimicrobials, by isolate morphology and host species.

Figure 4: Whole population treatment simulation, including antimicrobial cost per cure in (a) dogs and (b) cats.

Table 4: Summary of antimicrobial resistance detected in the most prevalent bacterial species/genera isolated from dog and cat urine

Figure 5: Proportion of *E. coli* (from animals from which ≥ 4 samples were cultured) classed as MDR, by sample sequence number.

Supplementary materials (Appendix 1)

Figure S1: Frequency of samples by dog breed and age

Figure S2: Changes in susceptibility over time for the most common species/genera

Table S1: Urine sample source by animal species, age and sex

Table S2: Multiple resistance patterns in *E. coli*

Table S3: Multiple resistance patterns in *Enterococcus faecalis*

Table S4: Multiple resistance patterns in *Staphylococcus pseudintermedius*

Table S5: Multiple resistance patterns in *Proteus mirabilis*

Chapter 3: Clavulanate and cephalosporins: what is the cost of convenience?

Figure 1: Example of a 'traffic light card' showing the different importance ratings (or level of AMR risk) of antimicrobials commonly used in dogs and cats

Figure 2: Prevalence of clavulanate-responsive beta-lactamase expression as a proportion of all isolates tested against amoxicillin and amoxicillin-clavulanate, Oct 2020-Sep 2021, by host species.

Figure 3: Prevalence of the most frequently isolated bacterial species cultured from urine samples, by host species.

Figure 4: Summary of 2015-2019 urinary isolate susceptibilities to selected antimicrobials from the six routinely tested by the laboratory

Table 1: Empirical, morphology-based treatment recommendations for sporadic lower UTIs in dogs and cats, based on the author's previously published 2015-2019 isolate *in vitro* susceptibility results.

Chapter 4: Pet Owners and Antibiotics: Knowledge, Opinions, Expectations, and Communication Preferences

Figure 1: Demographics of the 558 included survey participants (excluding insufficiently complete surveys).

Figure 2: Recency of visit to veterinarian, expectations of therapy and satisfaction with treatment decision.

Figure 3: Owner feelings about treatment decision in their most recent veterinary consultation for animal illness or injury, by expectation of medication and receipt of antibiotics.

Figure 4: Owner feelings about treatment decision, based on their expectations about medication for their pet and whether they received antibiotics.

Figure 5: Owner desire, hints and requests for antibiotics for their pets.

Figure 6: Pet owner expectations of the veterinary consultation, treatment preferences and trust.

Figure 7: Differences by respondent demographic category in pet owner expectations of a veterinary consultation, treatment preferences and trust.

Figure 8: Pet owner opinions on antibiotic use; knowledge of microbiology and antibiotic resistance.

Figure 9: Differences by respondent demographic category in pet owner opinions for antibiotic use, knowledge of microbiology and antibiotic resistance.

Figure 10: Communication preferences when not prescribing antibiotics, and delayed prescribing preferences.

Figure 11: Pet owner preferences for reasons to give a course of antibiotic tablets rather than a single, long-acting antibiotic injection.

Figure 12: Differences by respondent demographic category in popularity of reasons to give a course of antibiotic tablets instead of a long-acting antibiotic injection.

Figure 13: Owner behaviour and public health outcomes are linked by microbiological concepts that are poorly understood.

Supplementary materials (Appendix 2)

Figure S1: Demographics of respondents excluded from analysis

Chapter 5: ‘Brave enough’: a qualitative study of veterinary decisions to withhold or delay antimicrobial treatment in pets

Figure 1: Icek Ajzen’s Theory of Planned Behaviour (TPB) with background factors was used to organise the thematic analysis.

Table 1: Participant characteristics

Figure 2: Summary of factors influencing veterinarians’ decisions to withhold or delay antimicrobial treatment in the absence of a clear need, using an adaptation of the Theory of Planned Behaviour shown in Figure 1.

Figure 3: Background factors influencing the decision to withhold or delay antimicrobial treatment where there was no clear indication, and illustrative quotes.

Figure 4: Behavioural beliefs influencing the decision to withhold or delay antimicrobial treatment where there was no clear indication, and illustrative quotes. *(note: in the publication, this figure is mislabelled as background factors)*

Figure 5: Schema of the dominant behavioural beliefs that interviewees associated with withholding or delaying antimicrobial treatment.

Figure 6: Normative beliefs influencing decision to withhold or delay antimicrobial treatment where there is no clear indication, and illustrative quotes.

Figure 7: Control beliefs influencing decision to withhold or delay antimicrobial treatment where there is no clear indication, and illustrative quotes.

Supplementary materials (Appendix 3)

Table S1: Participant’s estimates of the contribution made by different sectors to the overall problem of AMR in Australia.

Document S2: Interview guide (for chapters 5 and 6)

Document S3: Codebook

Chapter 6: Seeking simplicity, navigating complexity: How veterinarians select an antimicrobial drug, dose, and duration for companion animals

Figure 1: Management selected by interview participants for the two case studies

Table 1: Overview of factors influencing veterinarians’ choices of antimicrobial drug, dose and duration

Table 2: Case factors (C) influencing veterinarians’ choice of antimicrobial drug, dose, and duration in companion animals.

Table 3: Antimicrobial drug (A) factors influencing veterinarians’ choices of antimicrobial drug, dose, and duration in companion animals.

Table 4: Pet owner (O) factors that influence veterinarians’ choice of antimicrobial drug, dose, and duration in companion animals.

Table 5a: Veterinarian (V) factors influencing choice of antimicrobial drug and dose in companion animals.

Table 5b: Veterinarian factors influencing choice of antimicrobial treatment duration (D) in companion animals.

Table 6: Practice and colleague (P) factors influencing veterinarians’ choice of antimicrobial drug, dose, and duration in companion animals.

Figure 2: The dispensary cycle

Table 7: External (E) factors influencing veterinarians’ choice of antimicrobial drug, dose, and duration in companion animals.

Supplementary materials (Appendix 4)

Document S1: Example of traffic-light AST report

Chapter 1: Literature Review

Introduction

Antimicrobials are some of the most important medications available to animals and humans, dramatically reducing morbidity and mortality from infectious diseases. However, their use is also associated with significant harms, including selection of antimicrobial resistance (AMR), disruption of normal microbiota and adverse effects that range from mild to fatal.

Antimicrobial resistance (AMR) is a ‘silent pandemic’¹ whose costs – in poorer health and welfare, lost lives and lower food production, and the associated economic burden – are undoubtedly enormous, but difficult to accurately quantify.² One rigorous study estimated that in 2019, the human deaths alone that were *directly* attributable to bacterial AMR totalled almost 1.3 million.³ Unfortunately, no estimates are available for animal mortality nor morbidity due to AMR.

AMR is a natural phenomenon that is accelerated by the use of antimicrobials. It has been described as the ‘quintessential One Health issue’,⁴ that is, a problem involving the health of humans, animals and the environment that requires a coordinated, multi-sector response. This is because antimicrobials are used in many species, and microbes and their antimicrobial resistance determinants can move between animals, humans and the environment. Selecting for AMR in any setting can therefore affect every setting, either directly or indirectly.⁵

Recognising the scale, complexity and urgency of this challenge, the Quadripartite of the World Health Organisation, World Organisation for Animal Health, Food and Animal Organisation, and the United Nations Environment Programme have committed to tackling AMR and developed a Global Action Plan in 2015.⁶ Most countries, including Australia, have their own National Action Plans on AMR.⁷

To maximise the benefits of antimicrobials and minimise the harms, it is important that all users use antimicrobials only when necessary, and that they optimise their choice of antimicrobial drug and regimen.

Scope and objectives of this thesis

The objective of this body of research is to improve our understanding of where suboptimal antimicrobial use occurs in Australian companion animal veterinary practice, and why it occurs, in order to develop and implement targeted interventions.

This work focuses on stewardship of antimicrobial drugs that act on bacteria, commonly referred to as antibiotics, as these are the most frequently applied antimicrobial type in the companion animal setting and the cause of most urgent concern.

Definition and goals of antimicrobial stewardship

Defined by Dyar *et al* as “a coherent set of actions which promote using antimicrobials responsibly,”⁸ antimicrobial stewardship (AMS), in its broadest sense, is an obligation shared by all members of society, including veterinary and medical prescribers, other health care workers, and consumers.

In the Australian companion animal setting, there are three central roles that influence AMS:

veterinarians, pet owners, and paraveterinary staff, including veterinary nurses, technicians and receptionists.

‘Responsible’ use of antimicrobials can be divided into two distinct categories:

- 1) minimising unnecessary use of antimicrobials; and
- 2) when antimicrobials are necessary, optimising the choice of drug, route, dose, timing and duration.

While the most commonly cited goal of AMS is to slow the development of AMR and thereby preserve the effectiveness of antimicrobials for all animals (including humans), for as long as possible, AMS also aims to minimise other important adverse effects of antimicrobial use (AMU).

Antimicrobial resistance in companion animals

Few data are available on AMR in companion animals. Where active surveillance programs exist for AMR in animals, these are almost exclusively focused on human health impacts i.e. monitoring food-producing animals and the animal-derived food products themselves. This reflects the prevailing societal concern around potential human health consequences from AMR bacteria from animal sources. To the author’s knowledge, no country in the world conducts routine surveillance of healthy companion animals for AMR isolates.

However, even AMR data from companion animal *clinical* samples – i.e. samples taken from unwell animals for diagnostic purposes - are rare in the scientific literature or elsewhere. There are some systems to consolidate clinical isolate data from diseased companion animals at national levels, but to date, only a few could be described as successful, e.g Sweden (SVARM),⁹ Norway (NORM-Vet),¹⁰ France (RESAPATH).¹¹ In contrast, the US FDA’s National AMR Monitoring System (NARMS) incorporated a small collection of companion animal clinical isolate data from 2017 to 2021, but none since.¹²

Undoubtedly, a lack of uniformity in antimicrobial susceptibility testing (AST) methods and reporting,¹³ and uncertainty surrounding clinical breakpoints in veterinary medicine¹⁴ are barriers to developing and maintaining such systems. An even greater barrier, perhaps, is the fact that in most countries, the majority of companion animal AST are performed by for-profit laboratories, that are not legally required to share data and have little incentive to volunteer it. Australia, like many countries, has never attempted to establish a national system to aggregate AST results from companion animal pathogens.

Hence, most publicly available data on AMR in companion animals comes from one-off analyses of clinical isolates from privately owned veterinary clinics or veterinary teaching hospitals. It can be difficult to use such analyses to form a clear picture of AMR trends, for several reasons. Firstly, there are geographical differences in pathogen prevalence within the same clinical syndrome¹⁵ and reports can come from different clinical cases, for example whether samples came from first-opinion, emergency or referral cases^{16, 17} will impact rates of resistance. Also, differences in laboratory techniques used, such as disc diffusion or microdilution plates¹⁸ and the breakpoints used to determine resistance to an antimicrobial¹⁴ can all impact the AMR rates reported.

Despite the variation in and paucity of data, there is evidence enough for concern that AMR pathogens are becoming more prevalent in companion animals worldwide. Of particular concern are methicillin-resistant *Staphylococcus pseudintermedius* (MRSP),^{19, 20} an

opportunistic canine skin pathogen that has acquired resistance to beta-lactam antimicrobials, which was first reported in 2006 and is now considered endemic worldwide.²¹ Another concern is extended-spectrum beta lactamase-producing (ESBL) *Enterobacteriaceae*^{22, 23}, that are resistant to most penicillins and cephalosporins. In a study from the Netherlands, ESBL *E. coli* was found in a concerning high 45% of healthy dogs and 55% of diarrhoeic dogs.²⁴ Resistance to carbapenems –a key ‘last-resort’ antimicrobial class for treatment of multi drug-resistant Gram-negative infections – has also been reported in companion animals around the world,²⁵ including in *Salmonella* from a cat in Australia.²⁶

Zoonotic risk and anthroponozoonotic risk of antimicrobial resistance

Although companion animals have historically been overlooked in the AMS space, there is no doubt that they play a role in AMR dynamics and should be included in One Health AMS efforts. Firstly, pets are very common; 69% of Australian households²⁷ and a similar percentage of US households²⁸ have a pet. Secondly, even in countries with relatively high levels of drug regulation, veterinarians are often at liberty to use many antimicrobials ‘off-label’ in companion animal patients, including last-resort antimicrobials for humans, such as carbapenems. Thirdly, many pets have very close physical relationships with their owners; an Australian survey conducted by a pet health insurance broker found almost half of pet owners shared their beds with their pets²⁹, similar to Portugal (60%)³⁰ and higher than in the UK (14%).³¹ The Portuguese study found almost 80% of owners kissed their pet and/or allowed their pet to lick their face, and one in five allowed their pet to eat from their plates.³⁰ In the UK study, dog owners also reported their pets licking their hands (~70%) and faces (~60%).³¹ These behaviours create high potential for AMR to develop and transfer from pets to humans. However, it must also be acknowledged that the same factors also create equally high potential for human-to-pet transmission of AMR.

Indeed, in Australia, humans may pose a greater AMR risk to their pets than vice versa; both the rate of antimicrobial exposure per life-year and the rate of high-importance antimicrobial use is higher in humans than in their pets.^{32, 33}

Yet despite the clear risk of bi-directional transmission of AMR between humans and their pets,³⁴ it remains unclear how much transmission actually occurs. One study looked at pets in the UK and Portugal presenting with urinary or skin infections and took samples from those pets and their owners. Core genome multilocus sequence typing – which provides high granularity of bacterial strain matching - showed 8 of 65 (12%) of pet-owner pairs shared the same strains of ESBL/Amp-C-producing *Enterobacteriaceae*³⁵, suggesting relatively frequent bacterial transfer between pets and owners, and/or a shared third source of ESBL-Amp-C *Enterobacteriaceae*, such as food or environment. Similarly, another study focused on MRSA-positive humans, found that in 6/66 (9%) of the households with cohabiting pets, at least one pet carried MRSA with the same sequence type.³⁶ However, a third study suggested that bacterial transfer between pets and owners could be much less frequent. This study recruited humans presenting to hospital and took samples from them and their pets, looking for frequently isolated multidrug-resistant organisms (MDRO), including MRSA. In 397 pet-owner pairs, only one pair (0.3%) was colonised with a matching MDRO.³⁷ More longitudinal research studies of pets and their owners would help to more accurately understand the frequency of inter-species transfer.³⁸

Determining the mechanism and direction of AMR spread between pets and their owners is more difficult. While some bacterial species are adapted to dogs and cats (e.g. *Staphylococcus pseudintermedius*, *Pasteurella multocida*) or to humans (e.g. *Staphylococcus*

aureus), suggesting those species as the original source, many bacteria e.g. *E. coli*, *Proteus* spp., *Enterococcus* spp. are common to humans and most other mammals, and re-circulation of bacteria within households makes it challenging to determine the source with certainty.

While the difficult process of identifying where AMR determinants originated and how and when they transmitted to other species is important to maximise AMS, meaningful progress can be made using basic principles of infection prevention, reducing unnecessary AMU, optimising antimicrobial drug selection and duration, and reducing transmission of all bacteria both within and between species through good hygiene and waste management.

Other risks associated with antimicrobial use

Other than selecting for AMR, the adverse effects of antimicrobial use in companion animals that cause most concern are gastrointestinal dysbiosis³⁹ and tissue toxicity.⁴⁰

Dysbiosis

Gastrointestinal dysbiosis – disruption to the normal intestinal microbiota and the metabolome - is an expected consequence of every dose of systemic antimicrobials, and is likely to have knock-on effects on many body functions, including metabolism, immunity,⁴¹ mood and behaviour.⁴² Our understanding of the scope, magnitude and duration of these effects is far from complete, but what is apparent so far is that recovery from iatrogenic dysbiosis is highly dependent on the type of antimicrobial drug used and the individual patient.⁴³ Dysbiosis in other body sites, such as the nasal cavity, oropharynx, genitourinary tract and skin is also expected with systemic antimicrobial use, however these effects have not been well studied in companion animals.

Several clinical trials have been conducted to understand the impact of commonly used antimicrobials (e.g. amoxicillin-clavulanate, metronidazole) on the gastrointestinal microbial diversity of healthy and sick dogs.⁴⁴⁻⁵⁰ All demonstrated dysbiosis induced by the antimicrobial therapy. One trial showed that healthy dogs given tylosin for 7 days developed no gastrointestinal signs, but all had marked dysbiosis at the end of treatment, which had partially resolved – in some dogs more than others - by the end of trial follow-up, 8 weeks after stopping the antimicrobial.⁴⁵ It is not known whether all treated dogs eventually returned to their baseline microbial diversity, or when. Only one similar trial on cats has been published; this showed persistent dysbiosis six weeks after clindamycin treatment.⁵¹ To fully understand the impact of systemic antimicrobial use in companion animals, more research on dysbiosis, with larger animal cohorts and longer follow-up periods, is needed.

In humans, some longer studies have been conducted. In one prospective study, 9 people who received oral vancomycin failed to recover their baseline faecal microbial diversity 22 weeks later.⁵² In a large Dutch retrospective study, both alpha- and beta- diversity of human gut microbiota were altered up to 4 years after treatment with macrolide and lincosamide antimicrobials, and for up to 1 year after beta-lactam antimicrobial use.⁵³

Outside of research studies, dysbiosis in companion animals is unlikely to be recognised, let alone actively managed, unless obvious gastrointestinal signs are present. Such signs can range from mild diarrhoea to severe, sometimes fatal, colitis caused by overgrowth of *Clostridioides difficile*⁵⁴ or other microbes.⁵⁵ In humans, the reported rate of antibiotic-associated diarrhoea ranges between 5% and 35%,⁵⁴ depending on the antimicrobial used, of which 15-25% of cases are due to *C. difficile*.⁵⁶ The incidence in companion animals is

unknown.

Toxicity and hypersensitivity

A less frequent, sometimes severe outcome of antimicrobial treatment is tissue toxicity,^{40, 57} for example chondrotoxicity from fluoroquinolone antimicrobial use in growing animals,⁵⁸ keratoconjunctivitis sicca associated with sulfonamide drugs⁵⁹ or ototoxicity⁴⁰ and nephrotoxicity from aminoglycoside antimicrobials.⁶⁰ These outcomes can often be avoided through careful selection of antimicrobial drug and regimen. However, increasing prevalence of AMR to relatively safe antimicrobials will force clinicians to make riskier treatment choices.

While immune-mediated hypersensitivity reactions to antimicrobials are recognised in companion animals,⁴⁰ the rate of such reactions is anecdotally very low, likely much lower than that reported in humans.⁶¹ Nevertheless, this rare but serious harm should be considered as part of the risk/benefit equation when prescribing.

Antimicrobial stewardship in companion animals

Antimicrobial importance ratings

To guide clinicians towards lower AMR-risk antimicrobial drug choices, and to help prioritise AMS efforts, the Australian Expert Advisory Group on AMR developed a system of antimicrobial importance ratings in 2002, which were updated by the Australian Strategic and Technical Advisory Group on AMR (ASTAG) in 2015⁶² and again in 2018.⁶³ The ASTAG system rates all antimicrobials available for animals and humans as 1) low; 2) medium; or 3) high importance,⁶³ indicating the severity of expected human health consequences if resistance should develop to that drug. Similarly, the World Health Organization (WHO) developed importance ratings for antimicrobial drugs at a meeting in Canberra in 2005.⁶⁴ Drugs are categorised by WHO into four levels: 1) important; 2) highly important; 3) critically important; and 4) highest priority critically important. The ASTAG importance ratings align closely with the WHO ratings, with a handful of differences based on local epidemiology, availability of drugs and antimicrobial susceptibility patterns. For example, the ASTAG system rates penicillins (such as amoxicillin) as low importance, whereas WHO had rated these as ‘critically important’, until they were downgraded to ‘highly important’ in the 2024 iteration.⁶⁵

Both ratings systems agree that quinolones (such as enrofloxacin) and late-generation cephalosporins, such as cefovecin – both of which are commonly used in companion animal practices in Australia⁶⁶ and elsewhere⁶⁷⁻⁶⁹ – are in the most important category and should be used with great care.

Antimicrobial use guidelines

Aside from antimicrobial importance ratings, another major pillar of AMS efforts are evidence-based prescribing guidelines. Given the infrequency of AST in companion animal practice,^{70, 71} veterinarians are almost always using antimicrobials empirically. Hence, syndrome-based prescribing guidelines, that take into account the locally expected pathogens, their relative prevalence, their antimicrobial susceptibility patterns and the local availability of various antimicrobial drugs for the animal species, are particularly important for companion animal AMS.

The International Society for Companion Animal Infectious Diseases (ISCAID) has released global guidelines for urinary tract infections,⁷² respiratory diseases,⁷³ and canine pyoderma.⁷⁴ The European Network for Optimization of Veterinary Antimicrobial Therapy (ENOVAT) has released guidelines on canine acute diarrhoea⁷⁵ and surgical prophylaxis.⁷⁶ The Federation of European Companion Animal Veterinary Associations (FECAVA) has also released AMU guidelines for a range of common dog and cat conditions⁷⁷ and several countries have their own national guidelines, including Denmark,⁷⁸ Canada⁷⁹ and Australia.⁸⁰

Developing such guidelines is not straightforward. Ideally, they should be based on evidence from clinical trials and supported by large-scale antibiograms, which require at least 30 clinical isolates of each relevant bacterial species for a given syndrome in a given animal species.⁸¹ While these requirements are relatively easy to meet in the context of a large human hospital that performs dozens of AST tests per day,⁸² for companion animal practice, they are much more challenging; veterinary guideline developers must make use of whatever published studies of AST data they can find. These studies are often focused on a single bacterial species, sometimes taken from different body sites (rather than all the potential causative pathogens for a syndrome in one body site),⁸³⁻⁸⁵ small in scale,⁸⁶ are taken from a non-representative cohort of patients (e.g. a veterinary referral hospital)^{87, 88} or a combination of these. When insufficient animal AST data or pharmacological data are available, it becomes necessary to extrapolate from human data⁸⁹ and use expert consensus.

Furthermore, given that the same bacterial species can have vastly different antimicrobial susceptibility patterns from one geographical area to another,⁹⁰⁻⁹⁴ and can shift over time,⁹⁵ isolates for an antibiogram should also be gathered from the area where the guidelines will be applied, as recently as possible. More data are needed from first-opinion companion animal practices in all geographical areas to validate locally used antimicrobial prescribing guidelines for their clinical context.

Clearly, developing antimicrobial guidelines is only part of the challenge – veterinarians also need to be aware of the guidelines and willing and able to follow them. One large US survey of veterinarians in 2019 found that an encouraging 60% were aware of antimicrobial prescribing guidelines. However, the effect of this awareness on prescribing intentions was weak. While veterinarians aware of guidelines were somewhat less likely to prescribe unnecessary antimicrobials for hypothetical scenarios than the guideline-unaware group, inappropriate prescribing intentions were high in both groups. For example, in the case of a young cat with urinary signs, which should not be treated with antimicrobials unless bacterial infection is confirmed with diagnostic testing, 44% of the guideline-aware group nevertheless intended to use antimicrobials, as did 54% of the guideline-unaware group. Similarly, for a well dog with 2-3 days of mild diarrhoea, for which guidelines similarly recommend no antimicrobials, 53% of guideline-aware veterinarians intended to treat with antimicrobials, compared with 59% of the guideline-unaware group.⁹⁶ Another study compared guideline recommendations with actual management of common dog and cat clinical presentations within a US academic veterinary

hospital; complete concordance with ISCAID guidelines even in this university hospital was low; 2.4% for upper respiratory tract infections and 2.6% for sporadic cystitis, for example.⁹⁷ It should, however, be noted that most deviations from guidelines in this centre were not in the choice of drug or the duration of treatment, but in the use of diagnostic testing. Earlier (2017) Swiss⁹⁸ studies had found much higher – but still suboptimal – rates of complete guideline concordance in dog prescriptions (38%)⁹⁹ and cat prescriptions (24%)¹⁰⁰ across both university hospitals and private practices, perhaps reflecting a stronger history of health education and AMS activity in many parts of Europe than in the US.

Antimicrobial use in companion animal practice

To design and evaluate AMS interventions for companion animal practice in Australia, it is important to understand current AMU practices and the drivers of suboptimal prescribing.

National data on antimicrobial use in companion animals

Similar to data on AMR in animals, national data on AMU in companion animals is scarce and of varying quality. Most countries report to WOAHA their total annual sales of antimicrobial products (in kilograms or tonnes of active ingredient) intended for use in any animal species¹⁰¹ and each country can select whether WOAHA makes their data publicly accessible through its digital platform, ANIMUSE.¹⁰²

Australia currently reports minimal AMU data to WOAHA, i.e. sales of kilograms of active antimicrobial ingredient in any products registered for animal use but does not make these public through ANIMUSE, which has led to controversial published assumptions about very high AMU in Australian food-producing animals.^{103, 104} The most recent Australian data publicly reported relate to sales of antimicrobials registered for animals from 2005 to 2010.¹⁰⁵

However, even if sales data were made available, these would not provide any useful insights into AMU in companion animals in Australia. There are three important reasons for this: sales data do not indicate how antimicrobials were actually used – how many animals of what size and species received which antimicrobials and how many were disposed of; some of the products registered for companion animals use are also registered for other animal species (e.g. *Noroclav* amoxicillin-clavulanate tablets are registered for both dogs and calves)¹⁰⁶, so could have been used ‘on-label’ in either of these species, and ‘off-label’ in several other animal species; some antimicrobial products (e.g. *Amoxil Forte*) registered only for human use¹⁰⁷ are commonly used ‘off-label’ in cats and dogs. Such usage is not currently accounted for in any routine data collection.

Currently, only France and Sweden additionally report how much active ingredient is used, and in how many companion animals by species,^{9, 108} but this level of AMU reporting will become mandatory for EU member states in 2029.¹⁰⁹ This is likely to lead to increased scrutiny on companion animal AMU globally. This will heighten risk to the public licence and regulatory settings that currently allow veterinarians to prescribe and sell a wide range of antimicrobials for companion animals, including antimicrobials of the highest importance for human health. These risks further underscore the importance of AMS efforts in this sector.

Suboptimal antimicrobial use in companion animal practice

Although Australia lacks systematic data on the patterns and appropriateness of AMU in companion animals, a small evidence base is emerging, thanks largely to two important data sources: VetCompass Australia and PetSure Pet Insurance. VetCompass Australia is a data repository funded and governed by the seven veterinary schools in Australia.¹¹⁰ It collects clinical notes, billing items and other data¹¹⁰ from the practice management software systems of almost 200 veterinary clinics around Australia, mostly first-opinion companion animal clinics. Data from around 200,000 dog and cat consultations per month are de-identified, collated and made available to approved veterinary researchers.¹¹⁰ PetSure is the largest provider of pet health insurance in Australia.¹¹¹ It assesses around two million insurance claims annually for veterinary care¹¹² and, in line with its commitment to supporting the veterinary community, has partnered with the University of Melbourne to use de-identified claims data to generate insights into antimicrobial use.

VetCompass Australia data from 2013 to 2017 revealed that almost 15% of dog consultations and 11% of cat consultations were associated with an antimicrobial prescription. In dogs, three medium-importance antimicrobial drugs accounted for 60% of all systemic antimicrobial prescriptions: amoxicillin-clavulanate (34%), cephalexin (16%) and metronidazole (10%). High-importance antimicrobials were uncommonly used in dogs; the most frequently applied drug in this category was enrofloxacin (3%). In cats, a more concerning picture emerged. The most frequently used systemic antimicrobial was high-importance cefovecin (32%), followed by medium-importance amoxicillin-clavulanate (31%) and low-importance doxycycline (13%).⁶⁶

An earlier study of VetCompass UK data showed similar patterns in the most frequently used antimicrobials in that country in 2012-2014: in dogs, the top three were amoxicillin-clavulanate (45%), cephalexin (15%) and metronidazole (10%) and in cats, cefovecin (30%), amoxicillin-clavulanate (29%) and clindamycin (9%).⁶⁷ One notable difference was that UK veterinarians were more likely to select low-importance amoxicillin in dogs (UK 9%, Australia 2%) and cats (UK 17%, Australia 2.5%) than Australian veterinarians,^{66, 67} although the overall proportion of use represented by amoxicillin in the UK is still low.

The total proportion of all (ASTAG) low-importance antimicrobials used was low in both Australia (13%)⁶⁶ and the UK (16%).⁶⁷ Veterinarians' apparent preference for the ASTAG medium-importance, broader spectrum amoxicillin-clavulanate over low-importance amoxicillin was also strongly reflected in 2022 sales data from across Europe.¹¹³ In 19 of 31 included countries, the ratio of amoxicillin to amoxicillin-clavulanate tablet sales (in kg of active ingredient) was less than 1:20. Only three countries had a ratio of more than 1:4, and within these only Sweden sold more amoxicillin than amoxicillin-clavulanate, at a ratio of 7:1. Interestingly, Sweden's direct neighbours Denmark (1:8) and Norway (1:5) had markedly lower ratios.¹¹³ Unfortunately, no species-level AMU data are available for Denmark or Norway, nor data to compare companion animal diseases or health outcomes across the three countries. But if Swedish veterinarians are using these tablets in a similar mix of animal diseases and achieving similar outcomes with similar pathogens, it would be reasonable to infer that much of the clavulanate used in Denmark and Norway provided no benefit.

In Australia, high use of amoxicillin-clavulanate, and the third-generation cephalosporin, cefovecin are a cause for concern, however without the clinical indications and local AST data, it is impossible to comment on the appropriateness of this use. Analysis of Australian AST data with accompanying clinical indications is needed to understand whether current patterns of AMU are appropriate.

In theory, both VetCompass Australia and PetSure data could be used to evaluate the appropriateness of AMU, across a wide range of conditions. However, there is no definition of what ‘appropriate’ antimicrobial use means in companion animals. Even when the task is simplified to assessing concordance with antimicrobial prescribing guidelines, it remains difficult to perform, as several things must be true for each prescription:

- a precise clinical indication for AMU must be discernible from the clinical notes;
- locally relevant, evidence-based antimicrobial prescribing guidelines for that clinical indication must be available;
- other relevant information that would influence drug selection must be present especially animal age, relevant comorbidities, clinical examination findings, AST results;
- the drugs dispensed (concentration, volume), animal weight and the dosage instructions must be present to evaluate route, dose, frequency and duration.

While the type and amount of antimicrobial drugs dispensed and the dosage instructions are usually available, and Australian guidelines⁸⁰ exist for many of the frequently seen indications, the remaining data items are often absent. In one study, fewer than 40% of systemic antimicrobial prescription events in VetCompass Australia had a dose, duration and indication recorded, or were able to be derived or calculated,¹¹⁴ highlighting challenges with clinical data quality. With regard to the indication, the NLP tools available at the time of analysis could only reliably narrow the diagnosis down to the body system involved, for example, ‘skin disorder’ or ‘urinary tract disorder’. Similarly, PetSure claims data shared with researchers have historically contained only enough detail to categorise diagnoses to a body system.

Nevertheless, broad indications of guideline concordance of veterinary antimicrobial prescribing in Australia can be gleaned from examining cat subcutaneous abscesses and cat and dog urinary tract infections in VetCompass Australia and PetSure data. These demonstrate that there is room for improvement in the decision to use antimicrobials, the use of AST, the choice of antimicrobial drug and the duration of treatment.

Cat subcutaneous abscesses

Cat abscesses are a common reason for presentation in veterinary general practice, representing around 3% of cat presentations in the UK.¹¹⁵ Australian AMU guidelines emphasise the need to establish drainage surgically (if not already draining) and thoroughly flush the abscess cavity. Systemic antimicrobials are only recommended as an additional measure if the animal is systemically unwell or immunocompromised, there is associated cellulitis or potential joint involvement.^{80, 116} While the proportion of abscess cases with such complications is unknown, anecdotally they are in the minority. Yet a VetCompass Australia study (albeit on data largely pre-dating the guidelines) found that 87% of cats with abscesses received systemic antimicrobials, with almost half of these receiving only antimicrobials and no surgical intervention.¹¹⁷

For abscess cases with an indication for antimicrobial treatment, the guideline-recommended antimicrobial drug is low-importance amoxicillin.^{80, 116} In the same study, only one percent of cases treated with an antimicrobial received amoxicillin; 53% received high-importance cefovecin, 34% medium-importance amoxicillin-clavulanate and 2% low-importance doxycycline.¹¹⁷ Since most abscesses are the result of territorial fights with other cats, these animals are more likely than the general cat population to have a free-roaming lifestyle and possibly more likely to display aggression, both of which likely make the route of antimicrobial

administration and frequency more salient for the treating veterinarian, encouraging the use of a single cefovecin injection.

Urinary tract infections

Taking urinary tract infections (UTIs) as another example, there are multiple apparent discrepancies between guideline recommendations and the way veterinarians manage cases. Starting with diagnostics, 2011 ISCAID guidelines recommended that AST be performed for all suspected bacterial infections of the urinary tract;¹¹⁸ the 2019 guidelines downgraded this to “preferred” for cases of sporadic cystitis.⁷² Although the rate of AST use in suspected urinary tract infections specifically is not known, a recent study found that only 4.5% of cats and dogs that received urinalysis (an in-house examination of urinary sediment that is commonly performed for animals with urinary signs) also received AST.^{119, unpublished data} Similarly, a VetCompass study of Australian dogs and cats that received cefovecin for any indication found that only 0.3% of recipients had had AST performed; this is despite AST being one of the requirements for using the drug, within the registered product information.⁷¹ Several local and international studies point to the cost to the owner and time delay involved in AST as major barriers to its use in high-income countries.^{70, 120-124}

With regard to antimicrobial drug choice, the recommended empirical treatments for sporadic bacterial cystitis (the most common cause of urinary signs in dogs) in the 2011 ISCAID guidelines¹¹⁸ were amoxicillin or trimethoprim-sulfonamide (TMS) or (the broadest-spectrum choice) amoxicillin-clavulanate. VetCompass Australia data from 2013-2017 showed that of the almost 11,000 dogs with urinary tract disorders that received antimicrobials – most of which would be expected to have bacterial cystitis – 74% received amoxicillin-clavulanate, with enrofloxacin (10%) and cephalexin (9%) the next most frequently used. Strikingly, neither amoxicillin nor TMS were used in *any* of the almost 11,000 identified urinary tract disorder cases in dogs⁶⁶. Analysis of PetSure claims data from the same time period showed similar results: of more than 7,000 dogs receiving antimicrobials for urinary tract disease, 68% received amoxicillin-clavulanate, 12% cephalexin and 8% enrofloxacin, although in this data set, 3% received amoxicillin and 2% received TMS, in accordance with guidelines.^{32, unpublished data}

In cats, urinary tract disorders are most commonly inflammatory, with no infectious component e.g. feline idiopathic cystitis¹²⁵, and thus antimicrobials are rarely indicated. Nevertheless, approximately 11,000 cats in the VetCompass Australia data from 2013-2017 were given antimicrobials for urinary tract disorders – higher than the number of dogs given antimicrobials for urinary tract disorders in the same time period - suggesting many cats were treated with antimicrobials unnecessarily. Moreover, only 2% received guideline-recommended amoxicillin and none received TMS. Almost half received high-importance cefovecin (47%) and the other half amoxicillin-clavulanate (45%).⁶⁶ PetSure data from the same time period showed an almost identical pattern of antimicrobial selection for more than 2,000 cats with urinary tract disease.^{32, unpublished data}

The reasons why veterinarians avoided the narrower-spectrum, inexpensive antimicrobials that were recommended in evidence-based guidelines for UTIs are unknown. Urinary pathogen susceptibility data and qualitative research with Australian veterinarians are required to understand the barriers to guideline-concordant AMU for this indication.

These datasets also reveal that inappropriate dosing of antimicrobials has been common in Australian companion animals. Across all conditions, a large proportion of animals received antimicrobial doses either too low or too high for their body weight. The rate of ‘correct’ dosing

(within 10% of guideline range) in VetCompass Australia data varied between antimicrobial drugs and was as low as 35% in dogs receiving doxycycline and 25% in cats receiving enrofloxacin.¹¹⁴ This is a cause for serious concern for both AMR and patient safety; doses that are too low or too infrequent still cause dysbiosis and select for AMR in all exposed bacteria, but may not achieve a therapeutic effect on the target pathogens; excessive doses are likely to be effective, but increase the risk of toxicity. The VetCompass Australia and PetSure data referenced are now several years old. It is not known whether the AMU patterns from 2013-2017 persist in Australian companion animal practice today.

Aside from the choice of drug and dosing, duration of treatment is another critical component of appropriate AMU. There is very little published veterinary research on this topic. A small Swiss study on cat antimicrobial use demonstrated that treatment duration exceeded guideline recommendations for approximately half the cases of FLUTD and abscesses treated with antimicrobials (whether or not the antimicrobials were judged to be indicated).¹²⁶ A more recent study in a single US veterinary teaching hospital used manual record review to evaluate antimicrobial guideline concordance for eight infectious diseases in dogs and cats in 2021-2022, but only included cases that received an antimicrobial rated as critically important by WHO, e.g. quinolones, 3rd and 4th-generation cephalosporins. In this limited study, concordance with guideline duration varied markedly for different conditions, e.g. 32% for pyelonephritis; 90% for sporadic cystitis, 93% for upper respiratory tract infections.⁹⁷

While VetCompass Australia and PetSure data have the potential to offer many insights on duration concordance with AMU guidelines, the primary challenge remains determining a precise indication for antimicrobial treatment, rather than a body system classification. Then there are two additional challenges; firstly, common conditions (e.g. skin infections) can have multiple episodes, consultation records and associated antimicrobial prescriptions¹¹⁴ over months or even years, making it difficult to separate episodes, and determine which antimicrobials relate to which episode. Secondly, some animals are treated for multiple conditions simultaneously, making it unclear which antimicrobial is for which condition. The best local data available on concordance of antimicrobial duration with guidelines come from the cat fight abscess study. Australian guidelines recommend that abscess cases that have an indication for antimicrobials receive five to ten days' treatment.^{80, 116} Fewer than 30% of cases in VetCompass Australia treated with antimicrobials received durations that could have been within the guideline range. Most of the durations exceeding ten days were due to cefovecin use; 47% of treated cats received one and 6% received two consecutive injections, lasting 14 days each.¹¹⁷ Again, it must be acknowledged that the analysed data (2013-2017) mostly preceded the first guideline release (2017), and it is unknown whether these patterns persist.

Evaluating whether treatment duration is optimal is even more challenging than evaluating concordance with guidelines. Optimal duration is not always the guideline-recommended duration, but rather the 'shortest duration necessary',¹²⁷ in other words, just long enough to assist that patient's immune system to clear the infection and no longer. While this seems simple, every infection is an interaction between a host and a pathogen, with a plethora of variables. Hence, determining the best stopping point for an individual is not always straightforward. In human medicine, patients can assess and verbalise improvements in their symptoms, which can be a useful guide to antibiotic cessation.¹²⁸ Sometimes functional tests such as forced expiratory volume for respiratory infections¹²⁹ or normalisation of acute phase protein levels such as C-reactive protein and procalcitonin¹³⁰⁻¹³² are monitored in conjunction with symptomatic improvement in order to tailor duration of treatment. In companion animals, functional tests that require active patient participation are not possible. However, C-reactive protein levels have been used successfully in two small studies to guide antimicrobial discontinuation in dogs with pneumonia, significantly shortening their duration of treatment.^{133,}

¹³⁴ No C-reactive protein trials have been conducted in cats. One study suggests that procalcitonin levels could be useful in cats¹³⁵ but it appears to be less useful in dogs.^{136, 137} To date, no acute phase protein tests have been widely adopted in veterinary practice for the purpose of guiding antimicrobial duration;¹³⁸ aside from the paucity of animal evidence, the cost to the pet owner of repeated tests is an expected barrier to routine use. For now, to decide on when to stop antimicrobial treatment, companion animal veterinarians must rely on clinical signs and/or antimicrobial use guidelines. It should be noted that companion animal guideline-recommended durations of treatment are currently based on minimal data, since there have been very few companion animal clinical trials published that compare two different treatment durations with the same drug,¹³⁹⁻¹⁴² let alone more complex trials designed to establish the shortest effective duration of treatment. A UK trial of this type, on dogs with UTI¹⁴³ is expected to report findings in the near future.

Factors influencing antimicrobial prescribing decisions

Clinical factors influencing antimicrobial prescribing decisions

In principle, the decision to prescribe systemic antibiotics to an unwell dog or cat, should be based only on the presence of a bacterial infection for which antimicrobials are expected to reduce morbidity. It is therefore unsurprising that there is seasonal variation in antimicrobial prescribing rates in temperate areas,¹⁴⁴ since there are seasonal disease peaks, most notably atopic skin disease in dogs over warmer months.¹⁴⁵ Similarly, in a large study using the VetCompass UK dataset (178 practices), unwell pets presenting to a veterinarian that were fully vaccinated (OR 0.93) or dogs that were desexed (OR 0.90) were significantly less likely to receive antibiotics compared with their undervaccinated and entire counterparts.¹⁴⁶ While there are many potential confounders and this study could not determine causality, the simplest explanation is that vaccinated animals are less likely to experience vaccine-preventable viral infections that can be mistaken for - or lead to - bacterial infections. Similarly, neutered animals are unlikely to suffer from infections associated with reproductive organs and hormones, such as prostatitis and pyometra.

Regarding the selection of antimicrobial drug and dosing regimen, there are few published qualitative studies exploring the clinical factors considered by companion animal veterinarians. Two European qualitative studies found veterinarians considered the diagnosis, severity of clinical signs, animal species, breed, age, living conditions, weight, temperament, pharmacokinetics, susceptibility of the known or presumptive pathogen and the drug's spectrum of activity.^{147, 148} Echoing those latter points, another study mentions that antimicrobial drug choice is influenced by the site of the infection and the perceived efficacy against the most likely pathogen.¹⁴⁸ In human general practice, additional clinical factors have been identified that doctors consider when selecting an antimicrobial regimen, including potential adverse effects, the patient's history of antimicrobial treatment, comorbidities, particularly renal insufficiency, and other relevant physical states such as pregnancy.¹⁴⁹ Interestingly, while clinic profit from antimicrobial drug sales is often raised as a potential driver of antimicrobial prescribing, an Australian survey of veterinarians showed that 72% strongly disagreed that profit motivated them.¹²⁰ This claimed disinterest in profit is supported by a survey of Dutch veterinarians¹²² and qualitative studies showing that veterinarians are, in fact, strongly motivated to minimise costs for clients.^{147, 150} On the other hand, Denmark's policy of limiting the profit that veterinary practices can make on antimicrobial sales was followed by a rapid decrease in total animal antimicrobial use in that country.¹⁵¹ The complexity of antimicrobial decision making in companion animal practice, and the added layer of socio-political complexity in which these decisions take place, means it is difficult to isolate the

effect of a single contributing factor.

Non-clinical factors influencing antimicrobial prescribing decisions

Aside from the effect of vaccination and desexing, VetCompass UK analyses also revealed some surprising factors associated with antimicrobial prescribing for unwell animals. Insured animals (OR 0.87) and animals treated at practices accredited by the Royal College of Veterinary Surgeons (OR 0.79) were significantly less likely to receive antimicrobials.¹⁴⁶ Assuming there was no significant difference in case mix between these groups - a possibility that was unfortunately not explored in the study – this suggests that in the decision to prescribe, non-clinical factors could play an even greater role than clinical factors in the decision.

In the companion animal veterinary literature, a wide range of non-clinical factors have been identified as influencing both the decision to prescribe antimicrobials, as well as the selection of drug and dosing regimen. The drivers of these two categories of suboptimal use appear to differ in potentially important ways. For example, the existence of non-antimicrobial treatments (e.g. medicated shampoos) could only influence the decision to prescribe antimicrobials, whereas antimicrobial label information would be expected to only influence the choice of drug and dosing regimen. However, these two decisions have not been separated in the existing literature. Qualitative research that differentiates between the decision to prescribe and the choice of drug and dosing regimen would help to better understand the drivers of suboptimal use.

The decision to use antimicrobials, even when the benefit is absent or unclear, has been associated most strongly with perceived or actual owner expectations of their pet receiving antimicrobials.^{147, 150, 152} These expectations are underpinned by owner's past ¹⁴⁷ experiences with veterinarians,¹⁵³ desire for a 'quick fix', ¹⁴⁷ beliefs that the risks of AMU are low or negligible¹⁵² as well as their level of anxiety about their animal's health.¹⁴⁸ Similarly, for the veterinarian, fear of missing an infection and the consequences of that can drive veterinarians to prescribe antimicrobials when uncertain.¹⁵⁰ This uncertainty can be in turn heightened when physical examination is hindered by animal aggression,¹⁴⁷ when the veterinarian is inexperienced,¹⁵⁰ and when there is perceived or actual owner reluctance to pursue further diagnostic testing, usually due to cost.^{150, 154} 'Just in case' antimicrobial prescribing can be viewed by veterinarians as a trade-off between current case priorities – safeguarding against clinical deterioration and satisfying owner expectations - and risks.¹⁵² Davis *et al* framed this as "tension between the immediate infection risks for individuals and longer-term, collective AMR risks",¹⁵⁵ the latter of which is easier to dismiss as it can seem abstract and distant for clinicians¹⁵⁶ and likely even more abstract for pet owners. The certain, immediate – and sometimes visible - consequences of dysbiosis could therefore prove a more effective deterrent to 'just in case' AMU. However, this remains to be tested.

Other drivers of unnecessary antimicrobial prescribing include time pressure on the veterinarian^{150, 152} and AMU norms within the veterinary practice.¹⁵⁷ One study additionally identified lower trust between a veterinarian and pet owner as motivator of unnecessary antimicrobial use, and availability of non-antimicrobial alternative treatments for the condition (e.g. medicated shampoo for canine superficial pyoderma) as a demotivator.¹⁴⁷

When considering the choice of antimicrobial drug, companion animal veterinarians are almost always selecting empirically, since they tend to perform AST only for refractory or relapsing cases.¹²⁰ This is at least in part due to perceived or actual unwillingness of pet owners

to pay out-of-pocket for AST; animals with insurance are more likely to receive AST.¹⁴⁷ Further supporting this was a recent Australian clinical trial that provided AST free of charge for animals with signs of urinary tract infection. During the free testing period, participating clinics showed a mean increase of 2.4 times [range 0.7 to 24.6 times] in their AST submission rates.¹⁵⁸

Veterinarians' empirical drug selections are based on many non-clinical factors, including the range of antimicrobials routinely kept in stock at the clinic and the formulations of drugs on the market.¹⁴⁸ In particular, veterinarians consider the palatability and ease of administration¹⁴⁷ along with animal aggression¹⁴⁷ and owners' physical capabilities¹⁵³, factors that are closely linked to concern about an animal failing to receive a 'complete' course of antimicrobials. This powerful concern about 'finishing the course' appears to be a primary driver for veterinarians to use long-acting cefovecin, a 14-day antimicrobial course given as subcutaneous injection by the veterinarian. This single injection effectively relieves veterinarians' concerns about owner compliance and owner safety, and simultaneously relieves the pet owner of the mental and physical burden of administering daily - or more frequent - oral medications at home. Unfortunately, as a third-generation cephalosporin which remains detectable in the plasma for at least four weeks,^{159, 160} it follows that it also maintains dysbiosis and exerts selection pressure for ESBL-producing bacteria for this duration.

Other major influences on drug selection include what other veterinarians in their practice tend to prescribe for a given syndrome^{147, 148} and minimising the drug costs for the client.^{148, 150} Habits,^{147, 150} clinic protocols,^{120, 148} pharmaceutical company marketing¹⁴⁷ and local requirements for AST prior to using particular antimicrobials in some countries¹⁴⁷ have also been identified as playing a role in drug selection. While one might hope that AMU guidelines would have a major influence, only 28% of Australian veterinarians had referred to AMU guidelines in a 2017 survey.¹²⁰ Interviews with veterinarians in the Netherlands suggested that guidelines had been less influential on veterinarians' antimicrobial choices than force of habit.¹⁴⁷

No studies have explored the factors influencing the duration of veterinary antimicrobial treatment, however the medical literature shows that doctors strongly favour durations that are "five or seven days, or multiples thereof",¹⁶¹ which also aligns with the way that human antimicrobials often come packaged.¹⁶² This seems more related to the way people conceptualise time than any biological reason,¹⁶³ making it likely that veterinarians also favour these durations when prescribing antimicrobials. VetCompass Australia data could reveal such patterns, if they exist, in companion animal treatment duration.

Strategies for improving antimicrobial use in companion animal practice

Both involuntary and voluntary approaches have been employed to improve veterinary antimicrobial use. Involuntary approaches have the advantage of being relatively simple to enact, however, their enforcement can be difficult and costly, and can cause clinician pushback where they threaten professional autonomy¹⁶⁴ or cause welfare risks to sick animals that urgently require antimicrobials.¹⁶⁵ It should be noted that although reduced overall AMU is the metric most often mentioned with these strategies, the goal of AMS is not to reduce overall AMU *per se*, but to improve the appropriateness of AMU. Unfortunately, 'appropriate AMU' is yet to be defined for veterinary practice, much less actually measured.

Involuntary approaches

Denmark was an early adopter of an involuntary restriction on the profit veterinarians could make on prescription medication sales, including antimicrobials. Within one year of the 1994 implementation, total volume of animal therapeutic use of antimicrobials in Denmark dropped by 40%,¹⁵¹ although it seems likely this was primarily due to changes in livestock AMU. Norway, Sweden, Finland and Iceland have gone further than Denmark, decoupling veterinary prescribing and medication sales, meaning that veterinary clients must now purchase any prescribed antimicrobials from a pharmacy or other business, separate to the veterinary practice.¹⁶⁶ Although it is difficult to disentangle the effect of this policy from other AMS efforts, as well as the many cultural, climatic, animal management and other differences, it is notable that in 2022, these four countries had the four lowest rates of antimicrobial use in livestock of all 31 European countries, ranging from just 2.1 to 14.9 mg/PCU (Population Correction Unit), compared with 34.1mg/PCU in Denmark, 157.5mg/PCU in Italy and 254.7mg/PCU in Cyprus.¹¹³ In Australia, decoupling is unlikely to be practical outside major centres. Such a policy would cause disproportionate logistical challenges, treatment delays and compromised animal welfare for rural and remote veterinary clients, whose nearest pharmacy might be hundreds of kilometres away.¹⁶⁷

The government of the Netherlands explored the idea of decoupling in 2010, but determined that the administrative burden involved would be excessive.¹⁶⁸ Instead, it introduced national oversight of every individual veterinarian's antimicrobial prescribing, and imposed sanctions, including fines and professional suspensions, for non-compliance with prudent use policies.¹⁶⁹ AMU (by total mass of active ingredients) in livestock dropped by half in the following years¹⁷⁰, and 3rd and 4th generation cephalosporin use in all animals was practically eliminated by 2013.¹¹³ France introduced a national mandate in 2016 for veterinarians to have AST results before using high-importance antimicrobials;⁷⁰ sales of 3rd and 4th generation cephalosporins dropped by two-thirds in the first year and quinolone use dropped by half in the first five years after the mandate.¹¹³ In both cases, there were other concurrent AMS initiatives, as well as mainstream media attention on animal AMU, hence it is impossible to know how much change is attributable to these specific policies.

Other involuntary approaches that have been suggested include banning the use of all high-importance antimicrobials in animals. Almost all Dutch companion animal veterinarians surveyed in 2015 rejected this idea,¹²² as did 82% of veterinarians in a more recent global Delphi survey.¹⁷¹ A survey of Australian veterinarians revealed that concern for animal welfare is likely to be the primary reason for this objection.¹⁷²

Voluntary approaches

Voluntary strategies help avoid unintended consequences, such as compromised animal welfare. However, they are often more difficult to implement than involuntary strategies and can be less impactful, if a significant proportion of clinicians decline to engage with them. Voluntary strategies suggested by veterinarians include enhancing AMS content within veterinary undergraduate teaching¹⁷³; developing and disseminating evidence-based antimicrobial prescribing guidelines;^{73, 89, 97, 174-177} building clinical decision-support tools underpinned by AMS principles;^{122, 126, 158, 178} postgraduate veterinary education on AMU;^{122, 179} campaigns aimed at shifting veterinarians' and clients' attitudes towards antimicrobial use^{98, 180, 181} and audit and feedback on antimicrobial prescribing, without sanctions.¹⁸² AMS trials in companion animal practices in the Netherlands,¹⁸³ UK,^{184, 185} and Australia¹⁵⁴ have used a

combination of these strategies, and others, with success. One promising enhancement of standard audit and feedback that has been used in human general practice uses social norms to drive behaviour change. 'Nudge' letters are sent to individual prescribers with unexpectedly high rates of antimicrobial use, explaining their outlier status and the concern about their use.^{186, 187}

Veterinarians have been the focus of almost all companion animal AMS efforts in the literature to date, although it is clear that there are other important roles that deserve attention. The potential and actual role of paraveterinary staff in companion animal AMS has been recognised in the literature,^{188, 189} however no companion animal AMS trials to date have intentionally engaged these staff.

Pet owners are another group with an important role to play; clients' implicit or explicit desire to receive medication for an unwell animal, sometimes specifically antimicrobials, has been identified in UK qualitative studies as an influence on veterinary prescribing.^{152, 157} In the analogous setting of a parent presenting a sick child to a doctor, perceived or actual pressure from parents to prescribe antimicrobials has been repeatedly identified as a factor in qualitative research in multiple countries.¹⁹⁰⁻¹⁹⁵

A recent US survey study quantified pet owner expectations of antimicrobials, finding that 48% expected antimicrobials to be prescribed for their sick animal and 17% would still want antimicrobials prescribed, even if the veterinarian said these 'probably would not help'.¹⁹⁶ In contrast, a study of Swedes who presented to a veterinarian with a dog with diarrhoea found only 7% expected antimicrobials to treat it. Aside from differences in study design, and possible desirability bias in pet owner responses, there are many possible reasons for the disparity in these findings. The medical literature would suggest that public attitudes towards antimicrobial use in humans are intertwined with health beliefs, knowledge and education,^{197, 198} personal risk aversion,¹⁹⁷ national health policies,¹⁹⁸ and - perhaps less obviously - facets of local culture, including religiousness¹⁹⁹ and trust.²⁰⁰ Hence, to understand the prevalence and underlying reasons for such attitudes in Australian pet owners, local studies are needed.

The magnitude of the influence pet owner expectations of antimicrobials have on veterinary prescribing is also unknown. The only quantitative study performed (in human medicine) suggests that the influence could be significant; in 306 real parent-child medical consultations, where the child's illness had a presumed viral aetiology (e.g. ear pain, nasal congestion), antimicrobials were prescribed 62% of the time when the doctor perceived that the parent wanted antimicrobials, compared with only 7% of the time when the physician did not perceive parental desire for antimicrobials.¹⁹³

Despite a paucity of evidence, it is reasonable to infer that some proportion of Australian pet owners do expect a veterinarian to prescribe antimicrobials even when these are not necessary and that this increases the likelihood that a veterinarian will prescribe them. There is reason to be optimistic that pet owner expectations of antimicrobials are amenable to change. One recent AMS trial in the UK showed that owners who view a short animation about AMR prior to a veterinary consultation significantly increased their knowledge of AMR and reduced their intention to request antimicrobial treatment.¹⁸⁰ In contrast, a more passive pet owner AMS education campaign using waiting room posters had minimal impact on knowledge (only 10% could partially or completely reproduce the poster message) and no detectable impact on client pressure for antimicrobials.²⁰¹ In Victoria, a government-funded campaign called 'Not All Bugs Need Drugs' aimed to build veterinarian and animal owner awareness of unnecessary antimicrobial prescribing, however the effect of this campaign was not evaluated.

Conclusion

There is growing evidence that Australian companion animal veterinarians often deviate from local AMU guidelines and prudent use principles. This manifests as using antimicrobials when none are required, or as suboptimal choices of drug and treatment regimen, commonly selecting antimicrobial drugs of higher importance or durations of antimicrobial treatment that exceed guideline recommendations, or both.

The reasons for these behaviours have not yet been explored in depth with Australian companion animal veterinarians, and the two categories of suboptimal use have not been disentangled in the literature to date. Understanding the extent to which they are driven by microbiology, other clinical factors such as animal temperament and non-clinical factors, such as client expectations is an important step towards designing effective interventions to improve prescribing.

Research questions

The main research questions that will be explored in this thesis are:

Chapter 2

- Are the empirical antimicrobials recommended in international and Australia guidelines for dog and cat urinary tract infections effective against local urinary pathogens?

Chapter 3

- How frequently is the use of clavulanate and cefovecin justified in Australian companion animals?

Chapter 4

- Why do veterinarians sometimes prescribe antimicrobials to cats and dogs when there is uncertain (or no) clinical benefit?

Chapter 5

- What clinical and non-clinical factors influence veterinarians' selection of an antimicrobial drug, route and dosing regimen?

Chapter 6

- What do pet owners expect when they present a sick animal to a veterinarian? How can veterinarians communicate more effectively with pet owners about prudent antimicrobial use?

References

1. World Health Organization (WHO). Global antimicrobial resistance forum launched to help tackle common threat to planetary health. <https://www.who.int/news-room/articles-detail/global-antimicrobial-resistance-forum-launched-to-help-tackle-common-threat-to-planetary-health>. 2023
2. de Kraker ME, Stewardson AJ, Harbarth S. Will 10 Million People Die a Year due to Antimicrobial Resistance by 2050? *PLoS Medicine* 2016;13:e1002184.
3. Murray CJL, Ikuta KS, Sharara F et al. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *The Lancet* 2022;399:629-655.

4. Robinson TP, Bu D, Carrique-Mas J et al. Antibiotic resistance is the quintessential One Health issue. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 2016;110:377-380.
5. Da Costa PM, Loureiro L, Matos AJF. Transfer of Multidrug-Resistant Bacteria Between Intermingled Ecological Niches: The Interface Between Humans, Animals and the Environment. *International Journal of Environmental Research and Public Health* 2013;10:278-294.
6. World Health Organization (WHO). Global Action Plan on Antimicrobial Resistance <https://www.who.int/publications/i/item/9789241509763>. 2016. Retrieved:08/10/2025
7. Australian Government. Australia's National Antimicrobial Resistance Strategy – 2020 and beyond. <https://www.amr.gov.au/resources/australias-national-antimicrobial-resistance-strategy-2020-and-beyond>. 2020. Retrieved:08/10/2025
8. Dyar O, Huttner B, Schouten J, Pulcini C. What is antimicrobial stewardship? *Clinical Microbiology and Infection* 2017;23:793-798.
9. Statens Veterinärmedicinska Anstalt (SVA) Sweden. Swedish Veterinary Antimicrobial Resistance Monitoring (SVARM) Report 2024. <https://www.sva.se/media/amupibfr/swedres-svarm-2024-webb.pdf>. 2024. Retrieved:14/04/2025
10. Norwegian Veterinary Institute. NORM-VET - the monitoring program for antimicrobial resistance in the veterinary and food production sectors. <https://www.vetinst.no/en/surveillance-programmes/norm-norm-vet-report>. 2025. Retrieved:14/04/2025
11. ANSES-ANMV French Agency for Food Environmental and Occupational Health & Safety. French surveillance network for antimicrobial resistance in bacteria from diseased animals, 2023 Annual report. <https://www.anses.fr/fr/system/files/LABO-Ra-Resapath2023-EN.pdf>. 2024. Retrieved:10/10/2025
12. U.S. Food and Drug Administration (FDA). The National Antimicrobial Resistance Monitoring System (NARMS). <https://www.fda.gov/animal-veterinary/antimicrobial-resistance/national-antimicrobial-resistance-monitoring-system#:~:text=The%20NARMS%20program%20helps%20promote,limit%20the%20spread%20of%20resistance>. 2025. Retrieved:14/04/2025
13. Hardefeldt L, Marenda M, Crabb H et al. Antimicrobial susceptibility testing by Australian veterinary diagnostic laboratories. *Aus Vet J* 2018;96:142-146.
14. Feßler AT, Wang Y, Burbick CR et al. Antimicrobial susceptibility testing in veterinary medicine: performance, interpretation of results, best practices and pitfalls. *One Health Advances* 2023;1:26.
15. Turnidge J, Bell J, Biedenbach DJ, Jones RN. Pathogen occurrence and antimicrobial resistance trends among urinary tract infection isolates in the Asia-Western Pacific Region: report from the SENTRY Antimicrobial Surveillance Program, 1998–1999. *International Journal of Antimicrobial Agents* 2002;20:10-17.
16. Aika IN, Enato E. Antibigram of clinical isolates from primary and secondary healthcare facilities: a step towards antimicrobial stewardship. *PLoS Global Public Health* 2022;2:e0000644.
17. Saperston KN, Shapiro DJ, Hersh AL, Copp HL. A Comparison of Inpatient Versus Outpatient Resistance Patterns of Pediatric Urinary Tract Infection. *The Journal of Urology* 2014;191:1608-1613.

18. Annis DH, Craig BA. The effect of interlaboratory variability on antimicrobial susceptibility determination. *Diagnostic Microbiology and Infectious Disease* 2005;53:61-64.
19. Perreten V, Kadlec K, Schwarz S et al. Clonal spread of methicillin-resistant *Staphylococcus pseudintermedius* in Europe and North America: an international multicentre study. *J Antimicrob Chemother* 2010;65:1145-1154.
20. Pires dos Santos T, Damborg P, Moodley A, Guardabassi L. Systematic Review on Global Epidemiology of Methicillin-Resistant *Staphylococcus pseudintermedius*: Inference of Population Structure from Multilocus Sequence Typing Data. *Frontiers in Microbiology* 2016;7.
21. Nocera FP, De Martino L. Methicillin-resistant *Staphylococcus pseudintermedius*: epidemiological changes, antibiotic resistance, and alternative therapeutic strategies. *Veterinary Research Communications* 2024.
22. Zogg AL, Simmen S, Zurfluh K et al. High Prevalence of Extended-Spectrum β -Lactamase Producing Enterobacteriaceae Among Clinical Isolates From Cats and Dogs Admitted to a Veterinary Hospital in Switzerland. *Frontiers in Veterinary Science* 2018;5.
23. Salgado-Caxito M, Benavides JA, Adell AD, Paes AC, Moreno-Switt AI. Global prevalence and molecular characterization of extended-spectrum β -lactamase producing-*Escherichia coli* in dogs and cats – A scoping review and meta-analysis. *One Health* 2021;12:100236.
24. Hordijk J, Schoormans A, Kwakernaak M et al. High prevalence of fecal carriage of extended spectrum β -lactamase/AmpC-producing Enterobacteriaceae in cats and dogs. *Frontiers in Microbiology* 2013;4.
25. Rincón-Real AA, Suárez-Alfonso MC. Carbapenem resistance in critically important human pathogens isolated from companion animals: a systematic literature review. *Osong Public Health Res Perspect* 2022;13:407-423.
26. Abraham S, O’Dea M, Trott DJ et al. Isolation and plasmid characterization of carbapenemase (IMP-4) producing *Salmonella enterica* Typhimurium from cats. *Scientific reports* 2016;6:35527.
27. Animal Medicines Australia. Pets in Australia: A national survey of pets and people. Australia, 2022.
28. American Pet Products Association (APPA). National Pet Owners Survey. USA, 2025.
29. Hadnagy N. Let sleeping dogs lie in – alarming number of Aussies share their bed with pets. <https://www.comparethemarket.com.au/news/let-sleeping-dogs-lie-in-alarming-number-of-aussies-share-their-bed-with-pets/>. 2024. Retrieved:09/09/2025
30. do Vale B, Lopes AP, Fontes MdC et al. A Cross-Sectional Study of Knowledge on Ownership, Zoonoses and Practices among Pet Owners in Northern Portugal. *Animals* 2021;11:3543.
31. Westgarth C, Pinchbeck GL, Bradshaw JWS et al. Dog-human and dog-dog interactions of 260 dog-owning households in a community in Cheshire. *Veterinary Record* 2008;162:436-442.
32. Hardefeldt LY, Selinger J, Stevenson MA 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;225:34-39.
33. Australian Commission on Safety and Quality in Healthcare. AURA 2019: Third Australian report on antimicrobial use and resistance in human health. 2019.

34. Jin M, Osman M, Green BA et al. Evidence for the transmission of antimicrobial resistant bacteria between humans and companion animals: A scoping review. *One Health* 2023;17:100593.
35. Menezes J, Frosini S-M, Weese S et al. Transmission dynamics of ESBL/AmpC and carbapenemase-producing Enterobacterales between companion animals and humans. *Frontiers in Microbiology* 2024;15:1432240.
36. Morris DO, Lautenbach E, Zaoutis T et al. Potential for pet animals to harbour methicillin-resistant *Staphylococcus aureus* when residing with human MRSA patients. *Zoonoses Public Health* 2012;59:286-293.
37. Hackmann C, Genath A, Gruhl D et al. The transmission risk of multidrug-resistant organisms between hospital patients and their pets—a case– control study, Germany, 2019 to 2022. *Eurosurveillance* 2024;29:2300714.
38. Caddey B, Fisher S, Barkema Herman W, Nobrega Diego B. Companions in antimicrobial resistance: examining transmission of common antimicrobial-resistant organisms between people and their dogs, cats, and horses. *Clinical Microbiology Reviews* 2025;38:e00146-00122.
39. Deschamps C, Apper E, Brun M et al. Development of a new antibiotic-induced dysbiosis model of the canine colonic microbiota. *International Journal of Antimicrobial Agents* 2024;63:107102.
40. Arunvikram K, Ipsita Mohanty IM, Sardar K et al. Adverse drug reaction and toxicity caused by commonly used antimicrobials in canine practice. *Veterinary World* 2014;7:299-305.
41. Ji Y, Yang Y, Wu Z. Programming of metabolic and autoimmune diseases in canine and feline: linkage to the gut microbiome. *Microbial Pathogenesis* 2023;185:106436.
42. Sacoar C, Marugg JD, Lima NR, Empadinhas N, Montezinho L. Gut-brain axis impact on canine anxiety disorders: new challenges for behavioral veterinary medicine. *Journal of Veterinary Internal Medicine* 2024;2024:2856759.
43. Schwartz DJ, Langdon AE, Dantas G. Understanding the impact of antibiotic perturbation on the human microbiome. *Genome Medicine* 2020;12:82.
44. Pilla R, Gaschen FP, Barr JW et al. Effects of metronidazole on the fecal microbiome and metabolome in healthy dogs. *J Vet Intern Med* 2020;34:1853-1866.
45. Manchester AC, Webb CB, Blake AB et al. Long-term impact of tylosin on fecal microbiota and fecal bile acids of healthy dogs. *J Vet Intern Med* 2019;33:2605-2617.
46. Igarashi H, Maeda S, Ohno K et al. Effect of oral administration of metronidazole or prednisolone on fecal microbiota in dogs. *PloS One* 2014;9:e107909.
47. Suchodolski JS, Dowd SE, Westermarck E et al. The effect of the macrolide antibiotic tylosin on microbial diversity in the canine small intestine as demonstrated by massive parallel 16S rRNA gene sequencing. *BMC Microbiology* 2009;9:1-16.
48. Grønvold A-MR, L'Abée-Lund TM, Sørum H et al. Changes in fecal microbiota of healthy dogs administered amoxicillin. *FEMS Microbiology Ecology* 2009;71:313-326.
49. Werner M, Suchodolski JS, Straubinger RK et al. Effect of amoxicillin-clavulanic acid on clinical scores, intestinal microbiome, and amoxicillin-resistant *Escherichia coli* in dogs with uncomplicated acute diarrhea. *J Vet Intern Med* 2020;34:1166-1176.
50. Espinosa-Gongora C, Jessen LR, Kieler IN et al. Impact of oral amoxicillin and amoxicillin/clavulanic acid treatment on bacterial diversity and β -lactam resistance in the canine faecal microbiota. *J Antimicrob Chemother* 2020;75:351-361.

51. Whittemore JC, E. SJ, M. PJ, and Suchodolski JS. Effects of a synbiotic on the fecal microbiome and metabolomic profiles of healthy research cats administered clindamycin: a randomized, controlled trial. *Gut Microbes* 2019;10:521-539.
52. Isaac S, Scher JU, Djukovic A et al. Short- and long-term effects of oral vancomycin on the human intestinal microbiota. *J Antimicrob Chemother* 2016;72:128-136.
53. Mulder M, D. R, C. K-dJJ et al. Long-term effects of antimicrobial drugs on the composition of the human gut microbiota. *Gut Microbes* 2020;12:1791677.
54. McFarland LV. Antibiotic-associated diarrhea: epidemiology, trends and treatment. *Future Microbiology* 2008;3:563-578.
55. Willard MD, Berridge B, Braniecki A, Bouley D. Possible antibiotic-associated colitis in a dog. *Journal of the American Veterinary Medical Association* 1998;213:1775-1779.
56. Barbut F, Petit JC. Epidemiology of Clostridium difficile-associated infections. *Clinical Microbiology and Infection* 2001;7:405-410.
57. Randjelovic P, Veljkovic S, Stojiljkovic N, Sokolovic D, Ilic I. Gentamicin nephrotoxicity in animals: Current knowledge and future perspectives. *Experimental and Clinical Sciences Journal* 2017;16:388-399.
58. Hall MM, Finnoff JT, Smith J. Musculoskeletal Complications of Fluoroquinolones: Guidelines and Precautions for Usage in the Athletic Population. *Physical Medicine and Rehabilitation* 2011;3:132-142.
59. Trepanier LA, Danhof R, Toll J, Watrous D. Clinical findings in 40 dogs with hypersensitivity associated with administration of potentiated sulfonamides. *J Vet Intern Med* 2003;17:647-652.
60. Cronin R, Bulger R, Southern P, Henrich W. Natural history of aminoglycoside nephrotoxicity in the dog. *The Journal of Laboratory and Clinical Medicine* 1980;95:463-474.
61. Lee CE, Zembower TR, Fotis MA et al. The incidence of antimicrobial allergies in hospitalized patients: implications regarding prescribing patterns and emerging bacterial resistance. *Archives of Internal Medicine* 2000;160:2819-2822.
62. Australian Strategic and Technical Advisory Group on Antimicrobial Resistance (ASTAG). Importance Ratings and Summary of Antibacterial Uses in Humans in Australia, version 1.1. <https://www.amr.gov.au/sites/default/files/2022-10/importance-ratings-and-summary-of-antibacterial-uses-in-humans-in-australia.pdf>. 2015. Retrieved:22/10/2025
63. Australian Strategic and Technical Advisory Group on Antimicrobial Resistance (ASTAG). Importance ratings and summary of antibacterial uses in human and animal health in Australia. www.amr.gov.au/resources/importance-ratings-and-summary-antibacterial-uses-human-and-animal-health-australia. 2018. Retrieved:18 Feb 2023
64. Angulo FJ, Collignon P, Powers JH et al. World Health Organization ranking of antimicrobials according to their importance in human medicine: a critical step for developing risk management strategies for the use of antimicrobials in food production animals. *Clinical Infectious Diseases* 2009;49:132-141.
65. World Health Organization (WHO). WHO List of Medically Important Antimicrobials: a risk management tool for mitigating antimicrobial resistance due to non-human use. www.who.int/news/item/08-02-2024-who-medically-important-antimicrobial-list-2024. 2024. Retrieved:14 Feb 2024

66. Hur BA, Hardefeldt LY, Verspoor KM, Baldwin T, Gilkerson JR. 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:e0230049.
67. Buckland EL, O'Neill D, Summers J et al. Characterisation of antimicrobial usage in cats and dogs attending UK primary care companion animal veterinary practices. *Veterinary Record* 2016;179:489.
68. Galarce N, Arriagada G, Sánchez F et al. Antimicrobial Use in Companion Animals: Assessing Veterinarians' Prescription Patterns through the First National Survey in Chile. *Animals* 2021;11:348.
69. Karalliu E, Ngan SYL, Bęczkowski PM et al. Antimicrobial use practices among companion animal veterinarians in Hong Kong. *Vet J* 2025;314:106433.
70. Bourély C, Fortané N, Calavas D, Leblond A, Gay É. Why do veterinarians ask for antimicrobial susceptibility testing? A qualitative study exploring determinants and evaluating the impact of antibiotic reduction policy. *Prev Vet Med* 2018;159:123-134.
71. Hardefeldt L, Hur B, Verspoor K et al. Use of cefovecin in dogs and cats attending first-opinion veterinary practices in Australia. *Veterinary Record* 2020;187:e95-e95.
72. Weese JS, Blondeau J, Boothe D et al. International Society for Companion Animal Infectious Diseases (ISCAID) guidelines for the diagnosis and management of bacterial urinary tract infections in dogs and cats. *Veterinary Journal* 2019;247:8-25.
73. Lappin M, Blondeau J, Boothe D et al. Antimicrobial use guidelines for treatment of respiratory tract disease in dogs and cats: Antimicrobial Guidelines Working Group of the International Society for Companion Animal Infectious Diseases. *J Vet Intern Med* 2017;31:279-294.
74. Loeffler A, Cain CL, Ferrer L et al. Antimicrobial use guidelines for canine pyoderma by the International Society for Companion Animal Infectious Diseases (ISCAID). *Veterinary Dermatology* 2025;36:234-282.
75. Jessen L, Werner M, Singleton D et al. European Network for Optimization of Veterinary Antimicrobial Therapy (ENOVAT) guidelines for antimicrobial use in canine acute diarrhoea. *Vet J* 2024;307:106208.
76. Allerton F, Sørensen T, Scahill K et al. European Network for Optimization of Veterinary Antimicrobial Therapy (ENOVAT) 2025 guidelines for surgical antimicrobial prophylaxis in dogs and cats. *Journal of Small Animal Practice* 2025.
77. Federation of European Companion Animal Veterinary Associations (FECAVA). FECAVA Recommendations for Appropriate Antimicrobial Therapy. <https://www.fecava.org/wp-content/uploads/2020/01/FECAVA-Recommendations-for-Appropriate-Antimicrobial-ENGLISH-1.pdf>. 2018. Retrieved:06/10/2025
78. Den Danske Dyrlægeforening (Danish Veterinary Association). Antibiotic Use Guidelines for Companion Animal Practice (2nd Ed.). https://www.ddd.dk/media/2175/assembled_final.pdf. 2019. Retrieved:06/10/2025
79. Canadian Veterinary Medical Association (CVMA). Guidelines for Veterinary Antimicrobial Use. <https://www.canadianveterinarians.net/veterinary-resources/antimicrobial-stewardship-resources/cvma-guidelines-for-veterinary-antimicrobial-use/>. 2018. Retrieved:06/10/2025

80. The University of Melbourne. Australian Veterinary Prescribing Guidelines, Dogs and Cats (version 2). <https://vetantibiotics.science.unimelb.edu.au/about/resources/>. 2019. Retrieved:25 May 2022
81. Truong WR, Hidayat L, Bolaris MA, Nguyen L, Yamaki J. The antibiogram: key considerations for its development and utilization. *JAC-Antimicrobial Resistance* 2021;3.
82. Binkley S, Fishman NO, LaRosa LA et al. Comparison of Unit-Specific and Hospital-Wide Antibiograms Potential Implications for Selection of Empirical Antimicrobial Therapy. *Infection Control & Hospital Epidemiology* 2006;27:682-687.
83. Saputra S, Jordan D, Mitchell T et al. Antimicrobial resistance in clinical Escherichia coli isolated from companion animals in Australia. *Veterinary Microbiology* 2017;211:43-50.
84. Saputra S, Jordan D, Worthing KA et al. Antimicrobial resistance in coagulase-positive staphylococci isolated from companion animals in Australia: A one year study. *PloS One* 2017;12:e0176379.
85. KuKanich KS, Lubbers BV. Review of enterococci isolated from canine and feline urine specimens from 2006 to 2011. *Journal of the American Animal Hospital Association* 2015;51:148-154.
86. Almansa Ruiz JC, Jonker A, Bosman AM, Steenkamp G. Bacteria profile and antibiogram of the bacteria isolated from the exposed pulp of dog canine teeth. *Veterinary Record* 2018;183:97-97.
87. Leet-Otley K, Fellman CL, Wayne AS et al. Demonstrating the importance of local culture and susceptibility data: Antibiograms from dogs at a veterinary tertiary care center. *Journal of the American Veterinary Medical Association* 2023;261:1-7.
88. Wei AY, Thompson MF, Worthing KA et al. Frequency and antimicrobial susceptibility profiles of bacterial species isolated from canine and feline urine samples in Sydney, Australia, 2012-2021. *Veterinary Microbiology* 2025:110541.
89. Allerton F, Prior C, Bagcigil AF et al. Overview and evaluation of existing guidelines for rational antimicrobial use in small-animal veterinary practice in Europe. *Antibiotics* 2021;10:409.
90. Guardabassi L. Antimicrobial resistance: a global threat with remarkable geographical differences. *New Zealand Veterinary Journal* 2017;65:57-59.
91. Sader HS, Castanheira M, Arends SJR, Goossens H, Flamm RK. Geographical and temporal variation in the frequency and antimicrobial susceptibility of bacteria isolated from patients hospitalized with bacterial pneumonia: results from 20 years of the SENTRY Antimicrobial Surveillance Program (1997–2016). *J Antimicrob Chemother* 2019;74:1595-1606.
92. Hritcu OM, Schmidt VM, Salem SE et al. Geographical variations in virulence factors and antimicrobial resistance amongst staphylococci isolated from dogs from the United Kingdom and Romania. *Frontiers in Veterinary Science* 2020;7:414.
93. Ojasanya RA, Weese JS, Sobkowich KE et al. Assessment of Seasonality in Antimicrobial Susceptibility Testing and Resistance of Urinary Escherichia coli from Dogs and Cats in the United States (2019–2022). *Prev Vet Med* 2025:106684.
94. Marques C, Gama LT, Belas A et al. European multicenter study on antimicrobial resistance in bacteria isolated from companion animal urinary tract infections. *BMC Vet Res* 2016;12.

95. Conner JG, Smith J, Erol E et al. Temporal trends and predictors of antimicrobial resistance among *Staphylococcus* spp. isolated from canine specimens submitted to a diagnostic laboratory. *PLoS One* 2018;13:e0200719.
96. Taylor DD, Martin JN, Scallan Walter EJ. Survey of companion animal veterinarians' antimicrobial drug prescription practices and awareness of antimicrobial drug use guidelines in the United States. *Zoonoses Public Health* 2022;69:277-285.
97. Robbins SN, Goggs R, Kraus-Malett S, Goodman L. Effect of institutional antimicrobial stewardship guidelines on prescription of critically important antimicrobials for dogs and cats. *J Vet Intern Med* 2024;38:1706-1717.
98. Agriculture Victoria. Not all bugs need drugs: Play your part in preventing antibiotic resistant infections. <https://agriculture.vic.gov.au/livestock-and-animals/livestock-health-and-welfare/antibiotic-resistant-infections/information-for-vets>. Retrieved:25/06/2025
99. Lehner C, Hubbuch A, Schmitt K et al. Effect of antimicrobial stewardship on antimicrobial prescriptions for selected diseases of dogs in Switzerland. *J Vet Intern Med* 2020;34:2418-2431.
100. Schmitt K, Lehner C, Schuller S et al. Antimicrobial use for selected diseases in cats in Switzerland. *BMC Vet Res* 2019;15:94.
101. World Organisation for Animal Health (WOAH). Annual Report on Antimicrobial Agents Intended for Use in Animals, 8th report. <https://www.woah.org/app/uploads/2024/05/woah-amu-report-2024-final.pdf>. 2024. Retrieved:06/10/2025
102. World Organisation for Animal Health (WOAH). ANIMUSE: Global Database on Animal Antimicrobial Use. <https://amu.woah.org/amu-system-portal/home>. Retrieved:17/06/2025
103. Ellis S, Coombe J, Page S et al. Response to “Global trends in antimicrobial use in food-producing animals: 2020 to 2030”. *PLoS Global Public Health* 2025;4:e0003133.
104. Mulchandani R, Wang Y, Gilbert M, Van Boeckel TP. Global trends in antimicrobial use in food-producing animals: 2020 to 2030. *PLoS Global Public Health* 2023;3:e0001305.
105. Australian Pesticides and Veterinary Medicines Authority (APVMA). Quantity of Antimicrobial Products Sold for Veterinary Use in Australia: July 2005 to June 2010. Australian Government 2014.
106. Australian Pesticides and Veterinary Medicines Authority. Public Chemical Registration Information System Search (PubCRIS). <https://portal.apvma.gov.au/pubcris>. Retrieved:17/06/2025
107. Therapeutic Goods Administration (Australia). Australian Register of Therapeutic Goods (ARTG). <https://www.tga.gov.au/resources/artg>. Retrieved:17/06/2025
108. ANSES-ANMV FAff, Environmental and Occupational Health & Safety,. Médicaments antimicrobiens chez l'animal: Surveillance des ventes et des utilisations, Rapport annuel 2023. <https://www.anses.fr/fr/system/files/ANMV-Ra-Antibiotiques2023.pdf>. 2024. Retrieved:06/10/2025
109. European Medicines Agency (EMA). Advice on implementing measures under Article 57(4) of Regulation (EU) 2019/6 on veterinary medicinal products – Report on the format of the data to be collected on antimicrobial medicinal products used in animals. https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/advice-implementing-measures-under-article-574-regulation-eu-20196-veterinary-medicinal-products-report-format-data-be-collected-antimicrobial-medicinal-products-used-animals_en.pdf. 2020
110. VetCompass Australia. <https://www.vetcompass.com.au/>. Retrieved:14/04/2025

111. PetSure Australia. <https://petsure.com.au/>. Retrieved:11/09/2025
112. PetSure Australia. Impact Snapshot FY2024. 2024.
113. European Medicines Agency (EMA). 13th ESVAC report: Sales of veterinary antimicrobial agents in 31 European countries in 2022. https://www.ema.europa.eu/en/documents/report/sales-veterinary-antimicrobial-agents-31-european-countries-2022-trends-2010-2022-thirteenth-esvac-report_en.pdf. 2022. Retrieved:07/10/2025
114. Hur B, Hardefeldt LY, Verspoor KM, Baldwin T, Gilkerson JR. Evaluating the dose, indication and agreement with guidelines of antimicrobial use in companion animal practice with natural language processing. *JAC-Antimicrobial Resistance* 2022;4.
115. O'Neill DG, Church DB, McGreevy PD, Thomson PC, Brodbelt DC. Prevalence of disorders recorded in cats attending primary-care veterinary practices in England. *Vet J* 2014;202:286-291.
116. The University of Melbourne. Australian Veterinary Prescribing Guidelines, Dogs and Cats (version 1). <https://vetantibiotics.fvas.unimelb.edu.au>. 2017. Retrieved:19 June 2019
117. Hur B, Verspoor KM, Baldwin T et al. Using natural language processing and patient journey clustering for temporal phenotyping of antimicrobial therapies for cat bite abscesses. *Prev Vet Med* 2024;223:106112.
118. Weese JS, Blondeau JM, Boothe D et al. Antimicrobial use guidelines for treatment of urinary tract disease in dogs and cats: Antimicrobial Guidelines Working Group of the International Society for Companion Animal Infectious Diseases. *Veterinary Medicine International* 2011;2011:1-9.
119. Hii AW, Gilkerson JR, Bailey KE et al. Antimicrobial prescribing in dogs and cats with urinary tract disease in a prospective intervention trial. *J Vet Intern Med* 2026;40.
120. Hardefeldt LY, Gilkerson JR, Billman-Jacobe H et al. Barriers to and enablers of implementing antimicrobial stewardship programs in veterinary practices. *J Vet Intern Med* 2018;32:1092-1099.
121. Norris JM, Zhuo A, Govendir M et al. Factors influencing the behaviour and perceptions of Australian veterinarians towards antibiotic use and antimicrobial resistance. *PloS One* 2019;14:e0223534.
122. Hopman NEM, Mughini-Gras L, Speksnijder DC et al. Attitudes and perceptions of Dutch companion animal veterinarians towards antimicrobial use and antimicrobial resistance. *Prev Vet Med* 2019;170:104717.
123. Grayzel SE, Bender JB, Gumley N et al. Understanding companion animal practitioners' attitudes toward antimicrobial stewardship. *Journal of the American Veterinary Medical Association* 2015;247:883-884.
124. Fowler H, Davis MA, Perkins A et al. A survey of veterinary antimicrobial prescribing practices, Washington State 2015. *Veterinary Record* 2016;179:651.
125. Dorsch R, Teichmann-Knorrn S, Sjetne Lund H. Urinary tract infection and subclinical bacteriuria in cats: a clinical update. *Journal of Feline Medicine and Surgery* 2019;21:1023-1038.
126. Hubbuch A, Schmitt K, Lehner C et al. Antimicrobial prescriptions in cats in Switzerland before and after the introduction of an online antimicrobial stewardship tool. *BMC Vet Res* 2020;16:1-13.

127. Leekha S, Terrell CL, Edson RS. General principles of antimicrobial therapy. *Mayo Clinic Proceedings* 2011;86:156-167.
128. Llor C, Frimodt-Møller N, Miravittles M, Kahlmeter G, Bjerrum L. Optimising antibiotic exposure by customising the duration of treatment for respiratory tract infections based on patient needs in primary care. *eClinicalMedicine* 2024;74.
129. Waters V, Stanojevic S, Klingel M et al. Prolongation of antibiotic treatment for cystic fibrosis pulmonary exacerbations. *Journal of Cystic Fibrosis* 2015;14:770-776.
130. Pepper DJ, Sun J, Rhee C et al. Procalcitonin-guided antibiotic discontinuation and mortality in critically ill adults: a systematic review and meta-analysis. *Chest* 2019;155:1109-1118.
131. Kubo K, Sakuraya M, Sugimoto H et al. Benefits and harms of procalcitonin-or C-reactive protein-guided antimicrobial discontinuation in critically ill adults with sepsis: A systematic review and network meta-analysis. *Critical Care Medicine* 2024;52:e522-e534.
132. von Dach E, Albrich WC, Brunel A-S et al. Effect of C-reactive protein-guided antibiotic treatment duration, 7-day treatment, or 14-day treatment on 30-day clinical failure rate in patients with uncomplicated gram-negative bacteremia: a randomized clinical trial. *Journal of the American Medical Association* 2020;323:2160-2169.
133. Viitanen SJ, Lappalainen AK, Christensen M, Sankari S, Rajamäki M. The utility of acute-phase proteins in the assessment of treatment response in dogs with bacterial pneumonia. *J Vet Intern Med* 2017;31:124-133.
134. Fernandes Rodrigues N, Giraud L, Bolen G et al. Antimicrobial discontinuation in dogs with acute aspiration pneumonia based on clinical improvement and normalization of C-reactive protein concentration. *J Vet Intern Med* 2022;36:1082-1088.
135. Cho J-G, Oh Y-I, Song K-H, Seo K-W. Evaluation and comparison of serum procalcitonin and heparin-binding protein levels as biomarkers of bacterial infection in cats. *Journal of Feline Medicine and Surgery* 2021;23:370-374.
136. Koho N, Rajamäki MM, Viitanen SJ. Serum procalcitonin as a diagnostic biomarker in dogs with bacterial respiratory diseases. *Veterinary Clinical Pathology* 2024;53:273-279.
137. Rompf J, Lutz B, Adamik K-N et al. Plasma procalcitonin and C-reactive protein concentrations in dogs with bacterial sepsis and non-infectious systemic inflammatory response syndrome. *Frontiers in Veterinary Science* 2025;12:1609020.
138. Rossi G. Acute phase proteins in cats: Diagnostic and prognostic role, future directions, and analytical challenges. *Veterinary Clinical Pathology* 2023;52:37-49.
139. Vientós-Plotts AI, Masseau I, Reinero CR. Comparison of short-versus long-course antimicrobial therapy of uncomplicated bacterial pneumonia in dogs: a double-blinded, placebo-controlled pilot study. *Animals* 2021;11:3096.
140. Aiken MJ, Hughes TK, Abercromby RH, Holmes MA, Anderson AA. Prospective, randomized comparison of the effect of two antimicrobial regimes on surgical site infection rate in dogs undergoing orthopedic implant surgery. *Veterinary Surgery* 2015;44:661-667.
141. Turnwald GH, Gossett KA, Cox HU et al. Comparison of single-dose and conventional trimethoprim-sulfadiazine therapy in experimental *Staphylococcus intermedius* cystitis in the female dog. *American Journal of Veterinary Research* 1986;47:2621-2623.

142. Rogers KS, Lees GE, Simpson RB. Effects of single-dose and three-day trimethoprim-sulfadiazine and amikacin treatment of induced *Escherichia coli* urinary tract infections in dogs. *American Journal of Veterinary Research* 1988;49:345-349.
143. Allerton F, Pouwels KB, Bazelle J et al. Prospective trial of different antimicrobial treatment durations for presumptive canine urinary tract infections. *BMC Vet Res* 2021;17:299.
144. Hopman NE, Portengen L, Heederik DJ et al. Time trends, seasonal differences and determinants of systemic antimicrobial use in companion animal clinics (2012-2015). *Veterinary Microbiology* 2019;235:289-294.
145. Dong Y, Wang L, Zhang K, Zhang H, Guo D. Prevalence and association with environmental factors and establishment of prediction model of atopic dermatitis in pet dogs in China. *Frontiers in Veterinary Science* 2024;11:1428805.
146. Singleton DA, Pinchbeck GL, Radford AD et al. Factors associated with prescription of antimicrobial drugs for dogs and cats, United Kingdom, 2014–2016. *Emerging Infectious Diseases* 2020;26:1778.
147. Hopman NE, Hulscher ME, Graveland H et al. Factors influencing antimicrobial prescribing by Dutch companion animal veterinarians: A qualitative study. *Prev Vet Med* 2018;158:106-113.
148. Mateus AL, Brodbelt DC, Barber N, Stark KD. Qualitative study of factors associated with antimicrobial usage in seven small animal veterinary practices in the UK. *Prev Vet Med* 2014;117:68-78.
149. Krishnakumar J, Tsopra R. What rationale do GPs use to choose a particular antibiotic for a specific clinical situation? *BMC Family Practice* 2019;20:178.
150. King C, Smith M, Currie K et al. Exploring the behavioural drivers of veterinary surgeon antibiotic prescribing: a qualitative study of companion animal veterinary surgeons in the UK. *BMC Vet Res* 2018;14:332.
151. Grave K, Jensen VF, Odensvik K, Wierup M, Bangen M. Usage of veterinary therapeutic antimicrobials in Denmark, Norway and Sweden following termination of antimicrobial growth promoter use. *Prev Vet Med* 2006;75:123-132.
152. Smith M, King C, Davis M et al. Pet owner and vet interactions: exploring the drivers of AMR. *Antimicrob Resist Infect Control* 2018;7:46.
153. Tompson AC, Chandler CIR, Mateus ALP et al. What drives antimicrobial prescribing for companion animals? A mixed-methods study of UK veterinary clinics. *Prev Vet Med* 2020;183:105-117.
154. Hardefeldt LY, Hur B, Richards S et al. Antimicrobial stewardship in companion animal practice: an implementation trial in 135 general practice veterinary clinics. *JAC-Antimicrobial Resistance* 2022;4:dlac015.
155. Davis MDM, Schermuly A, Rajkhowa A et al. Risk individualisation and moral injury in the treatment of infection as impediments to the tackling of antimicrobial resistance. *Health, Risk & Society*:1-18.
156. Krockow EM, Colman AM, Chattoe-Brown E et al. Balancing the risks to individual and society: a systematic review and synthesis of qualitative research on antibiotic prescribing behaviour in hospitals. *Journal of Hospital Infection* 2019;101:428-439.

157. Currie K, King C, Nuttall T, Smith M, Flowers P. Expert consensus regarding drivers of antimicrobial stewardship in companion animal veterinary practice: a Delphi study. *Veterinary Record* 2018;182:691.
158. Hii AW, Gilkerson JR, Bailey KE et al. Outcomes from an intervention study implementing fee-free culture and susceptibility urine testing in dogs and cats. *Veterinary Record* 2025:e5500.
159. Stegemann MR, Sherington J, Coati N, Brown SA, Blanchflower S. Pharmacokinetics of cefovecin in cats. *J Vet Pharmacol Ther* 2006;29:513-524.
160. Stegemann MR, Sherington J, Blanchflower S. Pharmacokinetics and pharmacodynamics of cefovecin in dogs. *J Vet Pharmacol Ther* 2006;29:501-511.
161. Pouwels KB, Hopkins S, Llewelyn MJ et al. Duration of antibiotic treatment for common infections in English primary care: cross sectional analysis and comparison with guidelines. *Br Med J* 2019;364:l440.
162. McGuire TM, Smith J, Del Mar C. The match between common antibiotics packaging and guidelines for their use in Australia. *Australian and New Zealand Journal of Public Health* 2015;39:569-572.
163. Wong D. Antibiotic treatment durations are not based on scientific reasoning; they stem from an artificially created number system. *British Columbia Medical Journal* 2025;67:184-186.
164. Broom J, Broom A, Kenny K, Konecny P, Post JJ. Regulating antimicrobial use within hospitals: A qualitative study. *Infection, Disease & Health* 2024;29:81-90.
165. Golding SE, Ogden J, Higgins HM. Shared goals, different barriers: a qualitative study of UK veterinarians' and farmers' beliefs about antimicrobial resistance and stewardship. *Frontiers in Veterinary Science* 2019;6:132.
166. Törneke K, Torren-Edo J, Grave K, Mackay DKJ. The management of risk arising from the use of antimicrobial agents in veterinary medicine in EU/EEA countries – a review. *J Vet Pharmacol Ther* 2015;38:519-528.
167. Smith JD, White C, Roufeil L et al. A national study into the rural and remote pharmacist workforce. *Rural and Remote Health* 2013;13:1-11.
168. Beemer F, van Velzen G, van den Berg C et al. Rapport Berenschot: Wat zijn de effecten van het ontkoppelen van voorschrijven en verhandelen van diergeneesmiddelen door de dierenarts? (What are the effects of uncoupling the prescription and sales of veterinary medicines through veterinarians?). <https://app.1848.nl/document/tkapi/216587>. 2010. Retrieved:20/10/2025
169. Lloyd DH, Page SW. Antimicrobial Stewardship in Veterinary Medicine. *Microbiology Spectrum* 2018;6.
170. Speksnijder DC, Mevius DJ, Bruschke CJ, Wagenaar JA. Reduction of veterinary antimicrobial use in the Netherlands. The Dutch success model. *Zoonoses Public Health* 2015;62 Suppl 1:79-87.
171. Sri A, Bailey KE, Scarborough R et al. Reaching consensus amongst international experts on the use of high importance-rated antimicrobials in animals – a Delphi study. *One Health* 2024;19:100883.
172. Sri A, Bailey KE, Gilkerson JR, Browning GF, Hardefeldt LY. Attitudes towards Use of High-Importance Antimicrobials—A Cross-Sectional Study of Australian Veterinarians. *Antibiotics* 2022;11:1589.

173. Castro-Sánchez E, Drumright LN, Gharbi M, Farrell S, Holmes AH. Mapping antimicrobial stewardship in undergraduate medical, dental, pharmacy, nursing and veterinary education in the United Kingdom. *PLoS One* 2016;11:e0150056.
174. Weese JS. Investigation of antimicrobial use and the impact of antimicrobial use guidelines in a small animal veterinary teaching hospital: 1995–2004. *Journal of the American Veterinary Medical Association* 2006;228:553-558.
175. Hardefeldt L, Crabb H, Bailey K et al. Appraisal of the Australian Veterinary Prescribing Guidelines for antimicrobial prophylaxis for surgery in dogs and cats. *Aus Vet J* 2019;97:316-322.
176. Guardabassi L, Kruse H. Principles of prudent and rational use of antimicrobials in animals. *Guide to antimicrobial use in animals*, 2008:1-12.
177. Sarrazin S, Vandael F, Van Cleven A et al. The impact of antimicrobial use guidelines on prescription habits in fourteen Flemish small animal practices. *Vlaams Diergeneeskundig Tijdschrift* 2017;86.
178. GekkoVet. GekkoVet: The vet-created pet diagnostic platform. <https://www.gekkovet.com/>. Retrieved:25/06/2025
179. Allerton F, Russell J. Antimicrobial stewardship in veterinary medicine: a review of online resources. *JAC-Antimicrobial Resistance* 2023;5.
180. Wright E, Jessen LR, Tompson A et al. Influencing attitudes towards antimicrobial use and resistance in companion animals—the impact on pet owners of a short animation in a randomized controlled trial. *JAC-Antimicrobial Resistance* 2024;6.
181. Bhattacharya A, Hopkins S, Sallis A, Budd EL, Ashiru-Oredope D. A process evaluation of the UK-wide Antibiotic Guardian campaign: developing engagement on antimicrobial resistance. *Journal of Public Health (Oxf)* 2017;39:e40-e47.
182. Acharya KR, Cohen A, Brankston G et al. An Evaluation of the Impact of an OPEN Stewardship Generated Feedback Intervention on Antibiotic Prescribing among Primary Care Veterinarians in Canada and Israel. *Animals* 2024;14:626.
183. Hopman NEM, Portengen L, Hulscher MEJL et al. Implementation and evaluation of an antimicrobial stewardship programme in companion animal clinics: A stepped-wedge design intervention study. *PLoS One* 2019;14:e0225124.
184. Walker B, Sánchez-Vizcaíno F, Barker EN. Effect of an antimicrobial stewardship intervention on the prescribing behaviours of companion animal veterinarians: a pre–post study. *Veterinary Record* 2022;190:e1485.
185. Singleton DA, Rayner A, Brant B et al. A randomised controlled trial to reduce highest priority critically important antimicrobial prescription in companion animals. *Nature Communications* 2021;12.
186. Hallsworth M, Chadborn T, Sallis A et al. Provision of social norm feedback to high prescribers of antibiotics in general practice: a pragmatic national randomised controlled trial. *The Lancet* 2016;387:1743-1752.
187. Hendrie D. ‘Nudge’ letters prompt sustained drop in antibiotic prescribing. <https://www1.racgp.org.au/newsgp/professional/nudge-letters-prompt-sustained-drop-in-antibiotic#:~:text=The%20decreased%20prescribing%20results%20come,a%20major%20role%20to%20play>. 2020. Retrieved:01/10/2025

188. Redding LE, Reilly K, Radtke B, Bartholomew S, Cole SD. The potential role of veterinary technicians in promoting antimicrobial stewardship. *BMC Vet Res* 2023;19:142.
189. Kainga H, Phonera M, Kallu SA et al. Knowledge, attitudes and practices of veterinarians and para-veterinarians towards antimicrobial stewardship in Malawi: underutilized strength in the fight against antimicrobial resistance. *BMC Vet Res* 2025;21:390.
190. Tonkin-Crine S, Yardley L, Coenen S et al. GPs' views in five European countries of interventions to promote prudent antibiotic use. *The British Journal of General Practice* 2011;61:e252.
191. Petursson P. GPs' reasons for "non-pharmacological" prescribing of antibiotics A phenomenological study. *Scandinavian Journal of Primary Health Care* 2005;23:120-125.
192. Barden LS, Dowell SF, Schwartz B, Lackey C. Current attitudes regarding use of antimicrobial agents: results from physicians' and parents' focus group discussions. *Clinical Pediatrics* 1998;37:665-671.
193. Mangione-Smith R, McGlynn EA, Elliott MN, Krogstad P, Brook RH. The relationship between perceived parental expectations and pediatrician antimicrobial prescribing behavior. *Pediatrics* 1999;103:711-718.
194. Stivers T. Managing patient pressure to prescribe antibiotics in the clinic. *Pediatric Drugs* 2021;23:437-443.
195. Stivers T. Treatment decisions: Negotiations between doctors and parents in acute care encounters. *Communication in medical care: Interaction between primary care physicians and patients*. Cambridge University Press, 2006:279-312.
196. Frey E, Kedrowicz A, Hedgpeth MW. Decision making on antimicrobial use: Cat and dog owners' knowledge and preferences for veterinary communication. *Veterinary Record* 2024;194:no-no.
197. Roope LS, Tonkin-Crine S, Butler CC et al. Reducing demand for antibiotic prescriptions: evidence from an online survey of the general public on the interaction between preferences, beliefs and information, United Kingdom, 2015. *Eurosurveillance* 2018;23:1700424.
198. Hawkins O, Scott AM, Montgomery A 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:e0261917.
199. Blommaert A, Marais C, Hens N et al. Determinants of between-country differences in ambulatory antibiotic use and antibiotic resistance in Europe: a longitudinal observational study. *J Antimicrob Chemother* 2014;69:535-547.
200. Borg MA. National cultural dimensions as drivers of inappropriate ambulatory care consumption of antibiotics in Europe and their relevance to awareness campaigns. *J Antimicrob Chemother* 2011;67:763-767.
201. Redding LE, Cole SD. Posters have limited utility in conveying a message of antimicrobial stewardship to pet owners. *Frontiers in Veterinary Science* 2019;6:421.

Chapter 2: Use of local antibiogram data and antimicrobial importance ratings to select optimal empirical therapies for urinary tract infections in dogs and cats

A version of this paper has been published in *Antibiotics* (2020);
doi: 10.3390/antibiotics9120924

Ri Scarborough^{* 1,2}, Kirsten Bailey^{1,2}, Bradley Galgut³, Adam Williamson⁴, Laura Hardefeldt^{1,2}, James Gilkerson^{1,2}, Glenn Browning^{1,2}

¹ Asia-Pacific Centre for Animal Health, Department of Veterinary Biosciences, Melbourne Veterinary School, Faculty of Veterinary and Agricultural Sciences, University of Melbourne, Parkville, Victoria 3010, Australia; baileyk@unimelb.edu.au (K.B.); laura.hardefeldt@unimelb.edu.au (L.H.); jrgilk@unimelb.edu.au (J.G.); glenfb@unimelb.edu.au (G.B.)

² National Centre for Antimicrobial Stewardship, Peter Doherty Institute, Parkville, Victoria 3052, Australia

³ ASAP Laboratory, Mulgrave, Victoria 3170, Australia; bradley.galgut@asaplab.com.au

⁴ Make Data Useful, Fitzroy, Victoria 3065, Australia; adam.williamson@makedatauseful.com.au

* Correspondence: ri.scarborough@unimelb.edu.au

Abstract

International and Australian veterinary antimicrobial use guidelines recommend amoxicillin or trimethoprim-sulfonamide (TMS) for the empirical treatment of sporadic urinary tract infections (UTIs) in dogs and cats. However, in practice, these antibiotics are rarely used, and no large-scale analyses have examined the antibiograms of bacteria isolated from UTIs to validate these recommendations in Australia.

We analyzed five years of urine culture and antimicrobial susceptibility data from an Australian veterinary laboratory. The analysis included 6196 urinary isolates from dogs and cats, 78% of which were from samples submitted by first-opinion veterinary clinics. *Escherichia coli*, *Enterococcus faecalis*, *Staphylococcus pseudintermedius* and *Proteus* spp. were the most prevalent organisms. More than 80% of all isolated cocci were susceptible to amoxicillin, and more than 80% of bacilli were susceptible to TMS. A total of 94% of isolates were susceptible to at least one antimicrobial drug categorized as low-importance in Australia. The prevalence of multi-drug resistance (MDR) was highest in *E. coli*, at 9.7%; 84% of these MDR isolates were susceptible to amoxicillin-clavulanate. We performed population-level antimicrobial treatment simulations and proposed a novel method for integrating antimicrobial importance ratings with antibiogram data to optimize the selection of empirical therapy.

Our findings support current guideline recommendations to use amoxicillin or TMS. We also found that bacterial morphology assisted with selection; amoxicillin was a better choice for cocci and TMS for bacilli.

Introduction

Signs of lower urinary tract inflammation, such as stranguria, haematuria and pollakiuria, are a common presenting problem in dogs and cats. Although these signs are not always caused by bacterial infection, particularly in cats,¹ they are a common reason for antimicrobial therapy in small animal practice.² Microscopy, culture and antimicrobial susceptibility testing (MCAS) is not commonly performed on initial presentation in veterinary practice. Both in Australia³ and internationally,⁴ most cases of urinary tract infection (UTI) are treated empirically with antimicrobial drugs. Veterinarians are more likely to submit urine for MCAS after first-line empirical antimicrobial treatment has failed to resolve the problem or when there is a relapse.^{3, 4}

The most frequently isolated organism from lower UTI in dogs and cats is *Escherichia coli*. Other Enterobacteriaceae, including *Klebsiella* spp., *Proteus* spp. and *Enterobacter* spp., are also often encountered, as are staphylococci, streptococci and enterococci.⁵⁻⁷

Veterinary, agricultural and human medical organizations have developed importance ratings for antimicrobial agents to encourage greater care in the use of antimicrobials, particularly those of importance to human medicine for which there are few or no alternatives, should resistance develop.⁸ In Australia, the importance ratings of the Australian Strategic and Technical Advisory Group on Antimicrobial Resistance (ASTAG) are used.⁹ Antimicrobial prescribing guidelines have also proliferated. These take into account the likely pathogens, their susceptibility patterns and the best available evidence on the duration of therapy to guide empirical therapy, but only some consider antimicrobial importance ratings. International guidelines for the management of canine and feline UTIs have been available since 2011 from the International Society for Companion Animal Infectious Diseases (ISCAID), and these recommend trimethoprim-sulfonamide (TMS), amoxicillin or, where amoxicillin is unavailable, amoxicillin-clavulanate,^{1, 10} While the 2011 ISCAID guidelines suggested a duration of therapy of seven days, the current iteration (2019) recommends a duration of three to five days for sporadic UTIs.¹ Several national guidelines, including those in Denmark, Britain and Australia, also recommend amoxicillin or TMS.¹¹⁻¹³ However, neither of these options is commonly prescribed for UTIs in Australian cats and dogs.^{2, unpublished data}

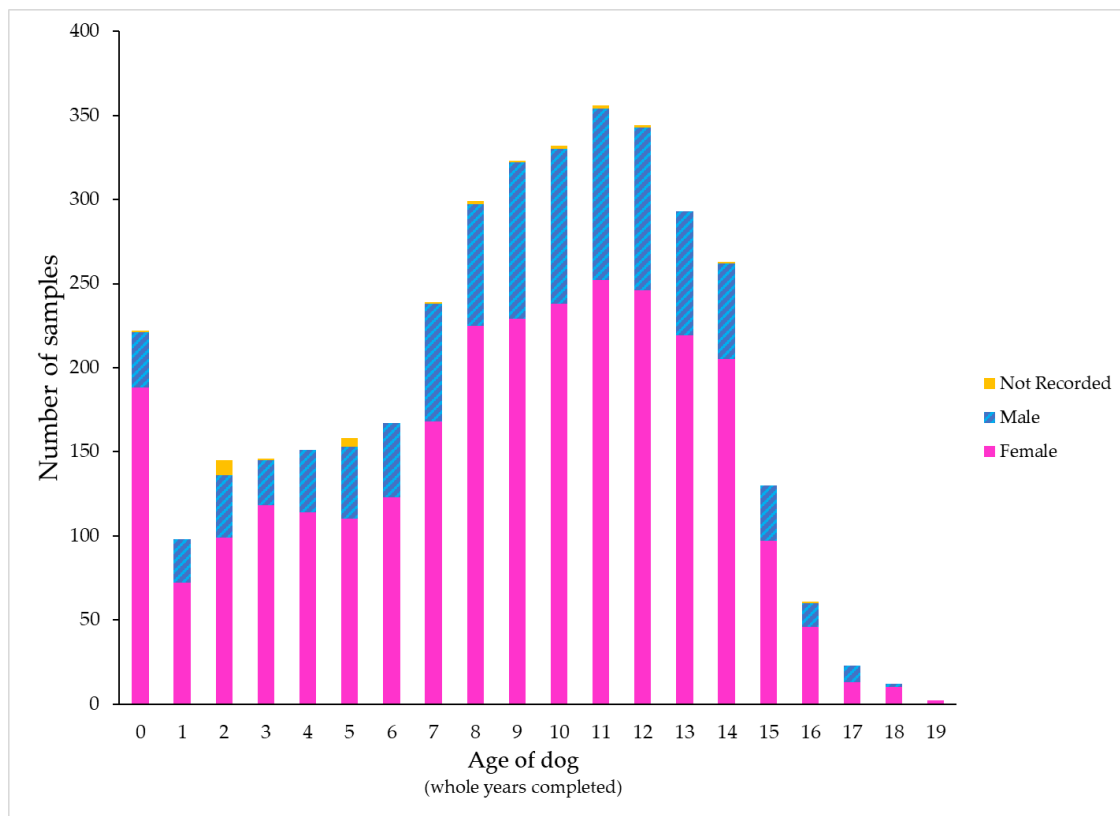
Antibiograms are tables of aggregated antimicrobial susceptibility results for isolates of a single bacterial species from one animal species over a defined period, from a particular geographical area and often a specific body site.¹⁴ They are useful as guides for empirical treatment in the clinical setting where the organisms were found, and, when generated in a regular and consistent manner, can allow changing trends in antimicrobial resistance to be monitored.¹⁵ The use of local and recent data to inform empirical therapy is important because of the substantial variations in microbial prevalence and antimicrobial susceptibility across geographical areas and time.^{16, 17} To date, there have been no large-scale analyses of Australian antibiograms to evaluate the suitability of the ISCAID and Australian treatment guidelines for UTIs, and there is evidence that guidelines are not being followed, with the broad-spectrum drugs amoxicillin-clavulanate and cefovecin the most popular treatments for canine and feline UTIs in Australia.^{2, 18}

This study aimed to describe the distribution, and antimicrobial susceptibility patterns, of organisms cultured from dog and cat urine samples in Australia and to formulate local empirical treatment recommendations. Recommendations can be based on two different approaches: an established method that uses only prevalence and susceptibility to calculate antimicrobial impact factors, and a novel method, used here, that also incorporates an antimicrobial importance “cost”. This novel method can help to select empirical treatment pathways that balance individual patient outcomes, which are highly visible and immediate, with the less tangible cost of antimicrobial resistance (AMR).¹⁹ We compared the treatment

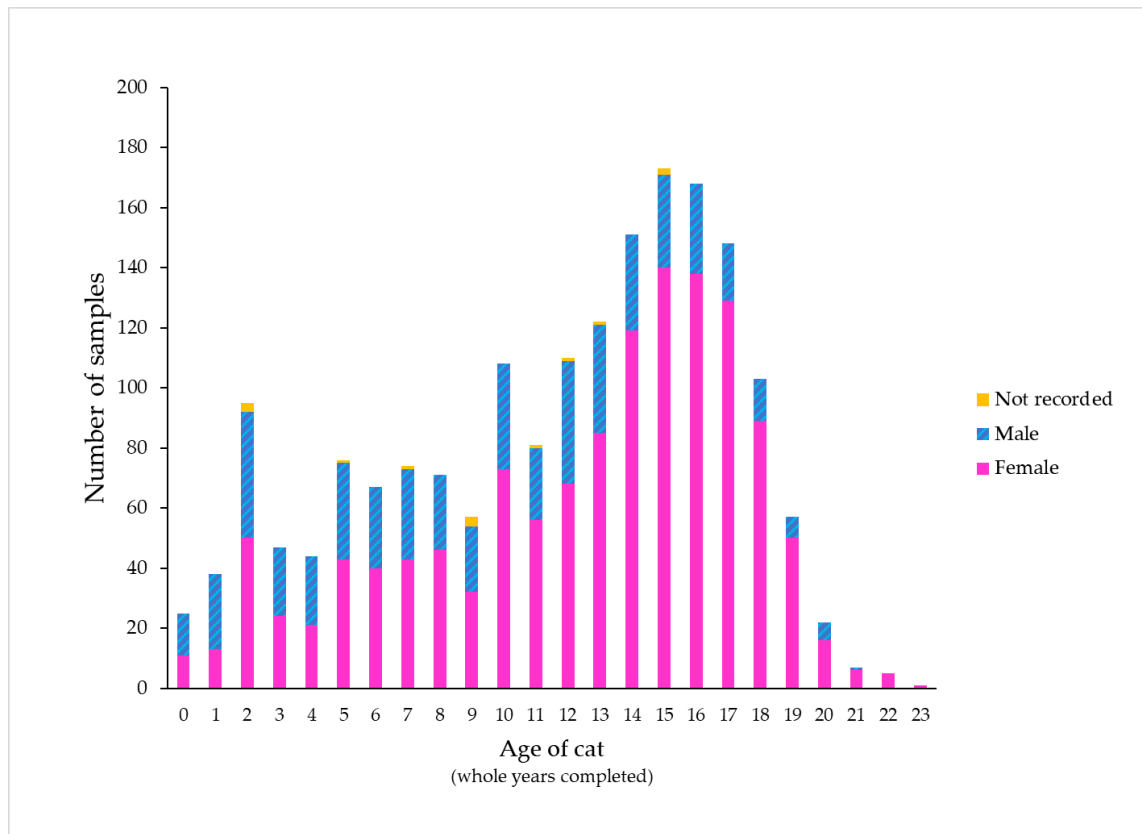
recommendations derived from these analyses with international and Australian antimicrobial prescribing guidelines for UTIs.

Results

During the study period, 263 veterinary clinics (246 first-opinion and 17 emergency/specialist practices) from a wide geographic area submitted urine samples to a commercial veterinary diagnostic laboratory. These practices included companion animal only and mixed (companion and farm animal) practices. A total of 5614 feline and canine urine samples from 4635 unique animals were present in the dataset. Twenty-two percent of the samples analyzed came from 17 emergency/specialist practices (7% of all clinics in the dataset); the remaining 78% were from first-opinion practices. Two-thirds of the samples tested came from dogs (3764 samples from 3093 dogs, 67%) and one-third came from cats (1850 samples from 1544 cats, 33%). Most samples tested from both dogs (74%) and cats (70%) were from females ($p < 0.001$). The median age was 9 years for dogs (interquartile range [IQR] 6 to 12) and 13 years for cats (IQR 7.5 to 16). In cats aged 3 years or less, males predominated (51%) compared to older cats (26%, $p < 0.001$) (Figure 1; Table S1, supplementary data). While most cats were recorded as Domestic Short Hair or Domestic Long Hair, many dog breeds were represented; samples came most often from Labrador Retrievers (287 samples), followed by Pugs, Golden Retrievers and Border Collies. No clear association could be discerned between breed size and age of peak presentation (Figure S1, supplementary data).



(a)



(b)

Figure 1. Distribution of samples by patient age and sex in (a) dogs and (b) cats.

Of the 4635 animals, 627 (14%) had two or more (range 1 to 10) urine cultures in the study period, with 180 (3.9%) having three or more and 84 (1.8%) having four or more. The median interval between consecutive urine cultures on the same animal was 75 days (range 0 to 1615 days, IQR 32–211 days). Animals that had multiple urine cultures during the study period were more likely to be female than animals that had only one urine culture (dogs, OR = 1.61, 95% confidence interval [CI] 1.25–2.06, $p < 0.001$; cats, OR = 1.49, 95% CI 1.07–2.09, $p = 0.02$). There was no association between the animal's age at the time of the first test and the probability of subsequent urine samples being submitted ($p = 0.131$).

The method used for urine collection was recorded for less than half of all samples (44%, 2443/5614). Most labeled samples were collected by cystocentesis (1641, 29%), followed by free catch (657, 12%) and catheterization (145, 3%), with no difference between dogs and cats. Free catch samples were more likely to yield a mixed growth of organisms than samples collected by cystocentesis (OR = 2.13, 95% CI 1.52–2.98, $p < 0.001$).

A single isolate was recorded for most of the dog (3403/3764, 90%) and cat (1730/1850, 94%) urine samples. Of the dog samples, 8% (314/3764) yielded two different isolates, 1% (42/3764) yielded three different isolates, and 0.08% (3/3764) yielded four different isolates. In cats, 6% (116/1850) yielded two different isolates, and 0.2% (3/1850) yielded three different isolates. Species other than those listed in Table 1 were found in fewer than 2% of samples, and most were found in fewer than 0.5% of samples. *Escherichia coli* (67% of cat and 55% of dog samples, $p < 0.0001$), *Enterococcus faecalis* (15% of cat and 9.3% of dog samples, $p < 0.0001$) and coagulase-negative *Staphylococcus* spp. (4.8% of cat and 2.4% of dog samples, $p < 0.0001$) were found in a higher proportion of samples from cats than samples from dogs. In contrast, *Staphylococcus pseudintermedius* (10% of dog and 7.2% of cat samples, $p = 0.0004$), *Proteus mirabilis* (11% of

dog and 2.1% of cat samples, $p = 0.0004$), other *Proteus* spp. (7.7% of dog and 1.2% of cat samples, $p < 0.0001$), *Enterobacter* spp. (4.2% of dog and 1.8% of cat samples, $p < 0.0001$) and *Streptococcus canis* (2.9% of dog and 0.8% of cat samples, $p < 0.0001$) were found in a higher proportion of samples from dogs than samples from cats.

Table 1. Organisms cultured for each collection method and proportion cultured as a pure growth.

Organism Species or Group	% of All Samples	Urine Collection Method, <i>n</i> (% as Pure Growth)				
		Cystocentesis	Catheter	Free Catch	Not Stated	Total
<i>Escherichia coli</i>	59%	1004 (94)	78 (89)	357 (86)	1855 (90)	3294 (90)
<i>Enterococcus faecalis</i>	11%	192 (72)	8 (63)	63 (54)	373 (55)	636 (61)
<i>Staphylococcus pseudintermedius</i>	9.1%	155 (92)	22 (96)	55 (87)	281 (75)	513 (87)
<i>Proteus mirabilis</i>	7.8%	110 (86)	8 (100)	72 (81)	250 (85)	440 (88)
<i>Proteus</i> spp.	5.5%	80 (89)	4 (50)	43 (88)	183 (78)	310 (76)
<i>Enterobacter</i> spp.	3.4%	36 (91)	8 (100)	35 (88)	111 (80)	190 (88)
Coagulase-negative <i>Staphylococcus</i> spp.	3.2%	55 (91)	8 (100)	16 (88)	98 (88)	177 (92)
<i>Streptococcus canis</i>	2.2%	13 (69)	8 (75)	31 (55)	73 (50)	125 (62)
All other organisms	8.2%	82	13	55	309	459

The organisms most commonly cultured as a pure growth were coagulase-negative staphylococci (92%) and *E. coli* (90%) (Table 1). Those most frequently found as a component of a mixed growth were *E. faecalis* (61%) and *S. canis* (62%). Where *E. faecalis* was cultured in mixed growth, it was most frequently found with *E. coli* (149/254, 59%), followed by *S. pseudintermedius* (41/254, 16%) and *P. mirabilis* (31/254, 12%).

The types of organisms grown were associated with the method of sample collection ($p < 0.001$). Catheterized samples were the most likely sample type to yield *Enterobacter* spp., *Staphylococcus* spp. and *Streptococcus* spp. Free catch samples were the most likely to yield *Proteus* spp. (Figure 2).

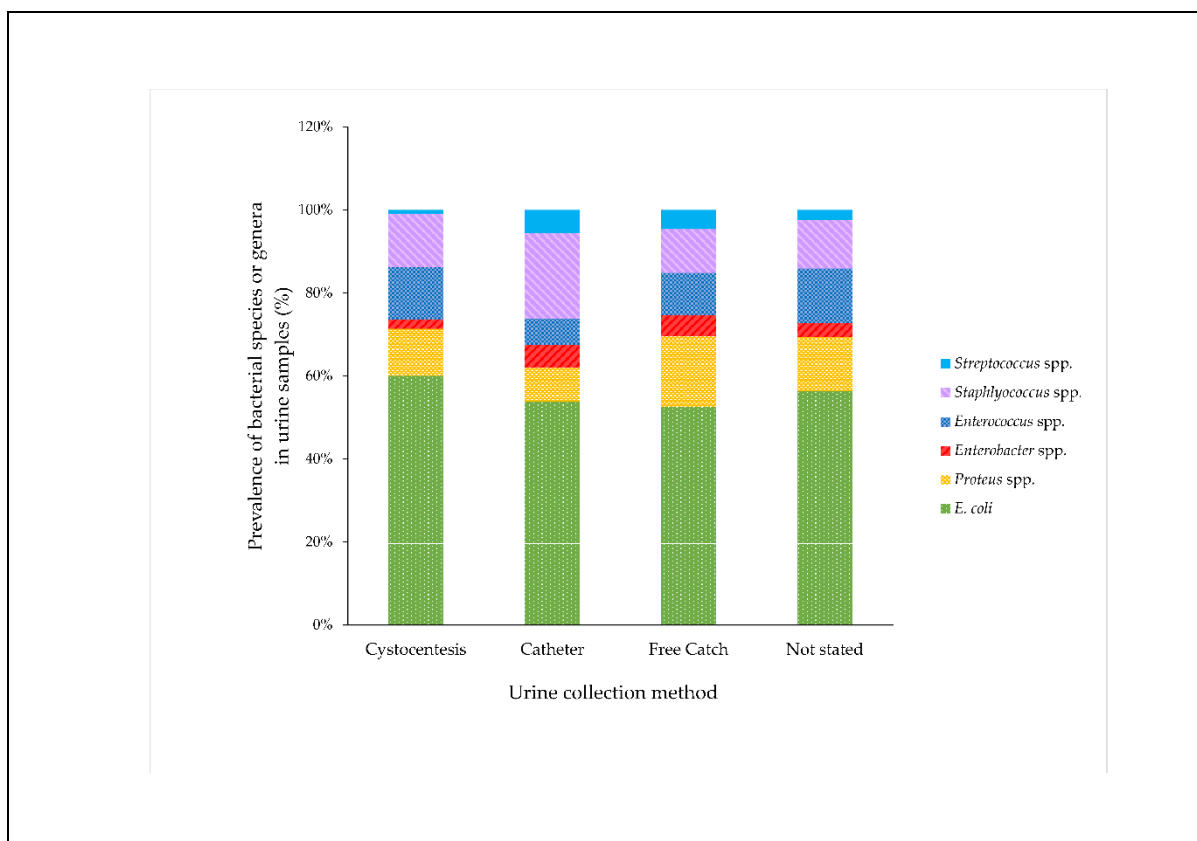


Figure 2. Bacterial species cultured, by collection method. Some totals are >100% because some samples yielded multiple bacterial species.

Most bacterial isolates in this study (5843/6196, 94%) were susceptible to one or more antimicrobials regarded as having low importance by the ASTAG (amoxicillin, TMS, doxycycline, erythromycin or tetracycline). Of those resistant to these drugs, more than two-thirds (250/353, 71%) were susceptible to an antimicrobial agent regarded as having medium importance by the ASTAG, amoxicillin-clavulanate. One percent (60/5614) of samples yielded isolates resistant to all low- and medium-importance agents tested. Of these, two-thirds (40/5614, 0.7%) were susceptible to enrofloxacin, but none was susceptible to cefovecin. More than 80% of the isolates of each species or genus were susceptible to each of the drugs tested (Tables 2 and 3). However, in both dogs and cats, *E. faecalis* showed low susceptibility to enrofloxacin (0.9% and 1.4% susceptible respectively), tetracycline (54% and 53% susceptible respectively) and erythromycin (76% and 77% susceptible). There were too few *S. canis* isolates from cats (14 isolates) for further analysis, however, in dogs (111 isolates) extensive resistance to enrofloxacin (95% resistant) and high-level resistance to gentamicin (97% resistant) were identified.

Table 2. Antimicrobial susceptibility and importance ratings for the most prevalent urinary isolates from dogs.

Amox: amoxicillin; TMS: trimethoprim-sulfonamide; Tetra: tetracycline; Doxy: doxycycline; Erythro: erythromycin; Gentam: Gentamicin; Amox-Clav: amoxicillin-clavulanate; Ceph: cephalaxin; Enroflox: enrofloxacin.

Organism	n	% of Dog Isolates	Low-Importance Antimicrobials					Medium-Importance Antimicrobials			High-Importance Antimicrobials	
			Amox	TMS	Tetra	Doxy	Erythro	Gentam	Amox-Clav	Ceph	Cefovecin	Enroflox
<i>Escherichia coli</i>	2058	55%	75%	93%	82%	98%	IR	93%	97%	90%	90%	95%
<i>Proteus mirabilis</i>	401	11%	91%	94%	IR	IR	IR	100%	99%	95%	97%	99%
<i>Staphylococcus pseudintermedius</i>	380	10%	91%	93%	76%	85%	75%	89%	98%	95%	95%	98%
<i>Enterococcus faecalis</i>	351	9.3%	96%	IR	54%	91%	76%	95% *	95%	IR	IR	0.9%
<i>Proteus</i> spp.	288	7.7%	87%	92%	1.6% **	0% **	IR	100%	98%	96%	94%	98%
<i>Enterobacter</i> spp.	157	4.2%	IR	86%	86%	100%	IR	100%	IR	IR	IR	96%
<i>Streptococcus canis</i>	111	2.9%	96%	96%	84%	97%	89%	IR	97%	90%	89%	4.8%
Coagulase-negative <i>Staphylococcus</i> spp.	89	2.4%	87%	93%	86%	86%	93%	95%	97%	94%	92%	98%

* Enterococci were tested against a higher-potency gentamicin disc (120 µg) to detect high-level resistance. ** Some *Proteus* spp. are intrinsically resistant, and others are not, but it was not possible to separate species with the data available. IR = intrinsic resistance. Gray = fewer than 30 isolates of this species/genus were tested against this antimicrobial, and/or this species/genus is intrinsically resistant to this antimicrobial; Green = more than 80% of isolates susceptible; Yellow = 60%–80% isolates susceptible; Pink = less than 60% of isolates susceptible.

Table 3. Antimicrobial susceptibility and importance ratings for the most prevalent urinary isolates from cats.

Amox: amoxicillin; TMS: trimethoprim-sulfonamide; Tetra: tetracycline; Doxy: doxycycline; Erythro: erythromycin; Gentam: Gentamicin; Amox-Clav: amoxicillin-clavulanate; Ceph: cephalixin; Enroflox: enrofloxacin.

Organism	n	% of Cat Isolates	Low-Importance Antimicrobials					Medium-Importance Antimicrobials			High-Importance Antimicrobials	
			Amox	TMS	Tetra	Doxy	Erythro	Gentam	Amox-Clav	Ceph	Cefovecin	Enroflox
<i>Escherichia coli</i>	1236	67%	80%	94%	82%	82%	IR	100%	99%	92%	93%	97%
<i>Enterococcus faecalis</i>	285	15%	98%	IR	53%	87%	77%	95% *	99%	IR	IR	1.4%
<i>Staphylococcus pseudintermedius</i>	133	7.2%	91%	97%	89%	100%	100%	100%	100%	93%	94%	100%
Coagulase-negative <i>Staphylococcus</i> spp.	88	4.8%	98%	100%	100%	100%	100%	100%	99%	98%	98%	100%
<i>Proteus mirabilis</i>	39	2.1%	87%	92%	IR	IR	IR	0.0%	100%	95%	95%	97%
<i>Enterobacter</i> spp.	33	1.8%	IR	76%	100%	100%	IR	100%	IR	IR	IR	97%
<i>Proteus</i> spp.	22	1.2%	82%	73%	0% **	0% **	IR	100%	96%	87%	82%	100%
<i>Streptococcus canis</i>	14	0.8%	100%	86%	86%	100%	100%	IR	100%	100%	100%	0%

* Enterococci were tested against a higher-potency gentamicin disc (120 µg) to detect high-level resistance. ** Some *Proteus* spp. are intrinsically resistant, and others are not, but it was not possible to separate species with the data available. IR = intrinsic resistance. Gray = fewer than 30 isolates of this species/genus were tested against this antimicrobial, and/or this species/genus is intrinsically resistant to this antimicrobial; Green = more than 80% of isolates susceptible; Yellow = 60%–80% isolates susceptible; Pink = less than 60% of isolates susceptible.

Antimicrobial Impact Factor

The impact factor was calculated using the formula for rational antimicrobial therapy (sum of % prevalence X% susceptible for organism 1 to n) for all species/genera found in at least 2% of cases.²⁰ This factor is an estimate of the percentage of UTI cases that are expected to respond to that antimicrobial when all cases are treated empirically.

The antimicrobials with the highest impact factors for dogs were amoxicillin-clavulanate (95), enrofloxacin (87), TMS (86) and amoxicillin (81). In cats, amoxicillin-clavulanate (95) was also ranked highest, followed by amoxicillin (81) and enrofloxacin (79), closely followed by TMS (77) (Figure 3).

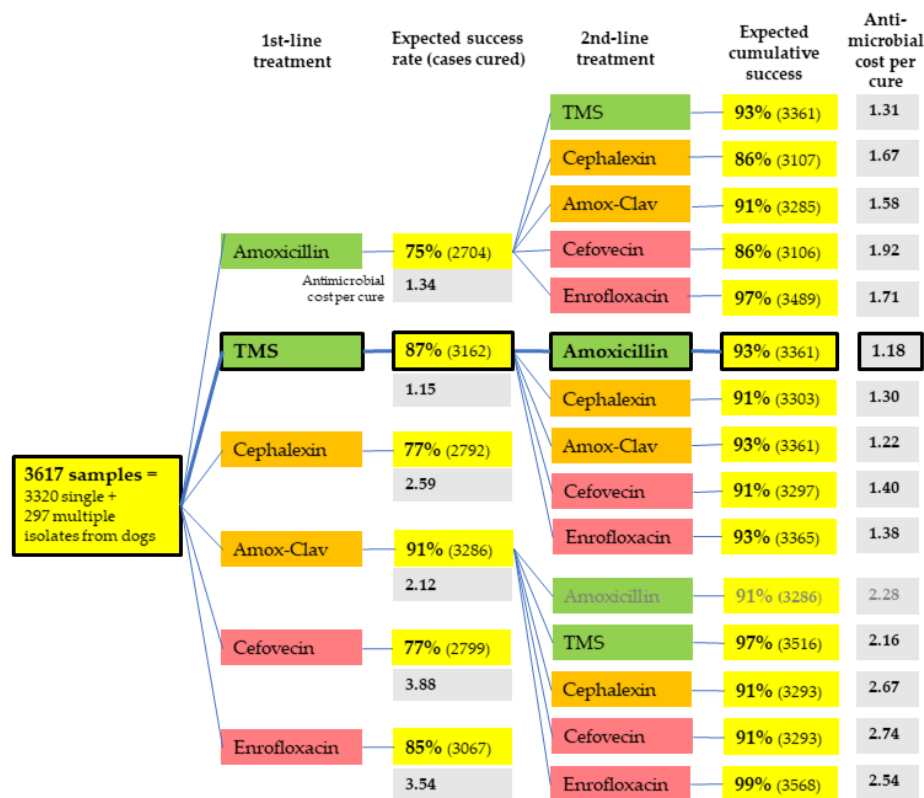
When the organisms were sorted by morphology (bacilli versus cocci), enrofloxacin had the highest impact factor for bacilli (92 in dogs and cats), however, amoxicillin-clavulanate (88 in dogs and 91 in cats) and TMS (82 in dogs and 89 in cats) also had high impact factors. For cocci, antimicrobial impact factors were lower across the board for cats, compared with dogs. Amoxicillin-clavulanate had the highest impact factor for both species (94 in dogs and 71 in cats), but amoxicillin (90 in dogs and 69 in cats) also had high impact factors.

Antimicrobial drug	Any morphology		Bacilli		Cocci	
	Dogs n=4172	Cats n=1972	Dogs n=3003	Cats n=1360	Dogs n=939	Cats n=566
TMS	86	77	82	89	55	22
Amoxicillin	81	81	70	74	90	69
Amoxicillin-clavulanate	95	95	88	91	94	71
Cephalexin	88	75	82	85	55	22
Cefovecin	81	75	82	86	55	21
Enrofloxacin	87	79	92	92	48	24

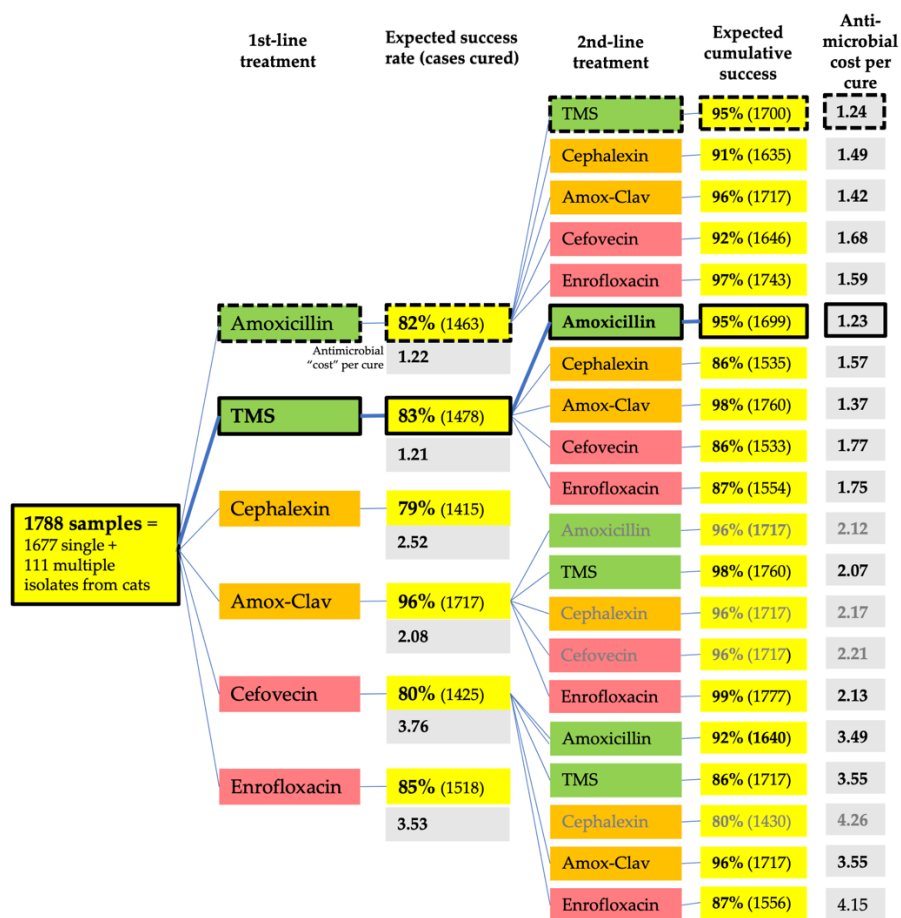
Figure 3. Impact factors of the six routinely tested antimicrobials, by isolate morphology and host species. The colors in the left column indicate the Australian Strategic and Technical Advisory Group on Antimicrobial Resistance (ASTAG) importance ratings of the antimicrobials, and the yellow and blue bars indicate the magnitude of the antimicrobial impact factor in each animal species.

2.2. Whole-Population Antimicrobial Simulation and Antimicrobial Cost per Cure

By accounting for the importance rating of each antimicrobial and the number of animals treated in each pathway, the treatment pathway with the lowest antimicrobial “cost” per cure for both dogs and cats was determined. This pathway was found to comprise initial treatment with TMS, followed by amoxicillin should this initial therapy fail (Figure 4).



(a)



(b)

Figure 4. Whole population treatment simulation, including antimicrobial cost per cure in (a) dogs and (b) cats. Amox-Clav = amoxicillin-clavulanate. Bold outlines indicate the best pathways by antimicrobial cost. Colors indicate the ASTAG importance ratings of antimicrobials⁹, where green are the least important (preferred choices), and red are the most important (least preferred choices), due to the risk that selection of resistance poses to human and animal health. Only selected second-line pathways are displayed—those with the lowest antimicrobial cost per cure and those following first-line choices that are most commonly used for UTIs in that animal species in Australia—amoxicillin-clavulanate in dogs and cefovecin and amoxicillin-clavulanate in cats.^{2, unpublished data}

*Note: Figure 4b differs from the published version. The cost per cure in the top right of the figure was published as 1.42 but should be **1.24** as shown here. The journal has declined to correct the published version.*

The proportions of each species/genus of bacteria recovered from urine samples with no acquired resistance or with MDR are shown in Table 4. MDR had the highest prevalence in *E. coli* (320/3294, 9.7%), most commonly involved beta-lactam resistance, but 268/320 (84%) of these MDR isolates were susceptible to amoxicillin-clavulanate. One *E. coli* isolate was resistant to ten antimicrobials tested (Table S2, Supplementary Materials). Resistance patterns for *E. faecalis*, *S. pseudintermedius* and *P. mirabilis* are also included in supplementary materials (Table S3, Table S4 and Table S5, Supplementary Materials). Oxacillin testing was not performed on *S. pseudintermedius* isolates, therefore the rate of methicillin resistance is unknown. As *Enterobacter* spp. are intrinsically resistant to most of the antimicrobials routinely tested at this laboratory, we could only assess susceptibility to TMS and enrofloxacin. Eighty-three percent (157/190) of the *Enterobacter* spp. isolates were susceptible to both these drugs. Thirty isolates (16%) were resistant to TMS, seven (3.7%) were resistant to enrofloxacin, and four (2.1%) were resistant to both. No association was found between the animal's age and the antimicrobial susceptibilities of the most common isolates.

Table 4. Summary of antimicrobial resistance detected in the most prevalent bacterial species/genera isolated from dog and cat urine. MDR: multi-drug resistance.

Organism	Total Number of Isolates	Intrinsic Resistances	Isolates with no Acquired Resistance Detected n (%)	MDR = Resistance to Three or More of:	MDR n (%)	Most Common MDR Combination (n)	Prevalence of Most Common MDR Combination # n (%)
<i>Escherichia coli</i>	3294	-	2450 (74)	AMX, AMC, LEX, CVN, TET, GEN, FQN, SXT	320 (9.7)	AMX + LEX + CVN	276 (8.4)
<i>Enterococcus faecalis</i>	636	LEX, CVN, SXT	22 (3.5)	AMX, TET, GEN*, ERY, FQN	19 (3.0)	TET + ERY + FQN	8 (1.3)
<i>Staphylococcus pseudintermedius</i>	513	-	433 (84)	AMX, AMC, LEX, CVN, TET, GEN, FQN, SXT	34 (6.6)	AMX + LEX + CVN	28 (5.5)
<i>Proteus mirabilis</i>	440	TET	378 (86)	AMX, AMC, LEX, CVN, FQN, SXT	16 (3.6)	AMX + LEX + CVN	13 (2.9)
<i>Proteus</i> spp.	310	#	249 (80)	AMX, AMC, LEX, CVN, FQN, SXT	16 (5.2)	AMX + LEX + CVN	8 (2.6)
<i>Enterobacter</i> spp.	190	AMX, AMC, LEX, CVN	157 (83)	Not assessable **			
Coagulase-negative <i>Staphylococcus</i> spp.	177	-	155 (88)	AMX, AMC, LEX, CVN, TET, GEN, FQN, SXT	8 (4.5)	AMX + LEX + CVN	6 (3.4)
<i>Strep. canis</i>	125	GEN	8 (6.4)	AMX, AMC, LEX, CVN, TET, GEN, FQN, SXT	2 (1.6)	AMX + FQN + SXT	1 (0.8)

AMX = amoxicillin (tested using ampicillin disc); AMC = amoxicillin-clavulanate; LEX = cephalexin; CVN = cefovecin; FQN = any fluoroquinolone (enrofloxacin most commonly tested); SXT = trimethoprim-sulfamethoxazole (TMS); ERY = erythromycin; GEN = gentamicin; TET = tetracyclines (doxycycline, tetracycline). Note: Not all isolates were tested against all antimicrobials. * Enterococci tested against a higher-potency gentamicin disc (120 µg) to detect high-level resistance. ** MDR cannot be assessed as only two antimicrobials (TMS, ENR) were routinely tested, apart from those to which *Enterobacter* spp. are intrinsically resistant. # Some *Proteus* spp. (other than *P. mirabilis*) have intrinsic resistance to TET, but the laboratory did not identify to the species level. ## Includes isolates that have this combination plus additional resistances.

Changes in Resistance

No changes in resistance patterns were detected across the population over time (Figure S2a–f, Supplementary Materials). However, in animals from which four or more urine samples were cultured during the study period, the proportion of *E. coli* classified as MDR increased by 7.3% with each successive sample, from sample 1 to 5 (95% CI: 4.3% to 10%) (Figure 5).

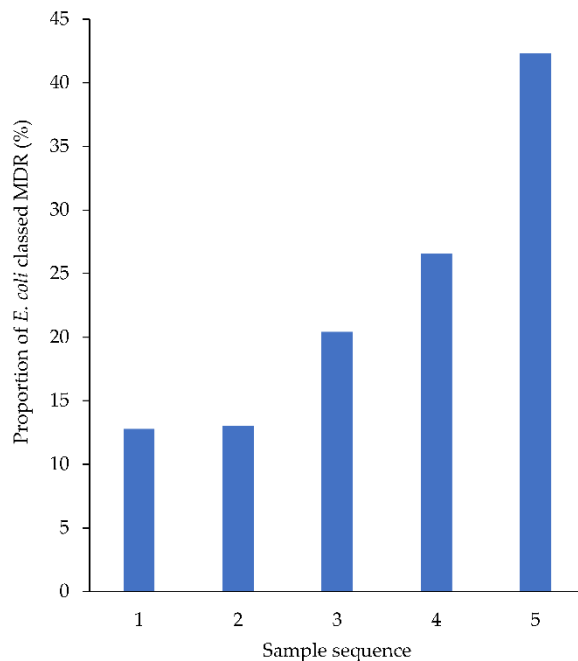


Figure 5. Proportion of *E. coli* (from animals from which ≥ 4 samples were cultured) classed as MDR, by sample sequence number.

Discussion

In general, little acquired antimicrobial resistance was observed in canine and feline urinary tract pathogens in this large Australian sample. The vast majority of the bacterial isolates were susceptible to the guideline-recommended antimicrobials, amoxicillin or TMS, and most bacteria isolated were susceptible to at least one of the antimicrobials tested that is classified as having low importance by the ASTAG (94% susceptible to one of amoxicillin, TMS, doxycycline, tetracycline or erythromycin). Two-thirds of the remainder (4%) were susceptible to amoxicillin-clavulanate.

These results should be considered to underestimate the effectiveness of these antimicrobials in first-opinion canine and feline UTI presentations for three reasons. Firstly, since veterinarians are more likely to submit urine samples for MCAS after first-line empirical antimicrobial treatment has failed to resolve the infection, or when there is a relapse,³ the isolates represented in these antibiograms are likely to have had previous exposure to antimicrobial therapy, increasing their chance of resistance,²¹ and more complicated UTI cases are probably over-represented. Secondly, the breakpoints used by the laboratory to determine whether an isolate is susceptible or resistant are based on drug concentrations achieved in plasma and tissues, in humans. However, some antimicrobials—including penicillins, cephalosporins and quinolones²²—reach considerably higher concentrations in the urine. This means that our results could be considered to underestimate the *in vivo* effectiveness of some of the antimicrobials in the lower urinary tract. Thirdly, *in vivo* cure rates for all antimicrobials are likely to be higher than *in vitro*

susceptibility would suggest, as laboratory results do not account for the activity of the animal's immune response, which augments the effect of antimicrobial therapy.²³ Thus, the actual UTI cure rate (as well as the antimicrobial impact factors) would probably be higher than we have assumed.

Almost three-quarters of samples from both dogs and cats were from females, consistent with the higher incidence of UTIs in females of many species.²⁴ However, in cats under three years of age, male cats outnumbered female cats, perhaps because idiopathic feline lower urinary tract disease (FLUTD)—which is sometimes accompanied by bacterial UTI²⁵ - is more common in young male cats.²⁶ This pattern of younger males and older females was also seen in a German study of cat UTIs.²⁷

E. coli was the most prevalent species isolated from dog and cat urine samples in this study (59% of samples), similar to international studies,^{6, 28, 29} but substantially higher than in another study from Australia⁷ and one from New Zealand.³⁰ *E. faecalis* (11.5%), *S. pseudintermedius* (9.2%), *P. mirabilis* (7.9%), other *Proteus* spp. (5.5%), *Enterobacter* spp. (3.6%), coagulase-negative staphylococci (3.2%) and *S. canis* (2.2%) were also detected in significant proportions of cases, as reported elsewhere.^{5, 29, 30} Notably, the proportion of MDR *E. coli* in this study (9.7%) was somewhat lower than in a previous Australian study, which found 16% of *E. coli* isolated from canine urine samples and 11% of *E. coli* isolated from feline urine samples to be MDR. However, this earlier study included fewer urinary tract isolates ($n = 672$), and the samples were from university and government laboratories,³¹ and thus a greater proportion may have come from more complex and refractory cases. Globally, there is substantial variation in resistance patterns among *E. coli* isolates from canine and feline urinary tract disease. In the USA, approximately 46% of *E. coli* isolates were resistant to amoxicillin in two studies,^{6, 32} compared with 23% of the isolates in our study, and the prevalence of resistance to amoxicillin-clavulanate as high as 35%,³² compared with 2% in our study. Another U.S. study found that only 35% of canine urinary *E. coli* isolates were susceptible in vitro to the first-generation cephalosporin, cefazolin,³³ while 90% of the isolates in our study were susceptible to cephalexin. In Europe, resistance to amoxicillin-clavulanate ranges from 2.9% (Sweden) to 32% (Spain) and MDR rates from 0.24% (Sweden) to 30% (Spain).²⁹ High rates of resistance have also been detected in South African (98% MDR, 11% extensively drug-resistant, 2% pan-drug-resistant)³⁴ and Brazilian (66% MDR)³⁵ urinary tract *E. coli* from dogs. While some overestimation of MDR can occur when authors do not account for intrinsic resistance, making it difficult to interpret MDR differences, it is clear that geographic differences in susceptibility rates exist, further underlining the need for the determination of local antibiograms to assist in the development and validation of local antimicrobial prescribing guidelines.

The canine and feline UTI isolates examined in our study were more susceptible than recent Australian UTI isolates from human patients to both amoxicillin (77% in dogs and cats vs. 54% in humans) and amoxicillin-clavulanate (97% in dogs and cats vs. 87% in humans).³⁶ However, a potentially concerning finding in our study was the high level of fluoroquinolone resistance in *E. faecalis*. Although enterococci have relatively low inherent susceptibility to fluoroquinolones,³⁷ resistance to enrofloxacin among *E. faecalis* isolates was nearly universal throughout the study period (99%). This level of fluoroquinolone resistance in enterococci has not been reported previously in Australia and is much higher than that detected in the USA (17/35, 49%)³⁸ and New Zealand (79/280, 28%).³⁰ However, there is some uncertainty about the pathogenicity of enterococci in the canine and feline urinary tract. Although acknowledged as an important urinary pathogen in humans³⁹ and known to invade urinary epithelial cells,⁴⁰ enterococci have commonly been considered an incidental finding in dog and cat urine. This is partly because enterococci are frequently found in mixed cultures^{29, 41} and are often found in the urine of animals

without clinical signs of UTI.³⁸ One author has stated that the “low pathogenicity of *Enterococcus* may not justify the risks and expense of antibiotic treatment”.^{42, p.1094} When enterococci are present in mixed bacterial cultures (as for almost 40% of all samples that yielded enterococci in this study), treatment aimed at the other bacterial species may result in clearance of enterococci without targeting therapy at these species.^{10, 42}

S. canis isolates in this study were also almost universally resistant to enrofloxacin (114/119, 96%). In contrast, in a New Zealand study, only 2% of beta-hemolytic streptococci were found resistant to enrofloxacin.³⁰ Genetic studies of *E. faecalis* and *S. canis* from local animal samples would be helpful to determine the mechanism and origin of enrofloxacin resistance. Enrofloxacin, marbofloxacin and pradofloxacin are registered for use in dogs and cats in Australia.¹⁸ Additionally, fluoroquinolones such as ciprofloxacin have been widely used in human medicine in Australia in the past and are increasingly prescribed to treat human UTIs. A 2011 trial in dogs found high-dose treatment with enrofloxacin for three days was effective for dog UTIs.⁴³ However, because of their high importance in both veterinary and human medicine, fluoroquinolones should be reserved for cases where MCAS demonstrates that no antimicrobials of lower importance are effective.

To avoid bacterial contamination from the urethra, perineum and other surfaces, cystocentesis samples are always preferable for MCAS, but these may be contraindicated in some circumstances and are not always readily obtained. This is reflected by the significant proportion of samples that were labeled as free catch (voided) or collected via a catheter in our study. Unsurprisingly, the urine collection method affected both the proportions of each of the bacterial genera cultured, as well as the likelihood of a mixed culture, as found in other studies.²⁷ This underlines the need for considered clinical interpretation of urine MCAS results, especially when a voided sample has been used.

A significant proportion of animals (627, 14%) had more than one urine MCAS performed by this laboratory in the study period. Although treatment data for these animals was not available, this subset can be reasonably assumed to represent animals that were treated with antimicrobials after their last MCAS and then returned to the veterinarian because of treatment failure, relapse or reinfection. The increased prevalence of MDR *E. coli* with each subsequent sample (from 8% in first samples to 29% in fourth samples) suggested that the intervening antimicrobial therapy had selected for MDR determinants, consistent with findings from other studies.^{31, 38}

Accepting the previously mentioned limitations of our susceptibility data, the impact factors calculated for each antimicrobial²⁰ suggest that amoxicillin-clavulanate is the most rational choice for the empirical treatment of UTIs. However, this potentiated penicillin is a medium-importance antimicrobial, therefore agents with lower importance should be chosen where clinically appropriate to reduce the risk of selection for antimicrobial resistance. Amoxicillin and TMS are both low-importance antimicrobials with high efficacy against the urinary isolates examined in this study, and we demonstrated that bacterial morphology clearly determines differing superior choices: TMS for bacilli and amoxicillin for cocci. Most veterinary clinics in Australia are equipped for this point-of-care determination. If bacilli are identified, the impact factor of TMS approaches that of amoxicillin-clavulanate (82 vs. 88 in dogs and 89 vs. 91 in cats); a treatment duration of three to five days is recommended,^{1, 12} and a trial in female dogs showed that three days of TMS was not inferior to 10 days of cephalexin.⁴⁴ Susceptibility results should always be interpreted by veterinarians in combination with their clinical judgment and consideration of relevant risk factors for individual patients. A number of adverse reactions to TMS have been reported in dogs and are outlined in the relevant guidelines. These include dose-dependent reactions, such as keratoconjunctivitis sicca and thyroid dysfunction, and delayed

hypersensitivity reactions, including hepatopathy, blood dyscrasias and polyarthritis, which typically occur with courses of more than five days of therapy.⁴⁵⁻⁴⁷ Challenges posed by hypersalivation in cats with oral TMS⁴⁸ can be overcome by using intact (not split) coated tablets, which are available in Australia and elsewhere. If cocci are identified, the expected efficacy of amoxicillin is very close to that of amoxicillin-clavulanate (antimicrobial impact factors of 90 vs. 94 in dogs, 69 vs. 71 in cats). In other words, 27 dogs or 40 cats would need to be treated with amoxicillin-clavulanate to achieve one additional cure, compared with amoxicillin.

Our novel population-level antimicrobial simulation, which accounts for the difference in antimicrobial importance ratings as well as the local prevalence of the different pathogens and their in vitro susceptibility, suggests that, where morphology and Gram stain are unknown, the most rational and appropriate first-line empirical choice is TMS, and, where this is not effective or clinically appropriate because of the risks of adverse effects, the most rational and appropriate second-line choice is amoxicillin. These findings support both the ISCAID¹ and the Australian Veterinary Prescribing Guidelines.¹² The use of evidence-based scores for AMR risk for each antimicrobial treatment, rather than the empirical scores of 1 to 3 applied in our study, would improve this simulation. It would also be valuable to repeat the antimicrobial simulation using Clinical and Laboratory Standards Institute (CLSI) susceptibility results and urine-specific breakpoints.

One limitation to our study is the laboratory's use of the calibrated dichotomous sensitivity (CDS) method. The CDS method is a validated antimicrobial susceptibility testing method developed in Australia in the late 1960s⁴⁹ that was widely used in both human and veterinary microbiology laboratories in Australia until recent years. It remains in use in a small number of accredited veterinary laboratories but is being phased out in favour of CLSI, which provides more information and has some veterinary breakpoints, including some that are urine-specific.

The CDS method uses the tables in Appendix 1: Document S6 to determine susceptibility when the radius of inhibition around a disc exceeds that calibrated to the listed MIC. The laboratory measured the radii of inhibition, but only recorded whether this indicated susceptibility or resistance according to the tables, which were developed for human samples and do not include urinary-specific breakpoints. These tables (and the relevant laboratory methods) remained unchanged during the study period,⁵⁰ hence temporal trends reported here can be relied upon. However, from the data available, we cannot estimate minimum inhibitory concentrations, or make adjustments for the high urine concentration of some antimicrobial drugs. The lack of oxacillin/cefoxitin testing of staphylococci also means that we have been unable to assess the prevalence of methicillin resistance, which is an important indicator for both AMR surveillance and clinical management. Another limitation was the absence of data on bacterial concentrations in urine samples, as well as corresponding clinical data and urinalysis results for these cases, prohibiting triangulation of susceptibility data with clinical signs and prior and subsequent antimicrobial therapy.

Materials and Methods

4.1. Source and Handling of Data

De-identified data were obtained from a veterinary diagnostic laboratory in Australia. Microscopy, culture and antimicrobial susceptibility test results from all cat and dog urine samples that were submitted to the laboratory over a 5-year period (1 January 2015 to 31 December 2019) were included in the study. A unique numerical code was assigned by the laboratory to each patient at the de-identification stage to allow recognition of multiple submissions from the same patient. Culture-negative results were excluded from the analysis.

For organisms with intrinsic resistance to an antimicrobial (including in vivo resistance despite in vitro susceptibility), any “susceptible” laboratory results were altered to resistant. Urinalysis and other clinical data were not available.

4.2. Sample Processing

Antimicrobial susceptibility testing was performed by the laboratory using the standardized calibrated dichotomous sensitivity (CDS) method⁵¹ by inoculation of urine samples directly onto agar plates then adding the antimicrobial discs: ampicillin 10 µg (reported as amoxicillin), amoxicillin/clavulanate 20/10 µg, cephalexin 30 µg, cefovecin 30 µg, enrofloxacin 5 µg and sulfamethoxazole/trimethoprim 1.25/23.75 µg. Some isolates were tested against additional antimicrobials—including marbofloxacin, clindamycin and tetracycline—either in response to special requests from the treating veterinarian or because of antimicrobial resistance seen in the initial tests. For enterococcal isolates, additional antimicrobial discs were applied: erythromycin 15 µg, doxycycline 30 µg and gentamicin 120 µg (to detect high-level resistance). The radius of the zone of inhibition was not recorded. Results were reported as either susceptible or resistant to each antimicrobial drug; there is no intermediate susceptibility result in CDS testing.

4.3. Antibigram, Antimicrobial Impact Factors and Antimicrobial Cost per Cure

The eight most prevalent bacterial species/groups were included in the antibiograms. As not all isolates were tested against the same antimicrobials, results were calculated as the susceptible proportion of the isolates tested against that antimicrobial. Groups of fewer than 30 isolates were excluded from calculations of antimicrobial impact factors and from resistance charts. Multi-drug resistance (MDR) was defined as non-intrinsic resistance to three or more of the antimicrobial categories tested. Antimicrobial categories were based on definitions published previously,⁵² with the addition of aminopenicillins, first-generation cephalosporins, third-generation cephalosporins and beta-lactam inhibitor combinations for staphylococci.

The formula for the selection of rational antimicrobial therapy²⁰ was applied to bacterial species that were present in at least 2% of urine samples from that host species to derive an “impact factor” for each antimicrobial agent. This is an estimate of the proportion of overall UTI cases expected to respond to empirical therapy with that antimicrobial. The impact factor calculation was repeated, differentiating isolates as bacilli and cocci; most veterinary clinics in Australia are equipped for the microscopy of urinary sediment, making morphology of bacteria a feasible approach to the selection of empirical therapy.

To further explore rational treatment pathways, we simulated the theoretical population-level effect of using two antimicrobials in sequence on the dog and cat urine samples that had been tested against all six antimicrobials in the laboratory’s standard panel, based on the in vitro susceptibility of the isolate/s in each sample. Treatment was considered successful once all the isolates in a single sample had been eliminated, or where the only remaining isolate from a sample containing multiple species was an *Enterococcus* spp. Each treatment course of the six antimicrobials was allocated an antimicrobial cost, according to the antimicrobial’s importance rating from the Australian Strategic and Technical Advisory Group on Antimicrobial Resistance,⁵³ with the highest importance antimicrobials given a cost score of three points, those with medium importance a score of two points and those with a low importance a score of one point. The antimicrobial cost per cure for each treatment pathway was then calculated as follows:

$$\frac{\text{Number of cases treated} \times \text{antimicrobial cost per treatment course}}{\text{Number of cases cured}}$$

Data were cleaned using Python and Microsoft Excel, and descriptive statistics were generated

in Microsoft Excel. Regressions and tests of proportions were performed using R Base Package,⁵⁴ dplyr,⁵⁵ tidyverse,⁵⁶ and epiDisplay.⁵⁷ The desexing status was inconsistently recorded, therefore spayed and entire females were combined, as were castrated and entire males.

Conclusions

Our study provided much-needed antimicrobial susceptibility data and practically applicable insights to assist small animal practitioners in the treatment of UTIs. This five-year sample, largely from first-opinion veterinary practices, showed relatively little acquired antimicrobial resistance overall, and very little multiple drug resistance, in urinary bacterial isolates from Australian dogs and cats. However, there were high levels of resistance to fluoroquinolones in *E. faecalis* and *S. canis*. For complicated cases, where animals had multiple urine cultures performed, there was a significant increase in the prevalence of MDR *E. coli* with each successive culture. These findings underscore the impact of veterinary antimicrobial prescribing on resistance patterns and the need for veterinarians to dispense antimicrobials with care.

The antibiograms and rational antimicrobial therapy simulation support current international and Australian guideline recommendations to use three to five days of TMS or amoxicillin as the first-line, empirical therapy for dog and cat UTIs. These agents remain effective against more than 80% of urinary isolates and pose a lower risk of selection for significant AMR than most of the other agents tested. The use of fluoroquinolones (which have a high importance rating) was microbiologically justified in only 0.7% of cases, while the use of the high-importance, third-generation cephalosporin, cefovecin, was not microbiologically justified for any cases.

Supplementary Materials: The following are available online at www.mdpi.com/xxx/s1, Table S1: Urine sample source by animal species, age and sex, Figure S1: Changes in susceptibility over time for the most common species/genera, Table S2: Multiple resistance patterns in *E. coli*, Table S3: Multiple resistance patterns in *Enterococcus faecalis*, Table S4: Multiple resistance patterns in *Staphylococcus pseudintermedius*, Table S5: Multiple resistance patterns in *Proteus mirabilis*.

Author Contributions: Data curation, B.G. and A.W.; Formal analysis, R.S.; Methodology, R.S., K.B., L.H. and J.G.; Resources, B.G.; Supervision, K.B., L.H. and G.B.; Writing—original draft, R.S.; Writing—review & editing, K.B., L.H., J.G. and G.B. All authors have read and agreed to the published version of the manuscript.

Funding: This research 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). K.B. is also funded by the NHMRC through the Centres of Research Excellence Scheme (National Centre for Antimicrobial Stewardship). L.H. is funded by the Australian Research Council through the Discovery Early Career Research Award program. R.S. was a recipient of an Australian Postgraduate Award scholarship.

Acknowledgments: We thank Alistair Legione for assistance with the data analysis program R and associated packages.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Weese JS, Blondeau J, Boothe D et al. International Society for Companion Animal Infectious Diseases (ISCAID) guidelines for the diagnosis and management of bacterial urinary tract infections in dogs and cats. *Vet J* 2019;247:8-25.
2. Hardefeldt LY, Selinger J, Stevenson MA 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;225:34-39.
3. Hardefeldt LY, Holloway S, Trott DJ et al. Antimicrobial Prescribing in Dogs and Cats in Australia: Results of the Australasian Infectious Disease Advisory Panel Survey. *J Vet Intern Med* 2017;31:1100-1107.
4. De Briyne N, Atkinson J, Pokludov L, Borriello SP, Price S. Factors influencing antibiotic prescribing habits and use of sensitivity testing amongst veterinarians in Europe. *Vet Rec* 2013;173:475-+.
5. Moyaert H, Morrissey I, de Jong A et al. Antimicrobial Susceptibility Monitoring of Bacterial Pathogens Isolated from Urinary Tract Infections in Dogs and Cats Across Europe: ComPath Results. *Microb Drug Resist* 2017;23:391-403.
6. Wong C, Epstein SE, Westropp JL. Antimicrobial Susceptibility Patterns in Urinary Tract Infections in Dogs (2010-2013). *J Vet Intern Med* 2015;29:1045-1052.
7. Litster A, Moss SM, Honnery M, Rees B, Trott DJ. Prevalence of bacterial species in cats with clinical signs of lower urinary tract disease: Recognition of *Staphylococcus felis* as a possible feline urinary tract pathogen. *Veterinary Microbiology* 2007;121:182-188.
8. Jordan D. Antimicrobial ratings: the importance of importance. *Aus Vet J* 2019.
9. Australian Strategic and Technical Advisory Group on Antimicrobial Resistance. Importance Ratings and Summary of Antibacterial Uses in Human and Animal Health in Australia. In: Department of Health, editor. Commonwealth of Australia, Canberra, Australia, 2018.
10. Weese JS, Blondeau JM, Boothe D et al. Antimicrobial use guidelines for treatment of urinary tract disease in dogs and cats: Antimicrobial Guidelines Working Group of the International Society for Companion Animal Infectious Diseases. *Veterinary Medicine International* 2011;2011:1-9.
11. British Small Animal Veterinary Association. PROTECT ME. https://www.bsavalibrary.com/content/chapter/10.22233/9781910443644.chap6_1. 2018. Retrieved:03/05/2022
12. University of Melbourne. Australian Veterinary Prescribing Guidelines, Dogs and Cats. <https://vetantibiotics.fvas.unimelb.edu.au/about/resources/>. 2019. Retrieved:24 May
13. Jessen LR, Damborg PP, Spohr A et al. Antibiotic Use Guidelines for Companion Animal Practice (2nd ed.). In: The Danish Small Animal Veterinary Association S, editor, 2019.
14. Lacy MK, Klutman NE, Horvat RT, Zapantis A. Antibigrams: New NCCLS Guidelines, Development, and Clinical Application. *Hospital Pharmacy* 2004;39:542-553.
15. Halstead DC, Gomez N, McCarter YS. Reality of Developing a Community-Wide Antibigram. *Journal of Clinical Microbiology* 2004;42:1-6.
16. Rizvi M, Malhotra S, Agarwal J et al. Regional variations in antimicrobial susceptibility of community-acquired uropathogenic *Escherichia coli* in India: Findings of a multicentric study highlighting the importance of local antibiograms. *IJID Regions* 2024;11:100370.
17. Smit CCH, Keighley C, Rogers K et al. Geo-Temporal Variation in the Antimicrobial Resistance of *Escherichia coli* in the Community. *Antibiotics* 2025;14:233.
18. Hur BA, Hardefeldt LY, Verspoor KM, Baldwin T, Gilkerson JR. 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:e0230049.
19. Charani E, Cooke J, Holmes A. Antibiotic stewardship programmes--what's missing? *J Antimicrob Chemother* 2010;65:2275-2277.

20. Blondeau JM, Tillotson GS. Formula to help select rational antimicrobial therapy (FRAT): its application to community- and hospital-acquired urinary tract infections. *Int J Antimicrob Ag* 1999;12:145-150.
21. Hernandez J, Bota D, Farbos M et al. Risk factors for urinary tract infection with multiple drug-resistant *Escherichia coli* in cats. *Journal of Feline Medicine and Surgery* 2013;16:75-81.
22. Turnidge J, Paterson DL. Setting and Revising Antibacterial Susceptibility Breakpoints. *Clinical Microbiology Reviews* 2007;20:391-408.
23. Doern GV, Brecher SM. The Clinical Predictive Value (or Lack Thereof) of the Results of In Vitro Antimicrobial Susceptibility Tests. *Journal of Clinical Microbiology* 2011;49:S11-S14.
24. Abelson B, Sun D, Que L et al. Sex differences in lower urinary tract biology and physiology. *Biology of Sex Differences* 2018;9.
25. Sævik BK, Trangerud C, Ottesen N, Sørsum H, Eggertsdóttir AV. Causes of lower urinary tract disease in Norwegian cats. *Journal of Feline Medicine and Surgery* 2011;13:410-417.
26. Piyarungsri K, Tangtrongsup S, Thitaram N, Lekklar P, Kittinuntasilp A. Prevalence and risk factors of feline lower urinary tract disease in Chiang Mai, Thailand. *Scientific Reports* 2020;10.
27. Dorsch R, Von Vopelius-Feldt C, Wolf G, Straubinger RK, Hartmann K. Feline urinary tract pathogens: prevalence of bacterial species and antimicrobial resistance over a 10-year period. *Veterinary Record* 2015;176:201-201.
28. Ball KR, Rubin JE, Chirino-Trejo M, Dowling PM. Antimicrobial resistance and prevalence of canine uropathogens at the Western College of Veterinary Medicine Veterinary Teaching Hospital, 2002-2007. *Canadian Veterinary Journal - Revue Veterinaire Canadienne* 2008;49:985-990.
29. Marques C, Gama LT, Belas A et al. European multicenter study on antimicrobial resistance in bacteria isolated from companion animal urinary tract infections. *BMC Vet Res* 2016;12.
30. McMeekin CH, Hill KE, Gibson IR, Bridges JP, Benschop J. Antimicrobial resistance patterns of bacteria isolated from canine urinary samples submitted to a New Zealand veterinary diagnostic laboratory between 2005–2012. *New Zealand Veterinary Journal* 2016;1-14.
31. Saputra S, Jordan D, Mitchell T et al. Antimicrobial resistance in clinical *Escherichia coli* isolated from companion animals in Australia. *Veterinary Microbiology* 2017;211:43-50.
32. Boothe D, Smaha T, Carpenter DM, Shaheen B, Hatchcock T. Antimicrobial resistance and pharmacodynamics of canine and feline pathogenic *E. coli* in the United States. *Journal of the American Animal Hospital Association* 2012;48:379-389.
33. Cummings KJ, Aprea VA, Altier C. Antimicrobial resistance trends among canine *Escherichia coli* isolates obtained from clinical samples in the northeastern USA, 2004-2011. *The Canadian veterinary journal = La revue veterinaire canadienne* 2015;56:393-398.
34. Qekwana DN, Phophi L, Naidoo V, Oguttu JW, Odoi A. Antimicrobial resistance among *Escherichia coli* isolates from dogs presented with urinary tract infections at a veterinary teaching hospital in South Africa. *BMC Vet Res* 2018;14:228.
35. Yamanaka AR, Hayakawa AT, Rocha ÍSM et al. The Occurrence of Multidrug Resistant Bacteria in the Urine of Healthy Dogs and Dogs with Cystitis. *Animals* 2019;9:1087.
36. Australian Commission on Safety and Quality in Healthcare. AURA 2019: Third Australian report on antimicrobial use and resistance in human health. 2019.
37. Arsène Sp, Leclercq R. Role of a *qnr*-Like Gene in the Intrinsic Resistance of *Enterococcus faecalis* to Fluoroquinolones. *Antimicrobial agents and chemotherapy* 2007;51:3254-3258.
38. KuKanich KS, Lubbers BV. Review of enterococci isolated from canine and feline urine specimens from 2006 to 2011. *J Am Anim Hosp Assoc* 2015;51:148-154.
39. Australian Commission on Safety and Quality in Healthcare. AURA 2019: Third Australian report on antimicrobial use and resistance in human health. 2019.
40. Horsley H, Malone-Lee J, Holland D et al. *Enterococcus faecalis* Subverts and Invades the Host Urothelium in Patients with Chronic Urinary Tract Infection. *PLoS One* 2013;8:e83637.
41. Hall JL, Holmes MA, Baines SJ. Prevalence and antimicrobial resistance of canine urinary tract pathogens. *Veterinary Record* 2013;173:549-549.

42. Papich MG. Antibiotic Treatment of Resistant Infections in Small Animals. *Veterinary Clinics of North America: Small Animal Practice* 2013;43:1091-1107.
43. Westropp JL, Sykes JE, Irom S et al. Evaluation of the Efficacy and Safety of High Dose Short Duration Enrofloxacin Treatment Regimen for Uncomplicated Urinary Tract Infections in Dogs. *J Vet Intern Med* 2012;26:506-512.
44. Clare S, Hartmann FA, Jooss M et al. Short- and long-term cure rates of short-duration trimethoprim-sulfamethoxazole treatment in female dogs with uncomplicated bacterial cystitis. *J Vet Intern Med* 2014;28:818-826.
45. Hall IA, Campbell KL, Chambers MD, Davis CN. Effect of trimethoprim/sulfamethoxazole on thyroid function in dogs with pyoderma. *Journal of the American Veterinary Medical Association* 1993;202:1959-1962.
46. Noli C, Koeman JP, Willemse T. A retrospective evaluation of adverse reactions to trimethoprim-sulphonamide combinations in dogs and cats. *Vet Quarterly* 1995;17:123-128.
47. Williamson NL, Frank LA, Hnilica KA. Effects of short-term trimethoprim-sulfamethoxazole administration on thyroid function in dogs. *J Am Vet Med Assoc* 2002;221:802-806.
48. Sykes JE. Antimicrobial Drug Use in Dogs and Cats. In: Giguère S, Prescott JF, Dowling PM, editors. *Antimicrobial Therapy in Veterinary Medicine, 5th Ed.* Wiley-Blackwell, New Jersey, USA, 2013:473-494.
49. CDS Reference Laboratory. The CDS Antibiotic Susceptibility Test. <https://cdstest.net/>. 2026. Retrieved:31/03/2026
50. CDS Reference Laboratory. Modifications to CDS testing manual. <https://cdstest.net/manual/modifications/>. 2018. Retrieved:31/03/2026
51. CDS Reference Laboratory. Antibiotic Susceptibility Testing by the CDS Method, 10th Edition. <http://cdstest.net/wordpress/wp-content/uploads/10th-Edition-Modified-September-2019.pdf>. 2019
52. Magiorakos AP, Srinivasan A, Carey RB et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. *Clinical Microbiology and Infection* 2012;18:268-281.
53. Australian Strategic and Technical Advisory Group on Antimicrobial Resistance (ASTAG). Importance ratings and summary of antibacterial uses in human and animal health in Australia. www.amr.gov.au/resources/importance-ratings-and-summary-antibacterial-uses-human-and-animal-health-australia. 2018. Retrieved:18 Feb 2023
54. R Development Core Team. R: A language and environment for statistical computing R Foundation for Statistical Computing, Vienna, Austria., 2019.
55. Wickham H, François R, Henry L, Müller K. dplyr: A Grammar of Data Manipulation. 2020.
56. Wickham H, Averick M, Bryan J et al. Welcome to the tidyverse. *Journal of Open Source Software* 2019;4:1686.
57. Chongsuvivatwong V. epiDisplay: Epidemiological Data Display Package. 2018.

Chapter 3: Clavulanate and cephalosporins: what is the cost of convenience?

A version of this chapter has been published in the Australian Veterinary Practitioner (2023).

This chapter synthesises some of the content of other chapters in this thesis, new antimicrobial susceptibility data from 2020-2021 and other relevant data from the first author's research group.

RO Scarborough^{1,2}, GF Browning^{1,2}, LY Hardefeldt^{1,2}, BI Galgut³, MS Marenda¹ and KE Bailey^{1,2}.

1. Asia-Pacific Centre for Animal Health, Department of Veterinary Biosciences, Melbourne Veterinary School, Faculty of Science, The University of Melbourne, Parkville
2. National Centre for Antimicrobial Stewardship, Peter Doherty Institute of Infection and Immunity, Parkville
3. ASAP Laboratory, Mulgrave

Abstract

Background: The systemic antimicrobial given most often to Australian dogs is a potentiated penicillin, amoxicillin-clavulanate. Cats are most likely to receive a long-acting (14-day) injection of a third-generation cephalosporin, cefovecin, or amoxicillin-clavulanate. These antimicrobial choices are non-concordant with local and international empirical prescribing guidelines for common bacterial infections in dogs and cats.

Aims and Methods: We undertook quantitative analysis of culture and susceptibility (C&S) data from dog and cat samples sent to an Australian veterinary pathology laboratory, to evaluate the appropriateness of antimicrobial choices. We then conducted semi-structured interviews with 22 Australian veterinarians who treat dogs and cats, to understand their antimicrobial decision-making.

Results: C&S results from dog and cat urinary isolates showed that the vast majority (94%) of urinary pathogens tested could be treated with either amoxicillin or trimethoprim-sulfonamide, as recommended in prescribing guidelines. Amoxicillin-clavulanate was justified in just 4% of cases; cefovecin was never microbiologically justified. In both urinary and non-urinary isolates, adding clavulanate to amoxicillin was helpful in fewer than 1 in 10 cases. Interviews revealed significant modifiable barriers to guideline-concordant prescribing: lack of veterinarian awareness of guidelines and antimicrobial importance ratings, practices not routinely holding stock of guideline-recommended, low-importance antimicrobials, and veterinarians prioritising animals 'finishing the course' of antimicrobials over the more important consideration of choosing the best antimicrobial for the shortest effective duration.

Conclusions: Current antimicrobial use in companion animal practice is suboptimal and overuse of clavulanate and cephalosporins, particularly third-generation cephalosporins, puts animals and people at unnecessary risk. There are simple changes veterinarians can make to improve their antimicrobial prescribing.

Introduction

The continued liberal use of antimicrobials in animals and humans – and the capacity of bacteria to acquire resistance to multiple antimicrobial agents on transmissible plasmids or transposons – threaten to propel us into a post-antibiotic era. The O'Neill report estimates that there are already 700,000 human deaths per year from antimicrobial-resistant infections and warns that this could balloon to 10 million human deaths per year by 2050¹, not to mention significant morbidity for many more living with resistant infections. The impact of antimicrobial resistance (AMR) on animal health, welfare and production is likely to be just as significant.

Few veterinarians would disagree that this One Health problem is already serious, and is worsening. As a result, all prescribers have an ethical obligation to optimise their antimicrobial choices and durations of therapy, and to avoid unnecessary antimicrobial use.²

To assist prescribers in these clinical decisions, antimicrobial prescribing guidelines have been developed for humans and animals. Australian guidelines for a range of animal species are available free online from the [University of Melbourne](https://www.unimelb.edu.au) or from the [AMR Vet Collective](https://www.amrvetcollective.org.au). Additionally, the World Health Organization³ and the Australian Strategic and Technical Advisory Group on AMR (ASTAG) have introduced importance ratings for all antimicrobials, categorising each as low, medium or high importance. To avoid the most serious consequences of AMR, veterinary and medical prescribers are urged to use low-importance antimicrobials preferentially, and reserve medium- and high-importance antimicrobials only for cases in which a lower importance antimicrobial would be ineffective or inappropriate. Some veterinarians will be familiar with 'traffic light cards'⁴ summarising antimicrobial importance ratings for different animal species (Figure 1).

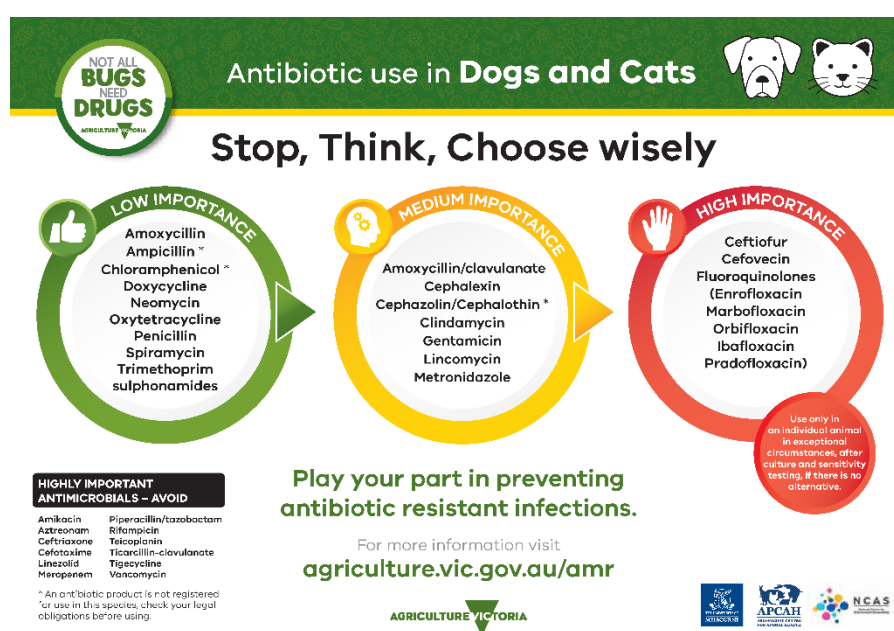


Figure 1: Example of a 'traffic light card' showing the different importance ratings (or level of AMR risk) of antimicrobials commonly used in dogs and cats. This resource and cards for other species are available for download from vetantibiotics.science.unimelb.edu.au/about/resources/

Many Australian companion animal veterinarians do not appear to have heeded this advice; our group's large-scale analyses of antimicrobial prescribing in companion animals^{5, 6} show a strong preference for medium- and high-importance systemic antimicrobials in dogs and cats, particularly amoxicillin-clavulanate and cefovecin.

Meanwhile, the low-importance antimicrobials recommended in the guidelines for many common bacterial infections are used infrequently – and, anecdotally, are often not even stocked in the practice dispensary.

While there are some situations where the choice of a higher importance antimicrobial is justified, we have robust evidence in at least one common condition - dog and cat urinary tract infections ⁷ - that the pathogens are overwhelmingly susceptible to the low-importance antimicrobials recommended in prescribing guidelines, yet are most commonly treated with medium-importance amoxicillin-clavulanate in dogs and high-importance cefovecin in cats.

Our interviews with veterinarians show that there are a number of factors contributing to these decisions, and lead us towards potential solutions.

Methods

We analysed culture and susceptibility (C&S) data from dog and cat urine and swab samples submitted in 2020-2021 to a Victorian veterinary laboratory that primarily serviced general practice clinics and used the calibrated dichotomous sensitivity (CDS) method. This is the same laboratory that provided data for our previously published study on urinary isolates, where more detail on the methods can be found.⁸ We focus on the susceptibility of the 2020-2021 isolates to amoxicillin and amoxicillin-clavulanate, presenting descriptive statistics.

We also present data from the aforementioned urinary isolate study⁸ and other, related studies^{5, 6, 9, 10} from our research group, to form a combined results and discussion that synthesises clinically relevant information for Australian veterinary practitioners.

Results and discussion

What are veterinarians prescribing?

In 2020, members of our research group used natural language processing to analyse 4.4 million consultation records from almost 200 Australian companion animal veterinary practices.⁵ Approximately 1 in 7 consultations resulted in the use of antimicrobials. In dogs, the three most common choices were all medium-importance antimicrobials: amoxicillin-clavulanate (34%), cephalexin (16%) and metronidazole (10%).

The most common systemic antimicrobial choice in cats was the high-importance third-generation cephalosporin, cefovecin (32%), followed closely by medium-importance amoxicillin-clavulanate (31%).

The low-importance drug amoxicillin was used infrequently (2% dogs, 2.5% cats), despite being recommended in 11 of 16 common canine and feline bacterial infections in the Australian Veterinary Prescribing Guidelines ¹¹. The trimethoprim-sulfonamide combination was one of the least commonly prescribed antimicrobial preparations (0.6% in dogs, 0.2% in cats), despite being recommended for first-line empirical treatment of lower urinary tract infections.¹¹

The high rate of use of amoxicillin-clavulanate and cefovecin in dogs and cats is not a recent phenomenon – antimicrobial choices in our 2020 study⁵ closely mirrored a 2018 analysis of almost 2 million pet insurance claims over a five-year period.⁶

These two studies demonstrate widespread and persistent antimicrobial prescribing patterns in

the Australian veterinary profession that appear to be non-concordant with prescribing guidelines.

What are the risks associated with overuse of clavulanate and third-generation cephalosporins?

Some bacteria can inactivate certain forms of penicillins by producing enzymes known as beta-lactamases. Early forms of beta-lactamases could hydrolyse amoxicillin or ampicillin, but not cephalosporins. Bacteria later evolved modified enzymes, known as extended-spectrum beta-lactamases (ESBLs), which can inactivate third-generation cephalosporins as well.

Clavulanate is a ‘false target’ for these enzymes. It binds irreversibly to beta-lactamases, thereby protecting amoxicillin from enzymatic degradation. Amoxicillin-clavulanate can therefore treat infections caused by bacteria that produce moderate amounts of beta-lactamases, whereas amoxicillin alone cannot.¹² However, overproduction of beta-lactamases, or mutations in the enzyme structure (‘inhibitor-resistant’ beta-lactamases), can overcome this protective effect, making the amoxicillin-clavulanate combination inefficient. Bacteria displaying these further enhanced resistance mechanisms can be selected for whenever the drug is used.¹³ Hence, amoxicillin-clavulanate should only be used when there is reasonable likelihood that the target pathogen *already* produces a clavulanate-responsive beta-lactamase.

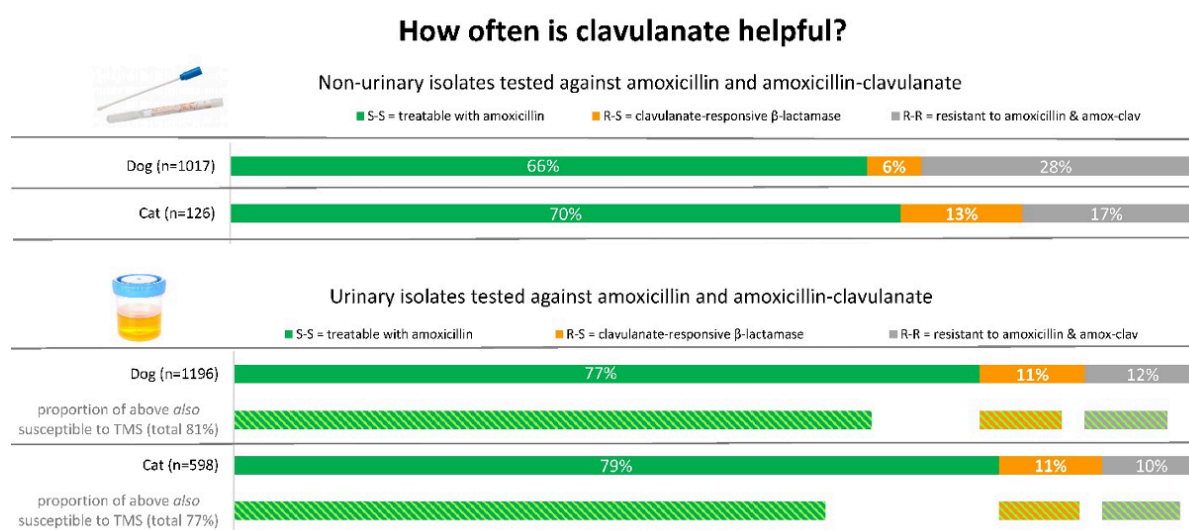


Figure 2: Prevalence of clavulanate-responsive beta-lactamase expression (orange) as a proportion of all isolates tested against both amoxicillin and amoxicillin-clavulanate (amox-clav), Oct 2020-Sep 2021, by host species. Top chart shows non-urinary isolates (n=1143) and bottom chart shows urinary isolates (n=1794). The laboratory used the CDS method for susceptibility testing.

* N.B. Many urinary isolates that test resistant in vitro may still respond clinically to amoxicillin, because in vivo amoxicillin concentrations in urine are many times higher than the cutoff levels used to declare resistance. Additionally, 79% of the urinary isolates producing beta lactamase were susceptible to low-importance TMS.

Veterinarians might be surprised how uncommonly beta-lactamase is produced by the pathogens they treat (Figure 2). Beta-lactamase production can be inferred when there is *susceptibility* to amoxicillin-clavulanate but *resistance* to amoxicillin (or ampicillin).

We analysed culture and susceptibility test results for samples sent to an Australian veterinary

diagnostic laboratory (ASAP Laboratory, Victoria) in 2020-2021. In dogs and cats, only about 1 in 10 isolates from urine and 1 in 15 isolates from swabs (body sites not specified) tested resistant to amoxicillin, but susceptible to amoxicillin-clavulanate. Importantly, the vast majority (153/193, 79%) of the beta lactamase-producing urinary isolates were susceptible to guideline-recommended TMS.

In other words, the addition of clavulanate to amoxicillin is helpful in fewer than 1 in 10 cases, and even then, can often be avoided by selecting a different low-importance antimicrobial. However, using clavulanate *always* applies selection pressure for clavulanate resistance, not only in the target pathogen, but also in commensal bacterial species, and increases the risk of direct toxic effects. In humans, treatment with amoxicillin-clavulanate, rather than amoxicillin, significantly increases the risk of adverse gastrointestinal, hepatic and haematological effects and more than doubles the risk of overgrowth of *Clostridioides difficile* in the gut.¹⁴ Although there is currently little published veterinary evidence, one can reasonably expect similar risks exist in companion animals.

These increased risks are clearly justified where the pathogen produces beta-lactamase and no lower importance antimicrobial would be effective. However, some veterinarians in our interview study (described later in this article) admitted that they routinely select amoxicillin-clavulanate over amoxicillin for reasons that have nothing to do with a microbiological imperative.

Cephalosporin use is under increasing scrutiny because of its role in selecting for some of the most problematic AMR pathogens, including *C. difficile*, methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci (VRE).¹⁵ Third-generation cephalosporins, including ceftiofur, are additionally associated with selection for ESBL-producing bacteria.¹⁶ The ESBLs can break down most penicillins (including amoxicillin) and cephalosporins (including cephalexin and ceftiofur).¹⁷ ESBLs are inhibited by clavulanate *in vitro*, but a significant proportion of ESBL-producing bacteria are *also* resistant to amoxicillin-clavulanate^{18,19} and other classes of antimicrobials, including fluoroquinolones (e.g. enrofloxacin), aminoglycosides (e.g. gentamicin) and trimethoprim-sulfonamide (TMS),^{17, 20} which can leave very few treatment options.

As bacterial populations can be transferred between animals, their owners and their environment, and these bacterial populations can also share their genes between each other, resistance that has been selected in one bacterial species and one animal host by the use of specific antimicrobials can be readily transferred to another organism and/or another host. As the two most frequently prescribed antimicrobials in cats are ceftiofur, which selects for bacteria producing ESBLs, and amoxicillin-clavulanate, which selects for clavulanate resistance, companion animal veterinarians are imposing considerable selection pressure for these two resistance mechanisms, and other resistance mechanisms that are often co-selected with them. While this selection may initially only develop in commensal bacteria and remain unnoticed, these organisms can act as a reservoir of resistance genes and subsequently transmit them to pathogens. AMR in the bacteria of an animal host appears to peak in the first month after antimicrobial exposure, but can persist for 12 months²¹⁻²³ and reduced diversity of intestinal microbiota can last up to two years.²⁴ Multi-drug resistant (MDR) infections in animals, for which we have no effective veterinary antimicrobials, are already occurring²⁵, and are likely to become much more common without significant behaviour change from the veterinary profession.

The high use of ceftiofur and amoxicillin-clavulanate in dogs and cats in Australia^{5, 6} cannot be justified, when lower-risk antimicrobials can often be substituted.

Urinary tract infections: a case in point

Urinary tract infections in dogs and cats provide a good example of guideline non-concordant prescribing in Australian veterinary practice.

Since 2011, international guidelines for managing uncomplicated lower UTIs have recommended amoxicillin or TMS as first-line empirical therapy.^{26, 27} The Australian Veterinary Prescribing Guidelines¹¹ make the same recommendation. The current recommended duration of therapy is 3-5 days.

Since susceptibility patterns can vary dramatically between different animal populations, and there were scant local susceptibility data, we aimed to validate these recommendations for the Australian context. In a previously published paper, we examined culture and susceptibility (C&S) results of more than 5000 culture-positive urine samples from Australian dogs and cats, submitted over a 5-year period, primarily from first-opinion veterinary practices.⁷

The most commonly isolated bacterial species was *E. coli* (59% of all samples). Other enteric Gram-negative bacilli, including various *Proteus* spp. (13% total) and *Enterobacter* spp. (3.3%) were found far less frequently. The other common species isolated were Gram-positive cocci: *Enterococcus faecalis* (11%), *Staphylococcus* spp. (12% total) and *Streptococcus canis* (2.2%) (Figure 3).

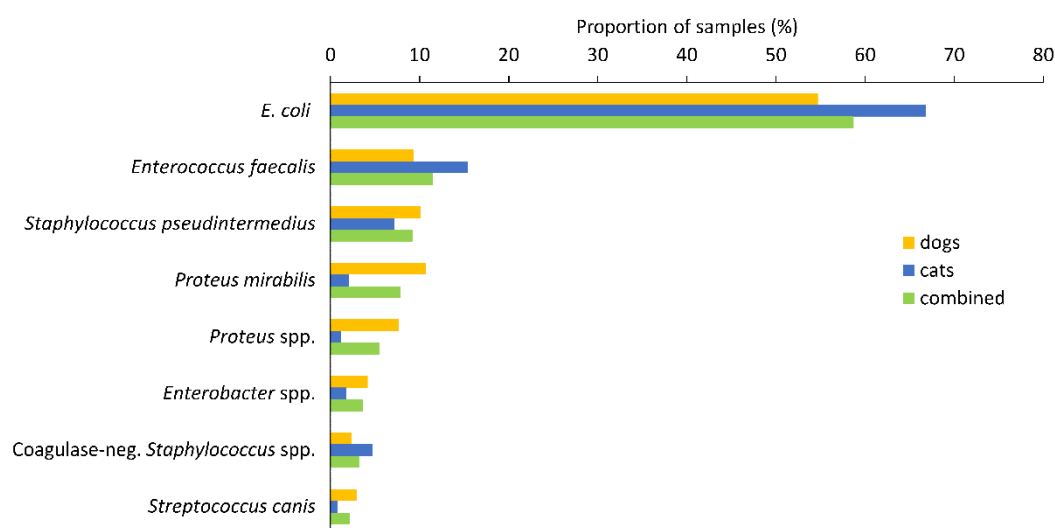


Figure 3: Prevalence of the most frequently isolated bacterial species cultured from urine samples, by host species. Total number of samples was 5614. The laboratory used standard microbiological methods to culture and identify isolates as previously reported.⁷

As most veterinarians rarely submit urine for C&S unless a UTI has failed to respond to empirical antimicrobial therapy, relapses or the case is complicated^{28, 29} the bacteria in this study represent a subgroup of UTIs, which is likely to have higher-than-typical levels of antimicrobial resistance. Additionally, some veterinary laboratories (including the one in this study) use a cutoff level for amoxicillin susceptibility that reflects serum amoxicillin concentrations more than 30 times lower than those actually achieved in urine^{30, 31}, and thus significantly underestimate the *in vivo* effectiveness of amoxicillin in the lower urinary tract.

Yet despite these two factors that would tend to underestimate typical antimicrobial susceptibility, the data were reassuring, as 5306/5614 (94%) of dog and cat urinary isolates were susceptible to amoxicillin and/or TMS. In only 236/5614 (4.2%) of cases was there a microbiological justification for use of the medium-importance antimicrobial amoxicillin-clavulanate, and in only 38/5614 (0.68%) was there a microbiological justification for use of the high-importance antimicrobial enrofloxacin. (Figure 4) Importantly, there was not a single isolate that required use of the high-importance antimicrobial cefovecin; every isolate that was susceptible to high-importance cefovecin (4594/5614, 82%) was also susceptible to medium-importance cephalixin, and the vast majority of these were also susceptible to lower importance TMS (4316/4594, 94%) and/or amoxicillin (3935/4594, 86%).

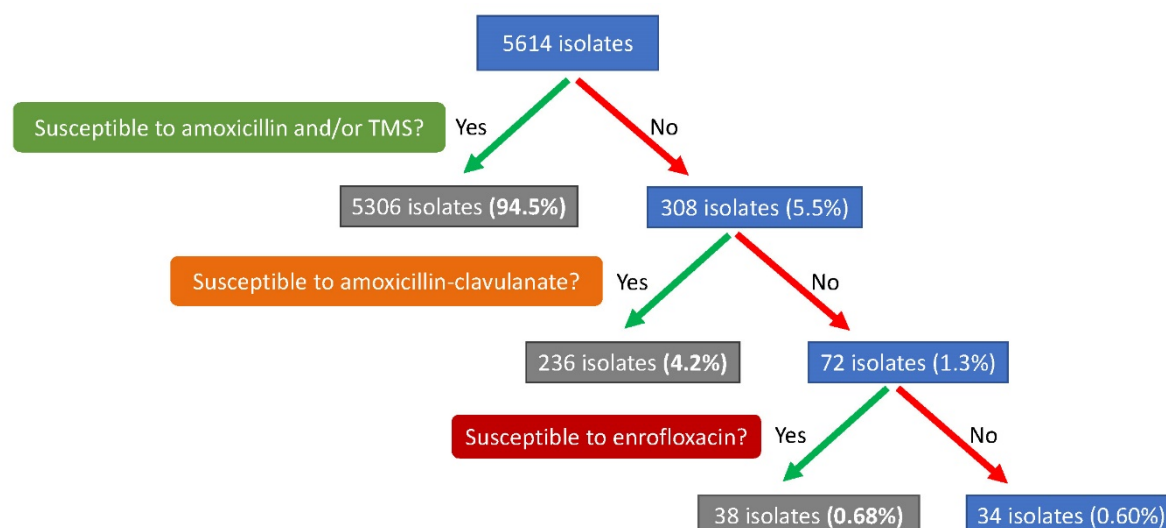


Figure 4: Summary of 2015-2019 urinary isolate susceptibilities to selected antimicrobials from the six routinely tested by the laboratory. Note: Medium-importance cephalixin was less effective than amoxicillin-clavulanate for isolates resistant to TMS and amoxicillin, and high-importance cefovecin was ineffective against all of the isolates resistant to amoxicillin-clavulanate. Therefore, both were omitted from this summary.

The most prevalent urinary tract pathogen, *E. coli*, provides the best opportunities for comparison of antimicrobial resistance results between species and countries. While there are challenges in comparing susceptibility patterns when laboratory methods and breakpoints are inconsistent, in our study, cat and dog *E. coli* isolates appeared to have higher rates of susceptibility than Australian human urinary *E. coli* isolates to amoxicillin (75%-80% vs 55% in humans) and amoxicillin-clavulanate (97%-99% vs 87% in humans).³² Compared with veterinary studies in China³³, the USA^{34,35}, the UK and much of Europe³⁶, the susceptibility of Australian dog and cat urinary *E. coli* to amoxicillin, TMS, amoxicillin-clavulanate, cephalixin and fluoroquinolones also appeared to be high. This is no reason for complacency, but rather a call to the veterinary profession to fiercely protect the fortunate position that we currently enjoy with urinary pathogens. It is a position that is unlikely to last long if veterinarians do not use antimicrobials with more care. The rise of methicillin-resistance in staphylococci (MRSP and MRSA) in companion animals since the early 2000s is a cautionary tale.³⁷⁻³⁹

Additional analyses of our local C&S data underlined that guideline-recommended amoxicillin and TMS were the most rational empirical choices for uncomplicated UTIs in dogs and cats. A new analysis demonstrates the value of in-clinic urinary cytology to choose between TMS and amoxicillin: in a UTI caused by rods, TMS was the better choice; if the UTI was caused by cocci, amoxicillin was clearly superior; expected effectiveness in this case came close to that of amoxicillin-clavulanate. (Table 1)

Table 1: Empirical, morphology-based treatment recommendations for sporadic lower UTIs in dogs and cats, based on the authors' previously published 2015-2019 isolate *in vitro* susceptibility results⁷

 Bacterial morphology	 Recommended empirical treatment	Expected success rate	Amoxicillin-clavulanate expected success rate
 Bacilli	TMS	93%	95%
 Cocci	Amoxicillin	88%*	92%
 Mixed or unknown	TMS	82%	93%

*amoxicillin effectiveness *in vivo* is likely to be higher than laboratory results suggest

Applying our own empirical recommendations in Table 1 to dog and cat urinary isolate data from the same laboratory in 2020-2021, 1363 isolates would have been treated with TMS and 445 with amoxicillin, with an overall projected success rate of 93%.

Keeping in mind the tendency of these C&S data to overestimate resistance, we can summarise this as follows: in Australian dog and cat UTIs, guideline-recommended TMS and amoxicillin are highly effective; selectively applying empirical TMS for rods or amoxicillin for cocci (or TMS if mixed or unknown) should cure more than 93% of all cases. Yet, according to a large pet insurance data set, Australian veterinarians are treating UTIs in cats almost exclusively with cefovecin (47%) or amoxicillin-clavulanate (39%) and in dogs with amoxicillin-clavulanate (68%) or cephalexin (12%).^{6, unpublished data}

One possible reason for guideline non-compliance is fear of adverse reactions to TMS, particularly in certain dog breeds. Although TMS should be avoided in Dobermanns, reactions such as dry eye, haematopoietic disorders, skin eruptions, and endocrinopathies, have been reported almost exclusively with TMS courses of ≥ 7 days^{40, 41} and are considered very unlikely with guideline-recommended^{11, 27} courses of 3-5 days. Another possible reason is fear of hypersalivation in cats, which should be avoidable by using unbroken, enteric-coated TMS tablets or by placing tablets into empty capsules. The University of Melbourne antimicrobial pocket guide for Australian companion animal veterinarians provides further guidance on adverse reactions and dose rates.⁴²

Our interviews with veterinarians showed that fear of treatment failure is another reason they use broader-spectrum antibiotics preferentially. In this regard, clinicians should draw significant reassurance from our analyses.

Why don't veterinarians follow the guidelines? And what can individuals do about it?

We conducted semi-structured interviews with 22 Australian veterinarians. The methods and results regarding delaying or withholding antimicrobials have been previously published.⁹ The median interview duration was 90 minutes. Two case studies (a dog with signs of a sporadic UTI and a cat with a skin abscess) and a core set of questions regarding prescribing behaviours were addressed in every interview, allowing some broad quantitation within this qualitative study. A range of additional, non-core questions was also asked, depending on previous responses.

The interviews revealed a number of reasons for non-compliance with antimicrobial prescribing guidelines, and for the frequent use of amoxicillin-clavulanate and cefovecin. We identified three key modifiable drivers of inappropriate amoxicillin-clavulanate and cefovecin use, and potential solutions that veterinarians can implement at little or no cost.

1. Display and discuss the guidelines and antimicrobial importance ‘traffic-light cards’ in the workplace

Many veterinarians were simply not aware of the availability of free, industry-independent Australian prescribing guidelines and ‘traffic-light’ antimicrobial importance ratings cards for different species (available at www.vetantibiotics.science.unimelb.edu.au). Two recent veterinary trials have demonstrated improvements in antimicrobial use in small animals at least partially attributable to the promotion of evidence-based guidelines within a practice.^{43, 44} Additional useful resources – including learning modules on antimicrobial resistance and stewardship - are available free at the AMR Vet Collective website: www.amrvetcollective.com

2. Keep stock of low-importance antibiotics, colour-code your antibiotic shelves

Several veterinarians admitted that medium-importance amoxicillin-clavulanate was their default or ‘go-to’ antimicrobial choice, simply because it is always in stock, it is effective in many infections and it felt familiar and ‘safe’ after years of habitual use.

Many interviewees said their practices simply did not routinely keep stock of the low-importance antimicrobials recommended in the guidelines; the inconvenience and delay of ordering in these drugs for an individual patient was reported as a barrier to their routine use. It follows that keeping stock of these inexpensive antimicrobials is an important adjunct to displaying the prescribing guidelines and traffic light cards.

Labelling antimicrobials (or the shelf they sit on) with traffic-light coloured dots corresponding to their ASTAG importance level (i.e. red for high-importance, yellow for medium-importance, green for low-importance) can also encourage responsible use. This simple intervention was part of a successful antimicrobial stewardship trial across 135 Australian veterinary practices⁴³ and was well received by veterinarians⁴⁵.

3. Think more about the right antibiotic for the shortest effective duration, and less about ‘finishing the course’

Some veterinarians interviewed lacked knowledge of the core principles of antimicrobial stewardship. For example, one interviewee could see no reason to use narrower-spectrum amoxicillin, because broad-spectrum amoxicillin-clavulanate could be used to treat all the same bacteria, *and more*.

Many more veterinarians expressed a concern about the risk of antimicrobial resistance if owners failed to finish the antimicrobial course they had selected. Although experts in infectious diseases and AMR have abandoned the old mantra of ‘finish the course’⁴⁶ - increasingly promoting the mantra ‘shorter is better’⁴⁷ and advocating for durations tailored to clinical signs or biomarkers^{48, 49} - the concept has proven stubbornly difficult to shift in the broader community. In the interviewed veterinarians, anxiety around unfinished antimicrobial courses – and the consequent concerns about clinical deterioration and AMR - were a major driver of the use of injections of high-importance, long-acting cefovecin, especially in cats. The same drivers have also been reported in a UK veterinarian interview study.²⁹

Overwhelmingly, the veterinarians who expressed concerns about finishing the course *also* selected durations of antimicrobial therapy (for the UTI case study discussed) in excess of guideline recommendations, as they believed these were more certain to clear an infection and thereby avoid AMR. In fact, longer-than-necessary antimicrobial courses increase the patient’s risk of developing a resistant infection⁵⁰.

A majority of the veterinarians interviewed also chose medium- or high-importance antimicrobials for both case studies discussed, whereas guidelines recommended a low-importance antimicrobial (UTI) or no antimicrobial at all (uncomplicated draining cat fight abscess).

These interview findings suggest that many veterinarians who are worried about the impact of their prescribing on AMR may be misdirecting their efforts. In fact, veterinarians would do well to shift their focus to:

- a) **avoiding antimicrobials where none are needed** (e.g. draining abscesses, clean surgeries, subclinical bacteriuria)
- b) **using low-importance antimicrobials preferentially***
- c) **keeping treatment durations as short as possible*** - longer antimicrobial exposure means more collateral damage

**check current [Australian Veterinary Prescribing Guidelines](#) for best empirical choices and suggested durations for common conditions in a range of species*

Guideline-recommended durations of therapy are becoming shorter as more evidence emerges that shorter courses are as effective as the traditional longer courses in many conditions ^{47, 51}. This is excellent news for our patients, because shorter courses lower three important risks: direct adverse effects, severe microbiome disruption, and AMR. They also make life easier for the client; shortening a course from a traditional 10-14 days to the guideline-recommended 3-5 days for a sporadic urinary tract infection makes it more feasible for clients to administer low-importance oral antimicrobials at home.

Providing tableting training for cat owners, and video tableting instructions that owners can refer to at home, could also help to avoid unnecessary use of cefovecin.

Implementing these changes will take time and effort, but if all veterinarians can reduce their reliance on cephalosporins and clavulanate, and follow prescribing guidelines, we have a better chance of protecting pets - and their owners - from the worst consequences of AMR in the longer term.

Acknowledgments: We gratefully acknowledge the support of ASAP Laboratory (part of Healix Pathology) in providing access to de-identified C&S data, and the veterinarians who generously gave their time for interviews.

Ethics: Ethical approval for the veterinarian interview study was provided by the University of Melbourne, Project ID 1955762.1

Conflict of interest: The authors declare no relevant conflicts of interest.

References

1. O'Neill J, et al. Tackling drug-resistant infections globally: Final report and recommendations. UK Review on Antimicrobial Resistance, Chaired by Jim O'Neill. https://amr-review.org/sites/default/files/160518_Final%20paper_with%20cover.pdf. 2016. Retrieved:02/11/2021
2. Bengtsson B, Greko C. Antibiotic resistance—consequences for animal health, welfare, and food production. *Ups J Med Sci* 2014;119:96-102.
3. World Health Organization. Critically important antimicrobials for human medicine. 6 edn, 2018.
4. Agriculture Victoria, The University of Melbourne. Traffic light card: Antibiotic use in dogs and cats <https://vetantibiotics.science.unimelb.edu.au/about/resources/>. 2020. Retrieved:01/11/2021
5. Hur BA, Hardefeldt LY, Verspoor KM, Baldwin T, Gilkerson JR. 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:e0230049.
6. Hardefeldt LY, Selinger J, Stevenson MA 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;225:34-39.
7. Scarborough R, Bailey K, Galgut B 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.
8. Scarborough R, Bailey K, Galgut B 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.
9. Scarborough RO, Sri AE, Browning GF, Hardefeldt LY, Bailey KE. 'Brave enough': A qualitative study of veterinary decisions to withhold or delay antimicrobial treatment in pets. *Antibiotics* 2023;12:540.
10. Scarborough RO, Bailey KE, Sri AE, Browning GF, Hardefeldt LY. Seeking simplicity, navigating complexity: How veterinarians select an antimicrobial drug, dose, and duration for companion animals. *J Vet Intern Med* 2024;38:3215-3234.
11. The University of Melbourne. Australian Veterinary Prescribing Guidelines, Dogs and Cats (version 2). <https://vetantibiotics.science.unimelb.edu.au/about/resources/>. 2019. Retrieved:01/10/2023
12. Reeves DS, Bywater MJ, Holt HA. Antibacterial synergism between beta-lactam antibiotics: Results using clavulanic acid (BRL 14151) with amoxycillin, carbenicillin or cephaloridine. *Infection* 1978;6:S9-S16.
13. Chaibi EB, Sirot D, Paul G, Labia R. Inhibitor-resistant TEM beta-lactamases: phenotypic, genetic and biochemical characteristics. *J Antimicrob Chemother* 1999;43:447-458.
14. Brown KA, Langford B, Schwartz KL et al. Antibiotic Prescribing Choices and Their Comparative C. Difficile Infection Risks: A Longitudinal Case-Cohort Study. *Clinical Infectious Diseases* 2021;72:836-844.
15. Dancer SJ. The problem with cephalosporins. *J Antimicrob Chemother* 2001;48:463-478.
16. Urbánek K, Kolář M, Lovečková Y, Strojil J, Šantavá L. Influence of third-generation cephalosporin utilization on the occurrence of ESBL-positive *Klebsiella pneumoniae* strains. *Journal of Clinical Pharmacy and Therapeutics* 2007;32:403-408.
17. Gharavi MJ, Zarei J, Roshani-Asl P et al. Comprehensive study of antimicrobial susceptibility pattern and extended spectrum beta-lactamase (ESBL) prevalence in bacteria isolated from urine samples. *Scientific Reports* 2021;11.
18. Fournier D, Chirouze C, Leroy J et al. Alternatives to carbapenems in ESBL-producing *Escherichia coli* infections. *Médecine et Maladies Infectieuses* 2013;43:62-66.

19. Prakash V, Lewis JS, 2nd, Herrera ML, Wickes BL, Jorgensen JH. Oral and parenteral therapeutic options for outpatient urinary infections caused by enterobacteriaceae producing CTX-M extended-spectrum beta-lactamases. *Antimicrobial Agents and Chemotherapy* 2009;53:1278-1280.
20. Kumar D, Singh AK, Ali MR, Chander Y. Antimicrobial Susceptibility Profile of Extended Spectrum β -Lactamase (ESBL) Producing *Escherichia coli* from Various Clinical Samples. *Infectious Diseases: Research and Treatment* 2014;7:IDRT.S13820.
21. Costelloe C, Metcalfe C, Lovering A, Mant D, Hay AD. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis. *Br Med J* 2010;340.
22. Lindgren M, Lofmark S, Edlund C, Huovinen P, Jalava J. Prolonged impact of a one-week course of clindamycin on *Enterococcus* spp. in human normal microbiota. *Scand J Infect Dis* 2009;41:215-219.
23. Nyberg SD, Osterblad M, Hakanen AJ et al. Long-term antimicrobial resistance in *Escherichia coli* from human intestinal microbiota after administration of clindamycin. *Scand J Infect Dis* 2007;39:514-520.
24. Jernberg C, Lofmark S, Edlund C, Jansson JK. Long-term ecological impacts of antibiotic administration on the human intestinal microbiota. *International Society for Microbial Ecology Journal* 2007;1:56-66.
25. Smith A, Wayne AS, Fellman CL, Rosenbaum MH. Usage patterns of carbapenem antimicrobials in dogs and cats at a veterinary tertiary care hospital. *J Vet Intern Med* 2019;33:1677-1685.
26. Weese JS, Blondeau JM, Boothe D et al. Antimicrobial use guidelines for treatment of urinary tract disease in dogs and cats: Antimicrobial Guidelines Working Group of the International Society for Companion Animal Infectious Diseases. *Veterinary Medicine International* 2011;2011:1-9.
27. Weese JS, Blondeau J, Boothe D et al. International Society for Companion Animal Infectious Diseases (ISCAID) guidelines for the diagnosis and management of bacterial urinary tract infections in dogs and cats. *Veterinary Journal* 2019;247:8-25.
28. De Briyne N, Atkinson J, Pokludov L, Borriello SP, Price S. Factors influencing antibiotic prescribing habits and use of sensitivity testing amongst veterinarians in Europe. *Veterinary Record* 2013;173:475-481.
29. Mateus ALP, Brodbelt DC, Barber N, Stärk KDC. Qualitative study of factors associated with antimicrobial usage in seven small animal veterinary practices in the UK. *Prev Vet Med* 2014;117:68-78.
30. Kukanich K, Woodruff K, Bieberly Z, Papich MG, Kukanich B. Evaluation of urine concentrations of amoxicillin and clavulanate in cats. *J Vet Intern Med* 2020.
31. Clinical and Laboratory Standards Institute (CLSI). Performance standards for antimicrobial disk and dilution susceptibility tests for bacteria isolated from animals, 5th Edition Clinical and Laboratory Standards Institute (CLSI), USA, 2021.
32. Australian Commission on Safety and Quality in Healthcare. AURA 2019: Third Australian report on antimicrobial use and resistance in human health. 2019.
33. Yu Z, Gunn L, Wall P, Fanning S. Antimicrobial resistance and its association with tolerance to heavy metals in agriculture production. *Food Microbiology* 2017;64:23-32.
34. Boothe D, Smaha T, Carpenter DM, Shaheen B, Hatchcock T. Antimicrobial resistance and pharmacodynamics of canine and feline pathogenic *E. coli* in the United States. *Journal of the American Animal Hospital Association* 2012;48:379-389.
35. Cummings KJ, Aprea VA, Altier C. Antimicrobial resistance trends among canine *Escherichia coli* isolates obtained from clinical samples in the northeastern USA, 2004-2011. *The Canadian Veterinary Journal* 2015;56:393-398.
36. Marques C, Gama LT, Belas A et al. European multicenter study on antimicrobial resistance in bacteria isolated from companion animal urinary tract infections. *BMC Vet Res* 2016;12.

37. Vincze S, Stamm I, Kopp PA et al. Alarming proportions of methicillin-resistant *Staphylococcus aureus* (MRSA) in wound samples from companion animals, Germany 2010–2012. *PLoS One* 2014;9:e85656.
38. Ventrella G, Moodley A, Grandolfo E et al. Frequency, antimicrobial susceptibility and clonal distribution of methicillin-resistant *Staphylococcus pseudintermedius* in canine clinical samples submitted to a veterinary diagnostic laboratory in Italy: A 3-year retrospective investigation. *Veterinary Microbiology* 2017;211:103-106.
39. Sasaki T, Kikuchi K, Tanaka Y et al. Methicillin-resistant *staphylococcus pseudintermedius* in a veterinary teaching hospital. *Journal of Clinical Microbiology* 2007;45:1118-1125.
40. Noli C, Koeman JP, Willemse T. A retrospective evaluation of adverse reactions to trimethoprim-sulphonamide combinations in dogs and cats. *Vet Quarterly* 1995;17:123-128.
41. Williamson NL, Frank LA, Hnilica KA. Effects of short-term trimethoprim-sulfamethoxazole administration on thyroid function in dogs. *Journal of the American Veterinary Medical Association* 2002;221:802-806.
42. The University of Melbourne. Guide for antimicrobial use in dogs and cats (version 1). <https://vetantibiotics.science.unimelb.edu.au/about/resources/>. 2021. Retrieved:01/10/2023
43. Hardefeldt LY, Hur B, Richards S et al. Antimicrobial stewardship in companion animal practice: an implementation trial in 135 general practice veterinary clinics (accepted for publication). *JAC-Antimicrobial Resistance* 2022
44. Singleton DA, Rayner A, Brant B et al. A randomised controlled trial to reduce highest priority critically important antimicrobial prescription in companion animals. *Nature Communications* 2021;12.
45. Richards S, Bailey KE, Scarborough R et al. Cross-sectional evaluation of a large-scale antimicrobial stewardship trial in Australian companion animal practices. *Veterinary Record*;n/a:e3268.
46. Del Mar C, Looke DFM. Should we abandon "finishing the course" of antimicrobials? *Br Med J* 2017;358.
47. Spellberg B. The new antibiotic mantra-"shorter is better". *JAMA Internal Medicine* 2016;176:1254-1255.
48. Borges I, Carneiro R, Bergo R et al. Duration of antibiotic therapy in critically ill patients: a randomized controlled trial of a clinical and C-reactive protein-based protocol versus an evidence-based best practice strategy without biomarkers. *Critical Care* 2020;24.
49. Yilmaz G, Salyan S, Aksoy F, Köksal İ. Individualized antibiotic therapy in patients with ventilator-associated pneumonia. *Journal of Medical Microbiology* 2017;66:78-82.
50. Hillier S, Roberts Z, Dunstan F et al. Prior antibiotics and risk of antibiotic-resistant community-acquired urinary tract infection: a case-control study. *J Antimicrob Chemother* 2007;60:92-99.
51. Dawson-Hahn EE, Mickan S, Onakpoya I et al. Short-course versus long-course oral antibiotic treatment for infections treated in outpatient settings: a review of systematic reviews. *Family Practice* 2017;34:511-519.

Chapter 4: Pet owners and antibiotics: knowledge, opinions, expectations, and communication preferences

A version of this paper has been published in *Antibiotics* (2021);
doi: 10.3390/antibiotics10111326

Ri Scarborough^{1,2*}, Laura Hardefeldt^{1,2}, Glenn Browning^{1,2} and Kirsten Bailey^{1,2}

¹ Asia-Pacific Centre for Animal Health, Department of Veterinary Biosciences, Melbourne Veterinary School, Faculty of Veterinary and Agricultural Sciences, University of Melbourne, Parkville, VIC 3010, Australia

² National Centre for Antimicrobial Stewardship, Peter Doherty Institute, Parkville, VIC 3052, Australia

* Correspondence: ri.scarborough@unimelb.edu.au

Abstract

Despite the important role of antimicrobial use in companion animals in the global challenge of antimicrobial resistance (AMR), very few studies have quantified pet owner factors that can contribute to suboptimal veterinary antimicrobial use.

We conducted an online survey of pet owners, asking about their experiences with veterinarians, their opinions on antibiotic use and knowledge of antibiotics, and their communication preferences regarding judicious prescribing.

Just over half (54%) of the 558 pet owners had received antibiotics for their pet at their last non-routine veterinary consultation and most owners were happy (83%) with the antibiotic prescribing decision of their veterinarian. A quarter (25%) indicated that they had been surprised, disappointed or frustrated when a veterinarian had not given their pet antibiotics; 15% had explicitly requested them.

Owners placed a higher priority on their pet receiving the most effective treatment than on treatment being cheap or convenient. Most respondents recognized the limitations of antibiotic therapy and the risks associated with antibiotic use, but 50% believed the risks were confined to the treated animal; only a minority was aware of inter-species transfer of bacteria. Pet owners indicated that they would find judicious prescribing messages focused on the direct risks of antibiotics to their pet more compelling than those about public health.

Our findings suggest that veterinary communications about responsible antibiotic use should focus on pet owners' priorities and address or bypass their gaps in understanding about antibiotic resistance.

Introduction

The preservation of the effectiveness of existing antimicrobial drugs, for all species, in the face of escalating bacterial antimicrobial resistance (AMR) is a shared responsibility, demanding effort from all sectors involved in the use of antimicrobial drugs.

There is significant overlap between the antimicrobial drugs used in companion animals and those used in humans. In addition, the popularity of companion animals and the physical closeness many people have with their pets as valued members of their families¹ increases the risk of antimicrobial-resistant bacteria – and resistance determinants – transferring from humans

to pets, and *vice versa*.

In Australia, 61% households have a pet; 40% have at least one dog and 27% have at least one cat.¹ Legally, pets can only be given antimicrobial drugs on prescription from a registered veterinary practitioner, who also usually dispenses the drugs from their clinic. Compared with human medical practice, companion animal practice in Australia uses antibiotics relatively infrequently; antimicrobial exposure per life-year in dogs and cats is less half that of Australian people, and the proportion of dog and cat prescriptions representing the highest priority critically important antimicrobials (HPCIA) is low.² While companion animal practitioners in several other countries use higher proportions of HPCIA, particularly third-generation cephalosporins and fluoroquinolones,³⁻⁸ there is undoubtedly scope in all countries to improve antimicrobial use in companion animal practice.⁹

Suboptimal antimicrobial use by prescribers can be conceptualized in two broad categories: firstly, using an antimicrobial drug where none is needed, for example, antibiotics for a viral infection, or for a bacterial infection which can usually be eliminated without antimicrobials (e.g. cat fight abscess); and secondly, where antimicrobials are indicated but the prescriber chooses a suboptimal drug, dose, timing, duration or route of administration. Expectations of pet owners that their pet should receive medication – often specifically antimicrobial drugs – combined with a lack of understanding of the risks associated with antimicrobial drugs, have been identified as drivers of suboptimal antimicrobial prescribing in companion animals.¹⁰⁻¹⁵ The availability of the long-acting HPCIA injection cefovecin (Convenia) for dogs and cats presents particular challenges for veterinarians. As a third-generation cephalosporin, it carries a high risk of selecting for resistant bacteria – including those producing extended-spectrum beta lactamases (ESBLs) – and its Australian product information states that it should only be used ‘*where indicated by antibiotic sensitivity testing, according to principles of prudent use*’.¹⁶ However, there is robust evidence that it is almost always being administered without prior antibiotic sensitivity testing^{17,18} and, anecdotally, it is being requested by some pet owners because of the ease of its administration compared with (more appropriate) oral antimicrobials.

Simple antimicrobial stewardship (AMS) interventions to tackle drivers of inappropriate use could include education of pet owners about antimicrobial resistance – for example, through informative posters in clinic waiting rooms – and training for veterinarians in communication skills. It is critical that such education and communication skills training are tailored to the knowledge and attitudes of pet owners with respect to antimicrobials for their pets.¹⁹ We identified only two previous quantitative studies of such factors in pet owners internationally: a discrete choice survey of dog owners, primarily from North America,²⁰ which elicited the priorities of dog owners when choosing between two antimicrobials; and a survey of cat owners in the UK,²¹ exploring attitudes to and knowledge about antimicrobials. Four qualitative studies have thematically documented a range of pet owner views of antibiotics in the UK^{14,15,22} and USA,²³ but no studies of Australian pet owners have been published. No studies to date have examined the preferences of pet owners for how veterinarians communicate when declining or delaying antimicrobial therapy, or when steering owners towards a more appropriate, but less convenient, treatment – despite the importance of these conversations for antimicrobial stewardship in companion animal medicine. The influence of pet owner characteristics on opinions, knowledge and preferences with respect to antimicrobial use has undergone very little examination.

The primary aim of this cross-sectional survey study was to investigate the opinions, expectations and preferences of cat and dog owners with respect to veterinary consultations and antimicrobial drugs, and to evaluate their understanding of the risks associated with antimicrobial use. The secondary aim was to determine whether there were differences in

responses between demographic groups, including age, socio-economic advantage, and educational background. The goal was to provide a basis for veterinarians to increase the effectiveness of their conversations with pet owners and inform future AMS interventions in companion animal veterinary practice.

Results

Respondents

A total of 662 responses were received. One hundred and four participants provided responses to fewer than 70% of questions, including key questions about attitudes and knowledge. These responses were disregarded and the remaining 558 responses were analysed. The demographics of participants whose responses were excluded were similar to those of the participants whose responses were included (Appendix 2, Table S1), suggesting that there were non-systematic reasons for the failure of some participants to complete the survey.

Participants were overwhelmingly female (92%). Most were aged 31-50 (58%), lived in the south-eastern Australian state of Victoria (59%), where the research team was based, and lived in the inner suburbs of a capital city (45%). A high proportion (41%) had a postgraduate educational qualification and 43% were in the highest quintile of socio-economic advantage (Figure 1).

More than half the participants cited a field of work or tertiary study that might have exposed them to the concept of AMR. Of particular note were the 44% of all participants who cited a background in human health and/or animal health. There was also considerable overlap between participants who cited a health background and those who had a postgraduate qualification; 51% (125/246) of postgraduate-qualified participants had a health background.

Category (% missing data)		n	Proportion	Histogram
Gender (0.4%)	Female	513	92%	
	Male	35	6%	
	Non-binary	8	1%	
Age group (0%)	30 or younger	80	14%	
	31-40	159	28%	
	41-50	162	29%	
	51-60	104	19%	
	61 or older	53	9%	
Pets owned (0%)	Dog(s) only	286	51%	
	Cat(s) only	131	23%	
	Dog(s) and cat(s)	128	23%	
	Past pets only	13	2%	
Australian state of residence (5%)	Victoria	328	59%	
	New South Wales	108	19%	
	Queensland	62	11%	
	All other states/territories (total)	33	6%	
Residential area description (0.2%)	Capital city, inner urban	251	45%	
	Capital city, outer urban	153	27%	
	Regional city or large town	92	16%	
	Small town or not in a town	61	11%	
SEIFA quintile of residential area (5%)	1 - least advantaged	45	8%	
	2	47	8%	
	3	85	15%	
	4	95	17%	
	5 - most advantaged	259	46%	
Highest education (0%)	School	47	8%	
	Diploma or Certificate	117	21%	
	Bachelor degree	164	29%	
	Postgraduate qualification	230	41%	
Fields of university study or work (0%)	Animal production or agriculture	29	5%	
	Animal health	56	10%	
	Human health	205	36%	
	Scientific research	78	14%	
	Science education	87	16%	
	None of the above	243	44%	

Figure 1. Demographics of survey participants (excluding insufficiently complete surveys)

Pet owner expectations of the veterinary consultation, treatment preferences and trust

Responses to these questions indicated that most owners viewed their veterinarians as trusted experts and perceived there was significant value in a veterinary consultation, even when no medications were given. However, a significant number of pet owners indicated that they had expected - and sometimes explicitly requested - antibiotics from a veterinarian.

Reflecting on their most recent veterinary consultation for an illness, injury or skin infection or wound, most participants (54%) reported having had an expectation that their animal would receive some sort of medication, and 54% said their animal received antibiotics (Figure). The vast majority (83%) were happy or very happy with the decision to use antibiotics, or not.

When did you last take your pet to a veterinarian for an illness, injury or skin wound/infection?			
Less than 6 months ago	331	59%	
6-12 months	105	19%	
1-2 years	72	13%	
More than 2 years	50	9.0%	
Did you expect your animal to receive medication for this problem?			
Yes	303	54%	
No	101	18%	
Not sure	106	19%	
(blank)	48	8.6%	
Did your animal receive antibiotics?			
Yes	301	54%	
No	199	36%	
Not sure	10	1.8%	
(blank)	48	8.6%	
How did you feel about this decision? (n=500)			
1 - Very unhappy	9	1.8%	
2 - Unhappy	12	2.4%	
3 - Neutral	65	13%	
4 - Happy	115	23%	
5 - Very happy	299	60%	

Figure 2: Recency of visit to veterinarian, expectations of therapy and satisfaction with treatment decision

The subgroups with the highest positive evaluations were those for whom the consultation outcome aligned with their expectations; either receiving antibiotics when they had expected some medication (91% positive), or not receiving antibiotics when they had not expected medication (89% positive) (Figure 3).

However, it is noteworthy that even in these ‘aligned’ groups, there was a small minority who were still unhappy with the decision to give or withhold antibiotics. The subgroup with the highest proportion of negative evaluations was owners who had *not* expected medication, but received antibiotics (Figure). Among owners who had expected medication, *not* receiving antibiotics decreased the proportion of positive owner evaluations by 15% and increased the proportion of neutral owner evaluations by a similar amount, but had no apparent impact on negative evaluations (4% negative with antibiotics, 3% negative without). No significant differences were found between participant subgroups, including between those with a health background (HB) and those with no health background (NHB).

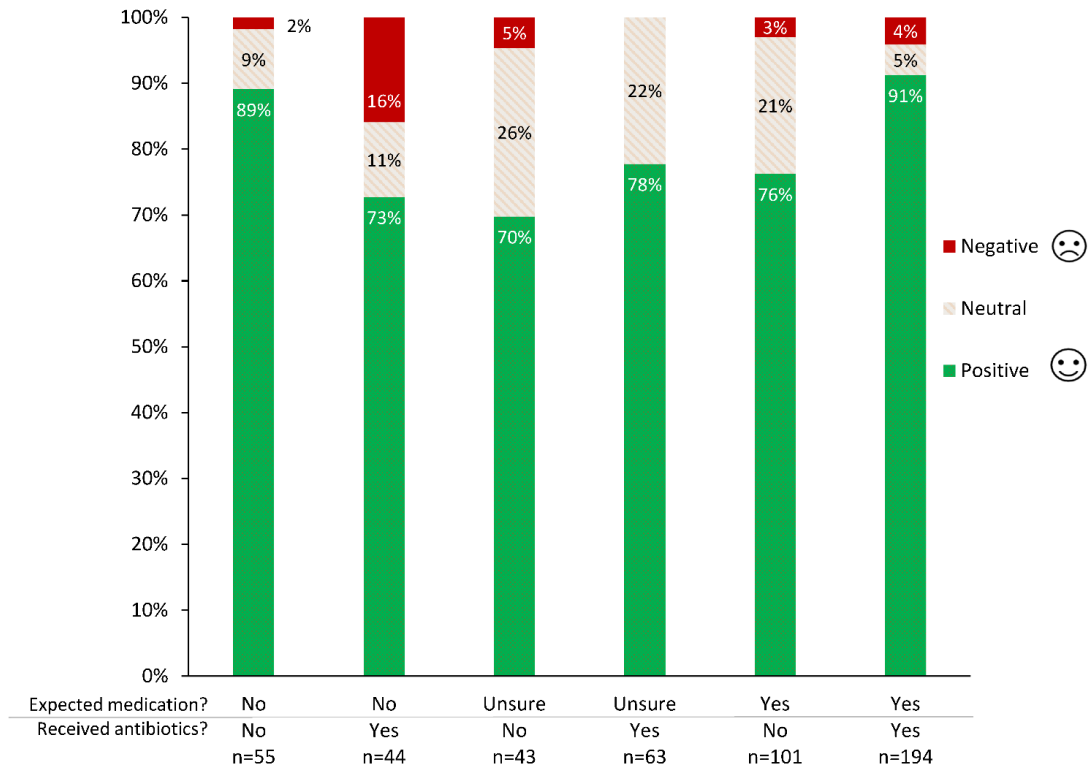


Figure 3: Owner feelings about treatment decision in their most recent veterinary consultation for animal illness or injury, by expectation of medication and receipt of antibiotics

Owners felt significantly more positive when their expectations about medication of their pet were aligned with the final decision about administering antibiotics [$p < 0.01$ for those expecting their pet to be medicated, $p < 0.001$ for those not expecting their pet to be medicated] (Figure).

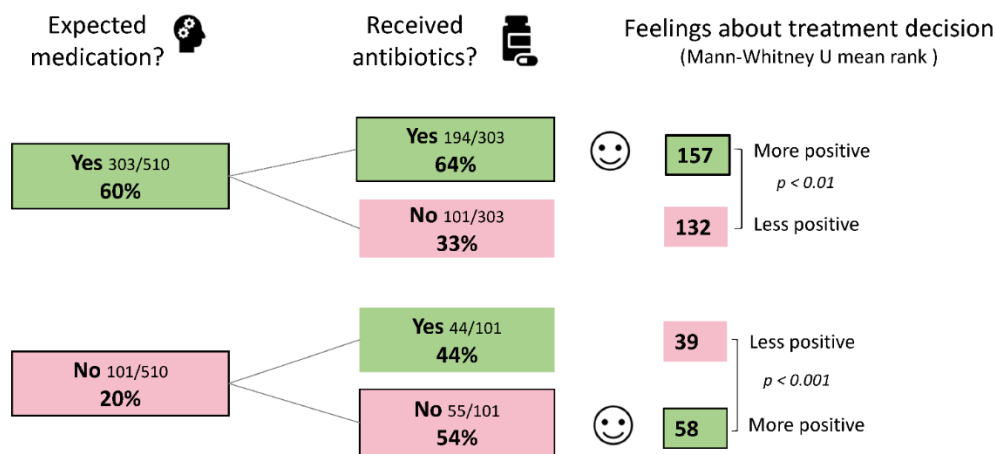


Figure 4: Owner feelings about treatment decision, based on their expectations about medication of their pet and whether they received antibiotics. 'Unsure' responses were removed from this figure, therefore totals are $< 100\%$.

Most owners (75%) said that they had never specifically wanted a veterinarian to give antibiotics to their pet (Figure). This proportion was similar for HB (78%) and NHB owners (72%). Within the 25% of respondents who said that they had been surprised, disappointed or frustrated when a

veterinarian had not given them antibiotics for their pet, 15% said they had specifically requested them, 2% said they had hinted but not asked specifically, and 8% said that they had not communicated their desire for prescription of antibiotics for their pet to the veterinarian. HB owners were almost twice as likely to have asked for antibiotics than NHB owners [OR 1.98, $p < 0.01$, 95% CI 1.2 to 3.2].

Have you ever wanted a veterinarian to give your cat or dog antibiotics, specifically?			
Never	418	75%	
Yes, and I have asked for them specifically	82	15%	
Yes, and I have hinted that I wanted them (never asked)	13	2.3%	
Yes, but I have never hinted or asked	45	8.1%	
Have you ever been surprised, disappointed or frustrated when a veterinarian did <i>not</i> give your cat or dog antibiotics?			
Never	514	92%	
Yes, a little	37	6.6%	
Yes, very	7	1.3%	

Figure 5: Owner desire, hints and requests for antibiotics for their pets



Figure 6: Pet owner expectations of the veterinary consultation, treatment preferences and trust. Pet owners were asked to what extent they agreed with each statement on the left. Proportions of responses to each statement corresponding to each of the five points on the Likert scale are shown. Data labels omitted where value is <4%.

	Disagree n (%)	Neutral n (%)	Agree n (%)
Veterinarians should make treatment as cheap as possible for owners			
Health background	55 (22)	73 (30)	118 (48)
No health background	53 (17)	72 (23)	186 (60)
I would probably choose an easier treatment option, over a more effective option that was more work for me			
Health background	216 (88)	15 (6.1)	15 (6.1)
No health background	238 (76)	26 (8.3)	48 (15)
If my sick pet doesn't get any medication, I feel that I haven't got good value from the veterinary consultation			
University degree	347 (88)	32 (8.1)	15 (3.8)
No university degree	134 (82)	17 (10)	13 (7.9)
When an animal is sick, sometimes all it needs is some nursing care and time			
University degree	50 (13)	75 (19)	269 (68)
No university degree	28 (17)	43 (26)	93 (57)
I would be annoyed if my animal was not cured the first time, and I had to go back to the veterinarian			
Less than 30 years old	35 (44)	17 (21)	28 (35)
61+ years old	27 (51)	16 (30)	10 (19)

Figure 7: Differences by respondent demographic category in pet owner expectations of a veterinary consultation, treatment preferences and trust. Bold text indicates a significantly higher subgroup result ($p < 0.05$).

Although owners mostly agreed that veterinarians should make treatment as cheap (55%) and convenient (55%) as possible for pet owners (Figure 6), higher proportions indicated that they would *not* prioritise effectiveness over cheapness (77%) nor over convenience (81%) (Figure 6). NHB owners were more likely to feel that veterinarians should make treatment cheap (60%) than HB owners (48%) [difference 12%, $p < 0.01$, 95%CI 3.7 to 20%] (Figure 7). Notably, the respondents' quintile of Socio-Economic Index For Area (SEIFA)²⁴, an Australian Government estimate of economic advantage based on residential postcode, did *not* make a significant difference to this response [$p = 0.20$]. HB owners were also significantly less likely (6.1%) than NHB owners (15%) to indicate that they would choose a more convenient treatment over a more effective treatment [difference 8%, $p < 0.001$, 95%CI 3.7 to 14%] (Figure 7).

More owners agreed (49%) than disagreed (29%) that they wanted to be given a few different treatment options. However, most pet owners (73%), including those who wanted multiple options, still wanted their veterinarian to recommend a single best option.

Very few pet owners indicated that they would feel upset if their sick pet did *not* receive any medication (5.2%) or that they hadn't got good value if they left the consultation without any medication (5.0%). Those *without* a university education were more likely (7.9%) than those with a university education (3.8%) to link consultation value with receiving medication [difference 4%, $p < 0.05$, 95%CI 1.4% to 8.1%] (Figure 7). Relatedly, most owners (65%) agreed that sometimes animals needed only nursing care and time to get better. Those *with* a university education were more likely to agree with this (68%) than those without (57%) [difference 12%, $p < 0.01$, 95%CI 2.8 to 20%] (Figure 7).

About one-quarter of owners (27%) indicated that they would be annoyed if their animal was not cured after the first veterinary consultation and needed to return to the clinic. Agreement with

this statement was significantly higher (35%) in owners aged under 30, than in those aged 61 or older (19%) [difference 16%, $p < 0.05$, 95%CI 0.42 to 32%] (Figure 7).

The level of trust that pet owners had in their veterinarians was extremely high; 96% agreed they trusted their veterinarian to do the right thing by their pet, including 71% who strongly agreed with this statement.

Pet owner opinions on antibiotic use; knowledge of microbiology and antibiotic resistance

Most respondents were broadly aware of the risks and limitations of antibiotics, and, accordingly, indicated a willingness to avoid them if possible, but there was limited awareness of risks beyond the treated animal, even in HB owners.

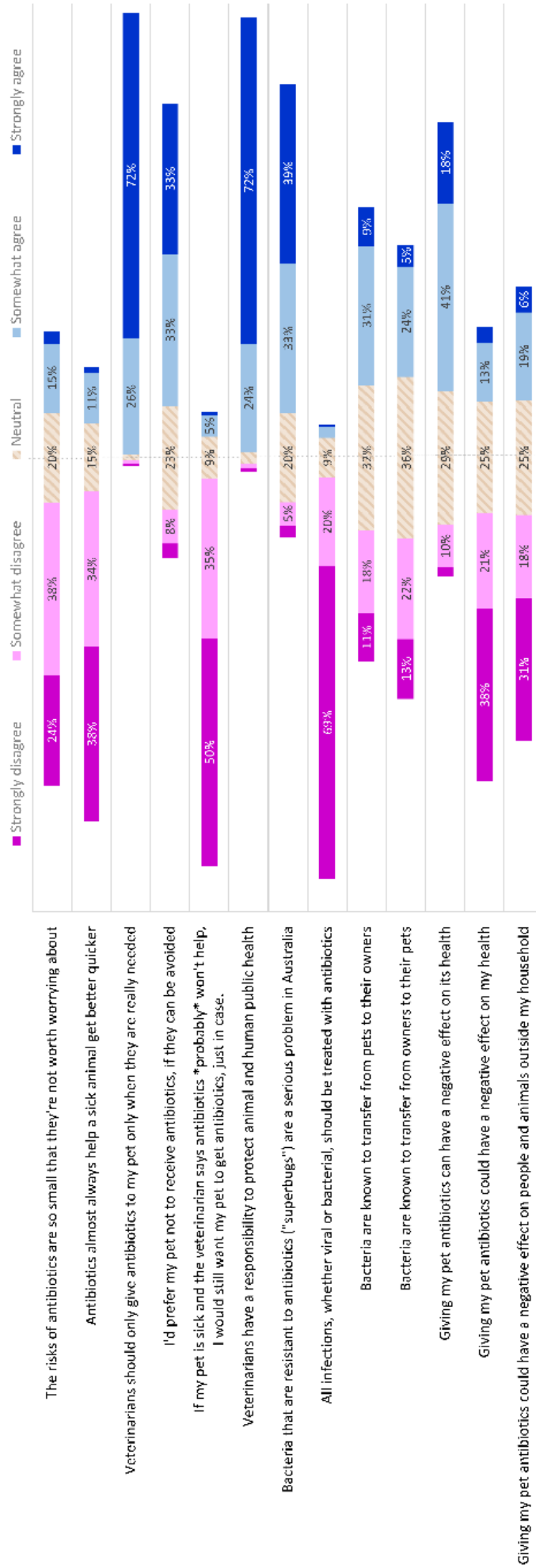


Figure 8: Pet owner opinions on antibiotic use; knowledge of microbiology and antibiotic resistance. Pet owners were asked to what extent they agreed with each statement on the left. Proportions of responses to each statement corresponding to each of the five points of the Likert scale are shown. Data labels omitted where value is <4%.

	Disagree n (%)	Neutral n (%)	Agree n (%)
The risks of antibiotics are so small that they're not worth worrying about			
University degree	259 (67)	73 (19)	57 (15)
No university degree	82 (52)	36 (23)	40 (25)
Antibiotics almost always help a sick animal get better quicker			
Health background	189 (78)	28 (12)	24 (10)
No health background	208 (68)	54 (18)	44 (14)
I'd prefer my pet not to receive antibiotics, if they can be avoided			
SEIFA tertile 1 (lowest)	14 (18)	14 (18)	49 (64)
SEIFA tertile 2 or 3	41 (9.3)	104 (23)	298 (67)
Health background	22 (9.1)	39 (16)	180 (75)
No health background	36 (12)	86 (28)	184 (60)
Bacteria that are resistant to antibiotics ("superbugs") are a serious problem in Australia			
University degree	30 (7.7)	54 (14)	305 (78)
No university degree	13 (8.2)	53 (34)	92 (58)
All infections, whether viral or bacterial, should be treated with antibiotics			
Health background	226 (94)	8 (3.3)	7 (2.9)
No health background	257 (84)	40 (13)	9 (2.9)
Bacteria are known to transfer from pets to their owners			
Animal health background	14 (25)	11 (20)	31 (55)
Human health background	57 (29)	54 (27)	89 (44)
Bacteria are known to transfer from owner to their pets			
Animal health background	19 (34)	14 (25)	23 (41)
Human health background	71 (36)	64 (32)	65 (33)
Giving my pet antibiotics can have a negative effect on its health			
Health background	24 (10)	50 (21)	167 (69)
No health background	38 (12)	111 (36)	157 (51)
Postgraduate qualification	16 (7.0)	52 (23)	159 (70)
No postgraduate qualification	46 (14)	109 (34)	165 (52)
Giving my pet antibiotics could have a negative effect on my health			
Health background	133 (55)	53 (22)	55 (23)
No health background	190 (62)	81 (26)	35 (11)
Giving my pet antibiotics could have a negative effect on people and animals outside my household			
Health background	104 (43)	58 (24)	79 (33)
No health background	168 (55)	80 (26)	58 (19)

Figure 9: Differences by respondent demographic category in pet owner opinions on antibiotic use; knowledge of microbiology and antibiotic resistance. Bold type indicates a significantly higher subgroup result ($p < 0.05$).

A minority of pet owners (18%) agreed with the statement that the risks of antibiotics were negligible (Figure 8). Although the majority (62%) believed that there were significant risks (by disagreeing with the statement), there was a substantial difference between those with (67% disagree) and those without a university education (52% disagree) [difference 15%, $p < 0.05$, 95%CI 5.7 to 24%]. Most (73%) also disagreed that antibiotics almost always make a sick animal better faster; a negative response was more common in HB owners (78%) than NHB owners (68%) [difference 10%, $p < 0.01$, 95%CI 2.9 to 18%] (Figure 9).

Pet owners felt very strongly that veterinarians should only give antibiotics to their pet when they were really needed (26% somewhat agree + 72% strongly agree = 97%). However, fewer agreed that they would prefer their pet *not* to receive antibiotics if they could be avoided (33% somewhat agree + 33% strongly agree = 67%) and 10% of all participants disagreed with this statement, with a higher proportion (18%) of those in the lowest socio-economic tertile disagreeing more than other tertiles combined [difference 8%, $p < 0.05$, 95%CI 1.5 to 16%]. The group that most wanted to avoid antibiotics for their pet if possible (75% agree) were HB owners, compared with 60% of

NHB owners [difference 15%, $p < 0.001$, 95%CI 6.6 to 23%] (Figure 9). Only 5% of pet owners indicated that they would want antibiotics for their pet when they probably wouldn't help, 'just in case'.

Pet owners were virtually unanimous (24% somewhat agree + 72% strongly agree = 96%) that veterinarians have a responsibility to protect both animal and human health.

Questions exploring pet owners' understanding of microbiology and antibiotic resistance (Figure 8) received a significantly greater proportion of neutral responses than the questions about their opinions, expectations and preferences (25% for knowledge questions; 14% for other survey questions) [difference 11%, $p < 0.001$, 95% CI 10 to 13%]. Most respondents (73%) agreed that antibiotic-resistant bacteria represented a serious problem in Australia, but agreement was much higher in those with a university degree (78%) than in those without a university education (59%) [difference 19%, $p < 0.001$, 95%CI 12 to 28%] (Figure 9).

The vast majority of respondents (89%) indicated an awareness of the therapeutic limitations of antibiotics, disagreeing with the statement that all bacterial and viral infections should be treated with antibiotics. Disagreement was significantly higher in HB owners (94%) than NHB owners (82%) [difference 9.8%, $p < 0.001$, 95%CI 4.4 to 15%].

The potential for transfer of bacteria between pets and their owners was not widely recognised, although a significantly higher proportion of respondents agreed that bacteria are known to move from pets to their owners (39%) than from owners to pets (29%) (difference 10%, $p < 0.001$, 95%CI 4.4 to 16%) (Figure 9). Of those who agreed with the first statement, only two-thirds agreed with the second statement (10% disagreed; 22% neutral).

HB owners were more likely than NHB owners to agree that bacteria are known to transfer from pets to their owners (46% compared to 34%) [difference 12%, $p < 0.01$, 95%CI 3.3 to 20%], and from owners to their pets (34% compared to 25%) [difference 8.8%, $p < 0.05$, 95%CI 3.2 to 18%]. Respondents with an *animal* health background were more likely to agree with each of these statements than those with a *human* health background (41% compared to 33%, and 55% compared to 44%, respectively), however these differences were not statistically significant (Figure 9). Post-hoc analysis showed that a sample size several times larger than this one would be required for this difference to reach significance.

Awareness of adverse effects of antibiotics on the individual animal was high (60%), but only 16% agreed that there was a potential risk to themselves when their pet had antibiotics. Again, a health background was associated with increased awareness of direct adverse effects on pet's health (69% compared to 51%) [difference 18%, $p < 0.001$, 95%CI 9.7 to 26%] as were postgraduate qualifications (70% compared to 52%) [difference 18%, $p < 0.001$, 95%CI 10 to 27%]. Those with a health background were also more aware than other respondents of the potential for antibiotics given to the pet to have negative effects on their own health (23% compared to 11%) [difference 11%, $p < 0.001$, 95%CI 5.1 to 18%].

Almost half (49%) of the respondents did not agree that antibiotics in their pet could pose a risk to animals and humans outside their household and only 25% agreed that this would pose a wider risk to animals and people outside their own household. HB owners were significantly more likely (33%) to recognise the broader risks of antibiotic use, compared with NHB owners (19%) [difference 14%, $p < 0.001$, 95%CI 6.5 to 21%] (Figure 9).

Communication preferences when not prescribing antibiotics, and delayed prescribing preferences

When a veterinarian declines to give antibiotics to an unwell pet or delays prescribing of antibiotics, owners indicated that reassurance was important, but different subgroups of owners expressed different preferences for how such reassurance was framed.

Participants were shown four sets of options about communication preferences and one set of options about delayed prescribing (Figure 10).

Communication preferences (select one from each group)				
1	Your pet doesn't need antibiotics today, but here are some things we can do to make him/her more comfortable.	375	67%	
	Here are some things we can do to make your pet more comfortable, but he/she doesn't need any antibiotics today.	183	33%	
2	Clinical trials have shown that using antibiotics does not help this to get better any faster.	235	42%	
	In my experience, giving antibiotics does not help this to get better any faster.	210	38%	
	Your pet's immune system can fight this off without antibiotics, if we just give it some time.	113	20%	
3	It's important that we use antibiotics only when they're needed, and your animal doesn't need them today.	265	47%	
	It's best for your animal not to have antibiotics unless they are really needed, and in this case he/she doesn't need them.	236	42%	
	Antibiotics can have negative effects on your pet, so it's good that he/she doesn't need them today.	57	10%	
4	Your pet is still eating and drinking, temperature is normal, gum colour is good and the chest is clear, so I am comfortable that he/she doesn't need antibiotics.	496	89%	
	I'm not too worried about your pet's condition at the moment, so I don't think he/she needs antibiotics.	62	11%	
Delayed prescribing preferences (select one)				
If it's not getting better in 3 days, please:				
	...come back in to the clinic and we'll re-check your animal, no charge, and decide on treatment then.	345	62%	
	...give me a call and I'll arrange some antibiotics for you to pick up.	97	17%	
	...come back in and pick up some antibiotics. I'll leave a note on your electronic file that any of our staff can give those to you, without another consultation.	78	14%	
	...come back in and pick up some antibiotics. Here is a prescription that you can bring back to this clinic and give to any member of our team. Then they can give you the antibiotics, without another consultation.	38	6.8%	

Figure 10: Communication preferences when not prescribing antibiotics, and delayed prescribing preferences

Most pet owners (67%) preferred to be told that their animal did not need antibiotics *before* being told about ways their pet can be made more comfortable; only 33% preferred to be told about ways their pet can be made more comfortable before being told their animal did not need antibiotics.

From a selection of three reasons why antibiotics were not needed, highlighting the role of the animal's immune system in controlling infection, the veterinarian's past experience and data from clinical trials, participants indicated that data on clinical trials were the preferred reason for not using antibiotics (42%). However, this varied with the respondent's level of education and background in human or animal health. Those whose highest level of education was completion of high school were twice as likely to prefer the veterinarian's experience (47%) over clinical trial data (23%). For HB owners and for those with any postgraduate qualification, this was reversed – 54% preferred to hear about clinical trial data and only 30% preferred to hear about the veterinarian's experience. Only 20% of all participants selected the argument that their animal's immune system would resolve the infection.

Fairly equal proportions of respondents preferred the explanations that veterinarians should only use antibiotics when they are needed (47%) and that avoiding antibiotics is best for the pet (42%) as reasons for not treating with antibiotics. The explanation that antibiotics can have adverse

effects was the least preferred of these three options (10%).

Given a choice between being reassured that their pet's clinical signs did not indicate a need for antibiotic therapy and the veterinarian's low level of concern about their pet's condition, most respondents (89%) preferred reassurance based on the animal's clinical signs. Participants with the lowest level of education (school only) were more likely than all other groups (23%) to select the veterinarian's low level of concern as a basis for not initiating antibiotic therapy, compared with just 11% of the participants with a postgraduate education [difference 13%, $p < 0.05$, 95%CI 2.0 to 23%].

With regard to delayed prescribing, the most preferred approach (62%) was to have the animal re-checked at the clinic if needed, without charge and without promising antibiotics. The least preferred option (6.8%) was receiving a paper prescription for antibiotics to present at the clinic if needed.

Reasons to give a course of antibiotic tablets, rather than a single, long-acting injection

Pet owners indicated that the risk of adverse effects and antibiotic resistance in their pet would be the reasons most likely to motivate them to select a course of antibiotic tablets (twice daily for 5 days) for their pet, over a single, long-acting antibiotic injection (Figure 11).

Reasons for course of antibiotic tablets over long-acting injection			
Adverse effects The tablets are much less likely to cause side effects in your pet	353	63%	
Antibiotic resistance in pet The tablets are much less likely to create antibiotic-resistant bacteria (superbugs) in your pet	255	46%	
Can't remove injection If the tablets don't work or cause nasty side effects, we can easily stop them and change to a different treatment. But if that happens with the injection, we can't take it out.	248	44%	
Effectiveness The tablets are 10% more likely to cure your pet	211	38%	
Prescribing guidelines The tablets are the best choice according to the Australian Veterinary Prescribing Guidelines	193	35%	
Lower cost The tablets are less than half the price of the injection	162	29%	
Public health The tablets are the most responsible choice for public health	31	5.6%	

Figure 11: Pet owner preferences for reasons to give a course of antibiotic tablets rather than a single, long-acting antibiotic injection. Respondents could select up to three statements that they found convincing, so the total is >100%.

	Selected n (%)
Lower cost	
Less than 30 years old	40 (50)
61+ years old	10 (19)
Can't remove injection	
No university degree	86 (52)
University degree	162 (41)
Prescribing guidelines	
Health background	102 (41)
No health background	91 (29)
Effectiveness	
Postgraduate qualification	93 (40)
Bachelor degree	65 (40)
Diploma or certificate	37 (33)
No post-school qualification	14 (30)

Figure 12: Differences by respondent demographic category in popularity of reasons to give a course of antibiotic tablets instead of a long-acting antibiotic injection. Bold type indicates a significantly higher subgroup result ($p < 0.05$).

The most popular response (selected by 63%) was a lower likelihood of adverse effects in their pet, followed by a decreased risk of antibiotic-resistant bacteria in their pet (46%). By far the least popular reason (6%) was that the tablets were the most responsible choice for public health. The lower cost of tablets was also a relatively unpopular reason (29%). Notably, there was no difference in the popularity of a lower cost between different quintiles of socio-economic advantage (based on residential postcode), but it was significantly more popular among those aged 30 or younger (50%) than in those aged 61 or older (19%) [difference 31%, $p < 0.01$, 95%CI 12 to 50%] (Figure 12).

The argument that an injected long-acting antibiotic could not be removed if it did not work or was to cause adverse effects was selected by 44% of all participants, but was more popular among owners who had no university education (52%) than among those who had a university qualification (41%) [difference 11%, $p < 0.05$, 95%CI 1.9 to 20%] (Figure 12).

Just over a third of all respondents (35%) favoured the argument that tablets were the option recommended by veterinary prescribing guidelines. In HB owners, this proportion was 41%, while for NHB owners it was 29% [difference 12%, $p < 0.01$, 95%CI 4.3 to 20%]. The argument that the course of tablets had increased effectiveness was more popular with participants with higher levels of education; 30% of those who had no post-secondary school qualifications chose this reason, increasing to 40% of those with a postgraduate qualifications, but this difference was not statistically significant (Figure 12).

Discussion

Our results indicate that pet owners often expect and sometimes hint at, or explicitly request, antibiotics for their sick pets, but appreciate that there are risks to their pet from antibiotic use. Pet owners expressed a great deal of trust in their veterinarians, and general satisfaction with the outcome of a consultation, even when no medication is given. Satisfaction with a consultation in which medication is not provided may be increased if the veterinarian provides reassurance and the option for re-examination.

Pet owner expectations of the veterinary consultation, treatment preferences and trust

Although a majority of pet owners felt that veterinarians should make treatment as cheap and convenient as possible for owners, a larger majority denied that when choosing between two treatment options, they would prioritise cheapness or convenience of treatment over effectiveness. This would suggest that owners care most about resolving their animal's problem. Veterinarians should therefore emphasise to owners that judicious treatment – whether using a non-antibiotic therapy, or using an antibiotic with a lower importance rating – is at least as effective as more convenient options they might request.

The relatively low priority owners placed on cost is seemingly at odds with the findings of a recent survey of dog owners from North America²⁰, which found that a low cost of treatment was more important (accounting for 47% of dog owner preferences) than ease (31% of owner preferences). However, the strong signal that convenience is less important to owners than effectiveness is also reflected in a cat owner survey in the United Kingdom (UK), in which 88% of owners indicated that getting the most *appropriate* antibiotic was more important than ease of administration.²¹ These findings are particularly encouraging for AMS interventions aimed at reducing use of high importance (but rarely the most appropriate) antibiotics, such as cefovecin and enrofloxacin.

Owners in this study indicated that the value they perceived in the veterinary consultation was not necessarily attached to the receipt of medication, however, more than half of surveyed pet owners (54%) had expected some sort of medication at their most recent presentation of an unwell animal. A similar proportion of parents (50%) expected antibiotics when they presented their children to a general practice doctor in a United States of America (US) study, but only 1% of parents had made an explicit request²⁵. Although the proportion of pet owners who *specifically* expected antibiotics at their most recent consultation cannot be determined from our survey, a quarter said they had, at some stage in the past, been surprised, disappointed or frustrated when a veterinarian had not provided antibiotics for their pet, and 15% had specifically asked for antibiotics. This indicates substantial public demand for antibiotics for pets, and is supported by qualitative studies of companion animal veterinarians in the UK^{14, 26, 27} and The Netherlands.¹¹ Several studies of doctors have found that implicit and explicit requests for antibiotics, and even the client simply questioning the treatment plan, increase the likelihood of prescription of antibiotics.²⁸⁻³⁰

Unsurprisingly, pet owners were happiest when their pre-consultation expectations of medications for their pet aligned with receiving antibiotics, or not. However, it is perhaps somewhat surprising that the highest proportion of unhappy respondents were those whose animals *had* received antibiotics when the owner had *not* expected any medication, rather than those who expected medication and were not provided antibiotics for their pet. One possible explanation is that many respondents who expected their pet to receive medication in fact received *non*-antibiotic medications, which satisfied the owners. Another possibility is that those

who had not expected medications for their pet felt that the antibiotics that they were given did not adequately address their animal's problem. Qualitative research with pet owners should be helpful in clarifying this.

Notably, respondents indicated a very high degree of trust in their veterinarians to do the right thing by their pet, a finding that is reflected in qualitative studies of pet owners in the UK.^{14, 22, 23} This degree of trust is helpful in facilitating conversations between veterinarians and pet owners about responsible antibiotic use.

Pet owner opinions on antibiotic use; knowledge of microbiology and antibiotic resistance

As expected, respondents with higher levels of education and those with health backgrounds had higher levels of knowledge about microbiology and antibiotic resistance and their opinions on antibiotic use aligned more closely with judicious prescribing principles.

Across all demographic groups, cat and dog owners appeared to understand that antibiotics are not indicated for viral infections, with a large majority disagreeing that all infections (viral and bacterial) should be treated with antibiotics, suggesting that this message has been successfully conveyed to the Australian public, including through initiatives such as 'Not All Bugs Need Drugs'.³¹ This is similar to the findings of a recent study of cat owners in the UK.²¹

Prescribing antibiotics 'just in case' was endorsed by only one in twenty of our participants, contrasting with interviews with pet owners in the US, where most participants said that they would like their pet to receive antibiotics even when there was no clear benefit.²³ It is uncertain whether these contrasts are a result of the methodological differences between the studies, true differences in the attitudes of the sample populations, or both.

However, One Health concepts were generally poorly understood. A minority of all pet owners appreciated that bacteria move from pets to their owners and a smaller minority knew that bacteria move from owners to pets. It is somewhat surprising that there was higher awareness of animal-to-human bacterial transfer than human-to-animal transfer, and even more surprising that this difference existed even among participants with animal and human health backgrounds. Similarly, only a small minority of pet owners recognised that giving antibiotics to their pet could have an adverse effect on them, on other animals in the household, and on animals and humans outside the household. This finding is supported by interviews with US pet owners,²³ none of whom were concerned that the same antimicrobials used in their pets are also used in humans; indeed some actually found it comforting. Therefore, AMS messages for the general public – whether in a veterinary or human medical setting - should not assume an understanding of One Health and the potential for bi-directional inter-species transmission of AMR.

Interestingly, 43% of cat owners in the UK agreed that using antibiotics in animals can reduce the effectiveness of antibiotics in humans, implying an understanding of inter-species transfer of resistant bacteria. However, interviews with pet owners in the UK suggested that most pet owners tend to attribute this effect to antibiotic use in food-producing animals (and human consumption of those products).¹⁴ Additionally, we know that many people conceptualise AMR as a property of the treated human or animal body, similar to the tolerance induced by opioid use, rather than a property of resident bacteria,^{15, 23} and that many lay people equate the presence of bacteria with infection.³² It follows that even pet owners who understand AMR as a property of bacteria, but who do not know that their pet is colonized by trillions of bacteria in the absence of infection, will struggle to understand the off-target and long-term effects of antibiotic

use. Interviews with veterinarians and pet owners have also highlighted significant gaps in pet owners' understanding of how AMR develops and spreads.^{14, 23}

Leveraging the public's concern about antibiotic resistance (as a broad concept) to drive change in their behaviour around use of antibiotics in pets would therefore first require pet owners to link their behaviour with antibiotic resistance at a broader level. However, the microbiological concepts that link pet owner behaviours and the 'big picture' outcomes of optimal antibiotic stewardship are, in fact, quite complex (Figure 13) and not commonly understood, even by our respondents with health backgrounds and high levels of education. As it is difficult to communicate these concepts concisely, public health arguments against unnecessary antibiotics are not well suited to waiting-room posters and 10-minute veterinary consultations. It is likely to be more effective to use messages about the potential for antibiotic-resistant infections in their pet, where the link is far more direct and is not hampered by common misunderstandings. However, individual owners who have very high health literacy, or owners in countries such as Sweden, where the population generally has high health literacy,³³ may respond to messages about the public health benefits of avoiding unnecessary antibiotic use.

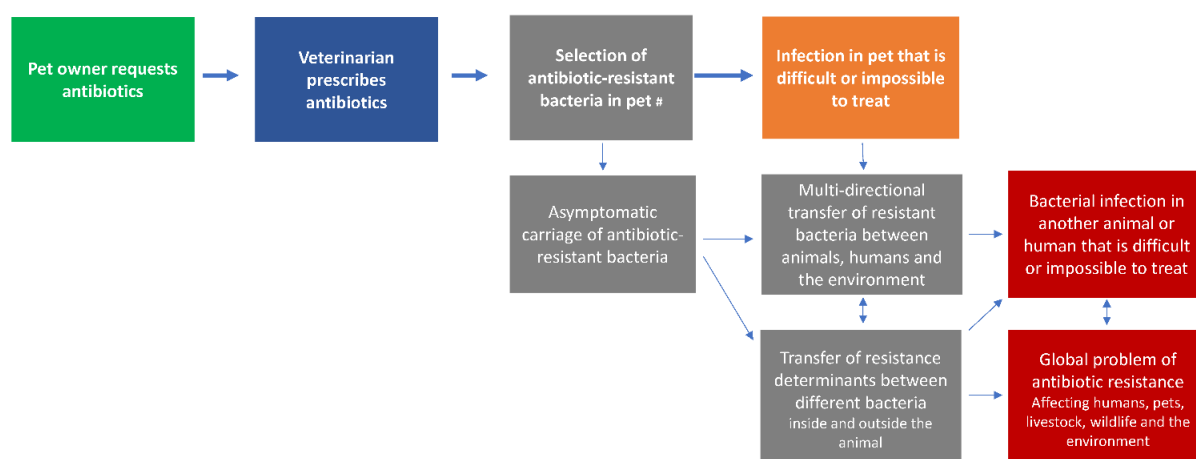


Figure 13: Owner behaviour (green) and public health outcomes (red) are linked by microbiological concepts (grey) that are poorly understood. The more direct potential adverse outcome for the pet (orange) is simpler to communicate, and remains logical even if the pet owner holds the #common misconception that antibiotic resistance is a property of the animal's body.

Communication preferences

To our knowledge, this is the first quantitative study eliciting the preferences of pet owners for the way veterinarians communicate with them about antibiotics. In the most closely analogous setting of a parent and child consulting a doctor, an in-depth study of 570 consultations³⁴ found that when antibiotics were not prescribed, parents were more satisfied when the doctor first explained what could be done to make the child feel better, before explaining that no antibiotics would be prescribed. We thus hypothesised that pet owners were likely to want to hear, *'Here are some things we can do to make your pet more comfortable,'* before being told their pet would not be prescribed antibiotics. In fact, the opposite was true, with two-thirds of owners preferring to first hear the message, *'Your pet doesn't need antibiotics today'*. However, as this was always the first of the questionnaire responses presented, order bias towards the first message on the list³⁵ may have contributed to the apparent preference for this message.

Different groups of respondents placed different importance on empirical data (*'Clinical trials have shown...'* and *'Your pet is still eating and drinking...'*) compared with the veterinarian's experience or personal concern (*'In my experience, giving antibiotics doesn't help...'* and *'I'm not too worried about...'*). Clients with lower levels of education clearly preferred messages about the veterinarian's experience or personal concern, whereas clients with higher levels of education preferred messages invoking empirical data. This suggests that when declining to give antibiotics, veterinarians – and indeed doctors – may have more success if they tailor their communication to the person's level of education, or, alternatively, they could incorporate both sets of messages when declining to provide antibiotics.

Delayed prescribing is an effective AMS strategy that is used commonly in both veterinary and medical consultations, when antibiotics are probably or definitely not indicated, and has been found to result in improved client satisfaction when no antibiotics are provided.²⁵ In a veterinary setting, the veterinarian would typically ask the owner to monitor the animal at home for particular changes, that would trigger either a re-examination, or beginning a course of antibiotics. In this study, pet owners overwhelmingly preferred to come back into the clinic for a recheck, at no charge, to simply collecting antibiotics without a re-check. This suggests that many owners are more interested in the reassurance provided by the re-check, than in receiving antibiotics specifically. However, it is unlikely to be financially sustainable for veterinary clinics to provide free re-checks on a routine basis. In future qualitative studies about pet owner attitudes to delayed prescribing, it would be worth exploring owner preferences for a re-check, if it attracted a consultation fee.

Apart from discussions with some pet owners when declining antibiotics, companion animal veterinarians also report challenging conversations with some pet owners – especially cat owners – who prefer a long-acting injectable antibiotic, cefovecin, over oral antibiotic courses. Although undeniably convenient, cefovecin is classified by the World Health Organization as a Highest Priority Critically Important Antimicrobial (HPCIA), and should not be used empirically. In addition, its 14-day duration of action is longer than the duration of treatment recommended in small animal prescribing guidelines for common indications for antimicrobial treatment.^{36, 37} Veterinarians therefore need effective ways to decline cefovecin and instead persuade pet owners to give alternative treatment (often tablets of a lower-importance antibiotic), while maintaining owner satisfaction. Our results show that owners prefer arguments centred on the health of their pet – the possibility of their pet experiencing direct adverse effects from the antibiotic, and the possibility of 'superbugs' developing in their pet, and effectiveness – over arguments around relative cost, public health or veterinary prescribing guidelines. Arguing for an antimicrobial because it is of lower importance to human and animal medicine is also unlikely to

be helpful; most dog owners in the North American study actually indicated a *preference* for their dog to receive high-importance antimicrobials over lower-importance antimicrobials.²⁰ Instead, framing a lower-importance antibiotic as a safer and more effective choice *for their pet* is likely to be more compelling.

Interestingly, the very strong positive responses (96%) to the statement '*Veterinarians have a responsibility to protect animal and human public health*' (see *Pet owner opinions*) are in stark contrast to the lack of popularity (5.6%) of the public health argument that a veterinarian could give for using the more responsible antibiotic tablets over the less responsible long-acting injection. It is possible that many pet owners simply do not see a link between their veterinarian's responsibility to public health (a broad concept that they might not associate with specific actions) and decisions about their pet, which are salient, personal and emotional. Alternatively, pet owners might feel that their veterinarian should execute their responsibility to public health when treating *other* animals, but not theirs. Again, qualitative research would be helpful to confirm and understand this apparent disagreement.

Strengths and limitations

Three quarters (74%) of respondents reported owning a dog and half (49%) had a cat; these proportions broadly mirror the relative popularity of these animals across Australian households.¹ Survey respondents were overwhelmingly female (92%), similar to a UK cat owner survey (91%),²¹ but approximately two-thirds of pet owners in a previous national survey were found to be women¹, and in our experience, an even higher proportion of the owners who present pets to veterinary clinics are women. The heavily urban distribution of responses is also largely reflective of the national population, 90% of whom reside in urban areas.³⁸ A more even spread of responses from different states of Australia would have been preferable. A very high proportion of respondents (70%) had tertiary qualifications, compared with a national average of 28% of those 15-64 years old, and a high proportion (43%) had postgraduate qualifications (the national average for those aged 15-64 years is 8.8%).³⁹ Additionally, a disproportionately high proportion of respondents (44%) were tertiary educated in and/or worked in health fields, compared with an estimated 10% of the national population.³⁹ Almost half of our respondents (46%) were in the socio-economic quintile of highest advantage, based on their postcode. This selection bias was anticipated, and is likely to have been in part a consequence of the social networks through which the survey was promoted. However, systematic subgroup analyses allowed us to distinguish the effects of this bias.

Respondents' recall of past veterinary interactions, and their prediction of their response to specific situations, may be imperfect, as people commonly idealise and oversimplify their mental representation of scenarios, ignoring factors that are salient in reality⁴⁰. For example, owners who indicate that convenience of treatment is not as important as effectiveness may be less likely to feel that way if their cat bites them while they are trying to administer tablets, and owners who indicate that cost is not important to them could well feel differently if their financial circumstances change. Nevertheless, knowing how owners would *like* to behave provides important insights into their idealised priorities and allows us to design effective communication strategies for AMS.

Materials and Methods

Dog and cat owners were recruited through a combination of social media posts (mainly in cat and dog interest groups on Facebook), posters with QR codes in veterinary clinic waiting rooms and through the authors' personal contacts. One personal contact shared the survey link in a

large social media group for Australian female doctors ('Medical Mums and Mums to Be') which would appear to explain the high proportion of respondents from a health background with high socio-economic advantage.

Recruitment materials invited pet owners who had taken their pet to a veterinarian for an illness or injury in the previous two years to participate. Veterinarians were not specifically excluded from participating, but because many practising veterinarians treat their own pets, the stipulation that the survey should be undertaken by those who had taken their pet to a veterinarian made it unlikely that veterinarians themselves would participate.

Participants undertook an anonymous online survey, using Qualtrics (Qualtrics, Provo, UT, USA), from February to April 2021. The survey is included in Appendix 2, Document S1. It asked a range of demographic questions, including gender, age, residential postcode and highest level of education. These data were deliberately sought in anticipation of the selection bias commonly seen in health studies, where older females with higher levels of education and higher socio-economic advantage are overrepresented.⁴¹⁻⁴³ Participants were also asked whether they had received university education or worked in scientific or health fields, as disproportionate responses were expected from these groups, and they could reasonably be expected to have a greater interest than the general population in antimicrobial use in animals.

The demographic questions were followed by questions about recent interactions with veterinary care, attitudes and knowledge about veterinary treatment and their preferences with respect to communication from veterinarians. Most of the questions were answered with a 5-point Likert scale, ranging from strongly agree to strongly disagree; questions on veterinary communication preferences asked the participant to select the most preferred message(s). There were two free-text questions that enabled the participant to provide context for their other responses. In some cases, owners provided their pet's diagnosis and outcome, or described the difficulty they experienced administering oral antimicrobials to their pet.

A question about owners' preferred reason for using a course of antibiotic tablets, rather than a single, long-acting antibiotic injection, was included in the survey (Q22) because veterinarians have reported having this conversation with pet owners who request a single injection of cefovecin, when multiple doses of an oral antibiotic would be a more appropriate choice.

In this survey of the general public, the term 'antibiotics' is used as it is in common parlance in the English-speaking world, to describe all antimicrobial medications directed at bacteria, including those not strictly classed as antibiotics. We have used it throughout the rest of this paper to mean all these medications. In the pet owner survey, the term 'vet' was used to mean veterinarian, as this is the most commonly used term used by the local population, however for international readability we have replaced it with the term 'veterinarian' throughout this manuscript.

Data were cleaned and analysed using Microsoft Excel and IBM SPSS. Differences in medians (the level of Likert scale agreement) between two groups were analysed using Mann-Whitney U tests, retaining all 5 levels of response. To examine proportions of responses across different participant groups, responses were collapsed into a 3-point Likert response, with 'strongly agree' and 'somewhat agree' combined, and 'somewhat disagree' and 'strongly disagree' also combined. Differences in proportions were analysed using a two-tailed z-test, with a significance level of 0.05. Pearson's chi-squared test was used to test the effect of participants' estimated socio-economic advantage on their responses.

The socio-economic advantage of participants was estimated using their residential postcode, and the corresponding Socio-Economic Index For Area (SEIFA) centile for that postcode, calculated by the Australian Bureau of Statistics using data from the most recent national Census.²⁴

Conclusions

This survey has provided the first data on pet owners' communication preferences when a veterinarian is declining to give antibiotics, using a delayed prescribing strategy, or encouraging a more appropriate (but less convenient) treatment. This study also provides new data on Australian pet owners' opinions, preferences and knowledge about antibiotics.

There is significant owner desire for antibiotics for unwell pets, but most owners also recognise antibiotic resistance as a serious problem, and are rarely disappointed when antibiotics are not given. Owners place a higher priority on their pet receiving the most effective treatment than on treatment being cheap or convenient. When declining to provide antibiotics, veterinarians would do well to detail the animal's reassuring clinical signs, mention supporting clinical trial data (where available) and speak of their experiences when the condition has resolved without antibiotics. If pressed, the prescriber could mention the importance of using antibiotics only when needed, and the direct risks of adverse effects and encouraging 'superbugs' in that particular animal. However, unless there is very high health literacy, or ample consultation time, it is probably wise to avoid invoking the broader risks of antibiotic use, as public understanding of normal microbiomes and transfer of bacteria between animals and humans is limited.

These findings can be applied by veterinarians – and indeed other antibiotic prescribers, including human medical practitioners, particularly those treating young children presented by their parents – to have more effective conversations about antibiotics with patients, parents and pet owners. Insights from this study should also be considered when devising public AMR education campaigns.

Author Contributions: Conceptualization, R.S., L.H., K.B., G.B.; methodology, R.S.; formal analysis, R.S.; investigation, R.S.; writing—original draft preparation, R.S.; writing—review and editing, L.H., K.B., G.B.; visualization, R.S.; supervision, G.B. All authors have read and agreed to the published version of the manuscript.

Funding: This research 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). K.B. is also funded by the NHMRC through the Centres of Research Excellence Scheme (National Centre for Antimicrobial Stewardship). L.H. is funded by the Australian Research Council through the Discovery Early Career Research Award program. R.S. was a recipient of an Australian Postgraduate Award scholarship.

Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Human Research Ethics Committee of The University of Melbourne (protocol code 2057499.1, date of approval 18 August 2020).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Acknowledgments: The authors gratefully acknowledge Mr Adam Williamson, who provided assistance with data management in Microsoft Excel, and Dr Anke Wietholter who assisted with analysis in SPSS.

Conflicts of Interest: The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the

manuscript, or in the decision to publish the results.

References

1. Animal Medicines Australia. Pets in Australia: A National Survey of Pets and People. <https://animalmedicinesaustralia.org.au/report/pets-in-australia-a-national-survey-of-pets-and-people/>. 2019. Retrieved:01/09/2021
2. Hardefeldt LY, Selinger J, Stevenson MA 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;225:34-39.
3. Buckland EL, O'Neill D, Summers J et al. Characterisation of antimicrobial usage in cats and dogs attending UK primary care companion animal veterinary practices. *Vet Rec* 2016;179:489-+.
4. Joosten P, Ceccarelli D, Odent E et al. Antimicrobial Usage and Resistance in Companion Animals: A Cross-Sectional Study in Three European Countries. *Antibiotics* 2020;9:87.
5. Schmitt K, Lehner C, Schuller S et al. Antimicrobial use for selected diseases in cats in Switzerland. *Bmc Vet Res* 2019;15.
6. Galarce N, Arriagada G, Sánchez F et al. Antimicrobial Use in Companion Animals: Assessing Veterinarians' Prescription Patterns through the First National Survey in Chile. *Animals* 2021;11:348.
7. Goggs R, Menard JM, Altier C et al. Patterns of antimicrobial drug use in veterinary primary care and specialty practice: A 6-year multi-institution study. *J Vet Intern Med* 2021.
8. Singleton DA, Sánchez-Vizcaíno F, Dawson S et al. Patterns of antimicrobial agent prescription in a sentinel population of canine and feline veterinary practices in the United Kingdom. *Veterinary Journal* 2017;224:18-24.
9. Hur BA, Hardefeldt LY, Verspoor KM, Baldwin T, Gilkerson JR. 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:e0230049.
10. Currie K, King C, Nuttall T, Smith M, Flowers P. Expert consensus regarding drivers of antimicrobial stewardship in companion animal veterinary practice: a Delphi study. *Vet Rec* 2018;182.
11. Hopman NEM, Hulscher MEJL, Graveland H et al. Factors influencing antimicrobial prescribing by Dutch companion animal veterinarians: A qualitative study. *Prev Vet Med* 2018;158:106-113.
12. King C, Smith M, Currie K et al. Exploring the behavioural drivers of veterinary surgeon antibiotic prescribing: a qualitative study of companion animal veterinary surgeons in the UK. *Bmc Vet Res* 2018;14.
13. De Briyne N, Atkinson J, Pokludov L, Borriello SP, Price S. Factors influencing antibiotic prescribing habits and use of sensitivity testing amongst veterinarians in Europe. *Vet Rec* 2013;173:475-+.
14. Smith M, King C, Davis M et al. Pet owner and vet interactions: exploring the drivers of AMR. *Antimicrob Resist Infect Control* 2018;7:46.
15. Dickson A, Smith M, Smith F et al. Understanding the relationship between pet owners and their companion animals as a key context for antimicrobial resistance-related behaviours: an interpretative phenomenological analysis. *Health Psychology and Behavioural Medicine* 2019;7:45-61.
16. Zoetis Australia Pty Ltd. Convenia (cefovecin sodium), product information. <https://websvr.infopest.com.au/LabelRouter?LabelType=L&Mode=1&ProductCode=60461>
17. Hardefeldt L, Hur B, Verspoor K et al. Use of cefovecin in dogs and cats attending first-opinion veterinary practices in Australia. *Vet Rec* 2020;vetrec-2020-2105.
18. Burke S, Black V, Sánchez-Vizcaíno F 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;19:687-692.

19. Thompson AC, Chandler CIR, Mateus ALP et al. What drives antimicrobial prescribing for companion animals? A mixed-methods study of UK veterinary clinics. *Prev Vet Med* 2020;105:117.
20. Stein MR, Evason MD, Stull JW, McClure JT, Weese JS. Knowledge, attitudes and influencers of North American dog-owners surrounding antimicrobials and antimicrobial stewardship. *Journal of Small Animal Practice* 2021.
21. Stallwood J, Shirlow A, Hibbert A. A UK-based survey of cat owners' perceptions and experiences of antibiotic usage. *Journal of Feline Medicine and Surgery* 2020;22:69-76.
22. Rhys-Davies L, Ogden J. Vets' and Pet Owners' Views About Antibiotics for Companion Animals and the Use of Phages as an Alternative. *Frontiers in Veterinary Science* 2020;7.
23. Redding LE, Cole SD. Pet owners' knowledge of and attitudes toward the judicious use of antimicrobials for companion animals. *Journal of the American Veterinary Medical Association* 2019;254:626-635.
24. Australian Bureau of Statistics. Census of Population and Housing: Socio-Economic Indexes for Areas (SEIFA), Australia, 2016.
<https://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/2033.0.55.0012016?OpenDocument>. 2018. Retrieved:10/06/2021
25. Mangione-Smith R, McGlynn EA, Elliott MN et al. Parent Expectations for Antibiotics, Physician-Parent Communication, and Satisfaction. *Archives of Pediatrics & Adolescent Medicine* 2001;155:800.
26. Mateus A, Brodbelt DC, Barber N, Stärk KDC. Antimicrobial usage in dogs and cats in first opinion veterinary practices in the UK. *Journal of Small Animal Practice* 2011;52:515-521.
27. Mateus ALP, Brodbelt DC, Barber N, Stärk KDC. Qualitative study of factors associated with antimicrobial usage in seven small animal veterinary practices in the UK. *Prev Vet Med* 2014;117:68-78.
28. Mangione-Smith R, Elliott MN, Stivers T, McDonald LL, Heritage J. Ruling Out the Need for Antibiotics. *Archives of Pediatrics & Adolescent Medicine* 2006;160.
29. Mangione-Smith R, McGlynn EA, Elliott MN, Krogstad P, Brook RH. The Relationship Between Perceived Parental Expectations and Pediatrician Antimicrobial Prescribing Behavior. *Pediatrics* 1999;103:711-718.
30. Ong S, Nakase J, Moran GJ et al. Antibiotic Use for Emergency Department Patients With Upper Respiratory Infections: Prescribing Practices, Patient Expectations, and Patient Satisfaction. *Annals of Emergency Medicine* 2007;50:213-220.
31. Agriculture Victoria. Not All Bugs Need Drugs. <https://agriculture.vic.gov.au/livestock-and-animals/livestock-health-and-welfare/antibiotic-resistant-infections/information-for-vets>
32. Galli I, Fasanelli R. Public understanding of science and common sense: Social representations of the human microbiome among the expert and non-expert public. *Health Psychology Open* 2020;7:205510292091323.
33. Vallin M, Polyzoi M, Marrone G et al. Knowledge and Attitudes towards Antibiotic Use and Resistance - A Latent Class Analysis of a Swedish Population-Based Sample. *PLoS One* 2016;11:e0152160.
34. Stivers T. Non-antibiotic treatment recommendations: delivery formats and implications for parent resistance. *Social Science & Medicine* 2005;60:949-964.
35. Feenberg D, Ganguli I, Gaulé P, Gruber J. It's Good to Be First: Order Bias in Reading and Citing NBER Working Papers. *Review of Economics and Statistics* 2017;99:32-39.
36. University of Melbourne. Australian Veterinary Prescribing Guidelines, Dogs and Cats. <https://vetantibiotics.fvas.unimelb.edu.au/about/resources/>. 2019. Retrieved:01/09/2021
37. Jessen LR, Damborg PP, Spohr A et al. Antibiotic Use Guidelines for Companion Animal Practice (2nd ed.).
www.ddd.dk/sektioner/familiedyr/antibiotikavejledning/Documents/Assembled_FINAL.pdf. 2019

38. Australian Bureau of Statistics. Historical population data, 2016.
<https://www.abs.gov.au/statistics/people/population/historical-population/latest-release#data-download>. 2019. Retrieved:10/06/2021
39. Australian Bureau of Statistics. Qualifications and work 2018-19.
<https://www.abs.gov.au/statistics/people/education/qualifications-and-work/2018-19#data-download>. 2020
40. Poon C, Koehler D, Buehler R. On the psychology of self-prediction: Consideration of situational barriers to intended actions. *Judgment and Decision Making* 2014;9:207-225.
41. Strandhagen E, Berg C, Lissner L et al. Selection bias in a population survey with registry linkage: potential effect on socioeconomic gradient in cardiovascular risk. *European Journal of Epidemiology* 2010;25:163-172.
42. Sjøgaard AJ, Selmer R, Bjertness E, Thelle D. The Oslo Health Study: The impact of self-selection in a large, population-based survey. *International Journal for Equity in Health* 2004;3.
43. Regber S, Novak M, Eiben G et al. Assessment of selection bias in a health survey of children and families – the IDEFICS Sweden-study. *BMC Public Health* 2013;13:418.

Chapter 5: ‘Brave Enough’: A Qualitative Study of Veterinary Decisions to Withhold or Delay Antimicrobial Treatment in Pets

Published manuscript

Ri O. Scarborough^{1,2,*}, Anna E. Sri^{1,2}, Glenn F. Browning^{1,2}, Laura Y. Hardefeldt^{1,2} and Kirsten E. Bailey^{1,2}

¹ Asia-Pacific Centre for Animal Health, Melbourne Veterinary School, University of Melbourne, Parkville, VIC 3010, Australia; laura.hardefeldt@unimelb.edu.au (L.H.); a.sri@unimelb.edu.au (A.S.); glenfb@unimelb.edu.au (G.B.); baileyk@unimelb.edu.au (K.B.)

² National Centre for Antimicrobial Stewardship, Peter Doherty Institute, Parkville, VIC 3052, Australia

* Correspondence: ri.scarborough@unimelb.edu.au

Abstract

Veterinarians sometimes prescribe antimicrobials even when they know or suspect that they are unnecessary. The drivers of this behaviour must be understood to design effective antimicrobial stewardship interventions.

Semi-structured interviews were conducted with 22 veterinarians who treated companion animals in Australia. The Theory of Planned Behaviour was used to organise interview themes, focusing on a decision to withhold antimicrobial therapy in the absence of a clear indication.

Many background factors influenced antimicrobial-withholding decisions, including the veterinarian’s communication skills, general attitudes towards antimicrobial resistance (AMR), habits and energy levels. Client awareness of AMR and the veterinarian–client relationship were also important. Beliefs about the consequences of withholding antimicrobials (behavioural beliefs) were dominated by fears of the animal’s condition deteriorating and of failing to meet client expectations. These fears, weighed against the seemingly distant consequences of AMR, were major barriers to withholding antimicrobials. Normative beliefs were primarily focused on the expected approval (or disapproval) of the client and of other veterinarians. Control beliefs about the difficulty of withholding antimicrobials centred around client factors, most importantly, their capacity to adequately monitor their animal, to pay for further investigations, or to undertake non-antimicrobial management, such as wound care, at home.

The use of antimicrobials by companion animal veterinarians in the absence of a clear indication is often powerfully driven by behavioural beliefs, chiefly, fears of clinical deterioration and of failing to meet client expectations.

Introduction

Antimicrobial resistance (AMR) is a major threat to environmental, animal and human health. In bacteria, AMR occurs as a result of the survival and proliferation of resistant bacterial subpopulations, and the transfer of AMR genes between bacteria.¹ This process is accelerated under the selection pressure of antimicrobial agents.² AMR bacteria can lead to serious adverse outcomes for the treated individual,³ in-contact animals (including humans),⁴ and wider animal populations.^{5, 6} To reduce morbidity and mortality attributable to AMR and to preserve the effectiveness of existing antimicrobials for as long as possible, prescribers should use antimicrobials only when they are needed and when they are likely to improve the health outcome of the patient. However, there is a significant body of evidence showing that prescribers in all sectors are still using antimicrobials in clinical syndromes where they are unlikely to be helpful, selecting empirical antimicrobials that have a broader spectrum of activity and prescribing antimicrobials for longer durations than is recommended in treatment guidelines.⁷⁻¹⁰

Although such prescribing can be driven by a limited understanding of microbiology and pharmacology, studies suggest that emotional reasons, socio-cultural factors and practical constraints often play a greater role in antimicrobial prescribing decisions than a lack of prescriber knowledge.¹¹⁻¹³ In other words, prescribers sometimes do things they are aware are not best practice. Despite the importance of qualitative research in understanding the drivers of suboptimal antimicrobial use,¹⁴ there are only four qualitative studies and one mixed-methods study of antimicrobial prescribing decisions by companion animal veterinarians in the English-language scientific literature,¹⁵⁻¹⁹ all conducted in the United Kingdom and the Netherlands. Australian veterinarians could have somewhat different approaches to antimicrobial use than their British and Dutch counterparts, due to differences in veterinary training, antimicrobial susceptibility of common pathogens, the availability and regulatory status of particular drugs, and the socio-economic, geographical and cultural context, including a much lower rate of pet health insurance compared with the UK.^{20, 21} A previous qualitative study that was focused on barriers to adoption of antimicrobial stewardship programs in Australian veterinary practices²² revealed a small number of non-clinical reasons Australian veterinarians used antimicrobials. This provided a foundation for this in-depth interview study on how veterinarians make prescribing decisions.

The framework of Ajzen's Theory of Planned Behaviour (TPB)²³ was used to structure the thematic analysis because it was felt to most accurately reflect the relationship between the contributory factors expressed by participants. The TPB has been previously applied in studies of prescribing behaviour.²⁴⁻²⁹ The TPB postulates that three groups of beliefs contribute to a person's intention to perform a behaviour, and that the strength of this intention is correlated with the likelihood of performing it. These groups of beliefs are: (1) behavioural beliefs, i.e., beliefs about the consequences of a behaviour and moral and ethical considerations of these consequences; (2) normative beliefs, i.e., perceived social pressure; and (3) control beliefs, i.e., the perceived barriers to and enablers of a behaviour, which lead to the perceived ease of executing it.²³ (Figure 1) It is important to note that a person's beliefs need not be formed through rational or even conscious thought³⁰ and that they are influenced by background factors, such as gender and knowledge.

The primary objective of this phenomenological, qualitative study was to explore the drivers of potentially unnecessary use of antimicrobials in Australian companion animal practice, by examining the decision to withhold or delay antimicrobial use. A secondary objective was to explore veterinarians' suggestions about how they could be better supported to withhold or delay use of antimicrobials, where clinically appropriate.

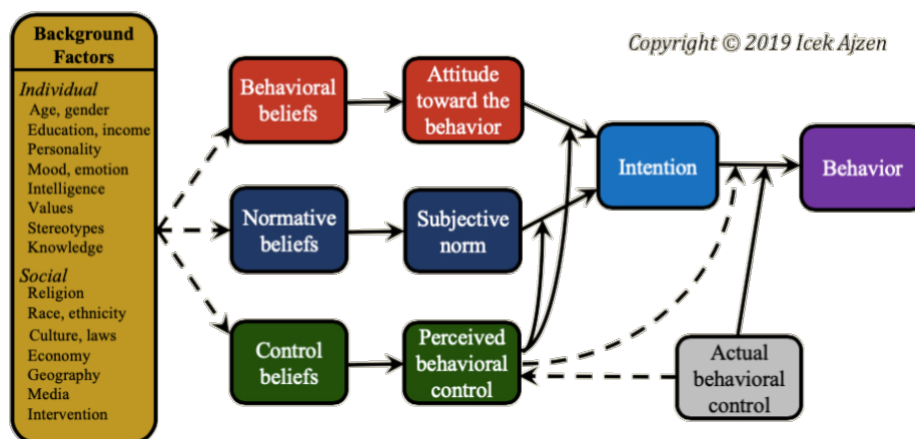


Figure 1. Icek Ajzen's Theory of Planned Behaviour (TPB) with background factors was used to organise the thematic analysis. Reproduction of this figure is permitted in journal articles, as stated on the University of Massachusetts website from which it is sourced: <https://people.umass.edu/aizen/tpb.background.html> (accessed on 12 July 2022).

Materials and Methods

In-depth, semi-structured one-on-one interviews were conducted with veterinarians registered in Australia who treat small companion animals. Most participants were recruited through two closed social media groups for Australian veterinarians, with purposive sampling of additional veterinarians approached through the authors' personal networks, to ensure inclusion of veterinarians across a broad demographic range and with diverse levels of interest in antimicrobial stewardship (AMS). None of the participants worked in the same practice as any of the other participants. Interview participants were offered an AUD 50 supermarket voucher as a token of appreciation for their time.

Pre-Interview Survey

Participants completed a short online survey in Qualtrics (www.qualtrics.com, accessed on 20 March 2020) to gather demographic and professional role information and understand the veterinarian's level of interest in antimicrobial resistance and stewardship. The pre-interview survey also asked participants to estimate the relative contributions of five different sectors (human hospitals, human primary practice, companion animals, livestock and other) to antimicrobial resistance in Australia. This question was used to gauge the participants' views of their own sector's contribution to AMR. Informed consent was obtained from all subjects involved in the study via the survey.

Interviews

In-depth, semi-structured one-on-one interviews were conducted by R.S., a veterinarian, in June and July 2020, using a video teleconferencing platform (www.zoom.us, accessed on 5 June 2020).

Positionality statement: The interviewer identifies as a female, formerly practising, Australian-born locally educated veterinarian, who had worked in both mixed practice and companion animal practices and was now studying for a PhD in Veterinary Medicine. This positionality was explained to the 18/22 participants who had not met the interviewer before; the others knew the interviewer from veterinary undergraduate studies.

The early part of each interview included the discussion of two clinical case studies (vignettes) for which national antimicrobial use guidelines exist: (a) a 2-year-old German Shepherd dog presenting with signs of lower urinary tract infection; and (b) an 8-year-old domestic short hair cat presenting with a cat fight abscess. The interview guide is provided in Appendix 3, Document S2. Participants were asked to explain the investigations and treatment they wished to undertake and why, and how they would respond to various additional pieces of information (e.g., what if the cat's owner says she cannot give tablets?) or alterations to the case story presented (e.g., what if the dog had already presented twice in the last three months with the same clinical signs?). The remainder of the interview was highly adaptive and guided by the participant's earlier responses. Interview participants were offered an AUD 50 supermarket voucher as a token of appreciation for their time.

Participants were interviewed (once each) until three consecutive interviews had not generated important new themes. Interviews were recorded using the video teleconferencing software, transcribed using online transcription software (otter.ai, accessed on 5 June 2020), and manually corrected by one author (R.S.). All identifying data, such as names of veterinary practices, colleagues and towns were redacted. R.S. used an inductive coding approach initially, to develop a draft codebook. Two authors (R.S., A.S.) independently coded a single interview according to the draft codebook, using NVivo12 (QSR International, 2020). Discrepancies in coding were discussed and the codebook refined. A second interview was then coded by both researchers in tandem to finalise the interview themes. Coding of all remaining interviews was completed by R.S. Themes related to a decision to withhold or prescribe antimicrobials were subsequently reorganised within the Theory of Planned Behaviour (Figure 1), focusing on the behaviour of withholding (or delaying) antimicrobial treatment. The final codebook is in Appendix 3, Document S3.

Results and Discussion

Pre-Interview Survey (Participant Characteristics)

The 22 interviewed veterinarians represented a broad range of relevant demographics. Participant characteristics are shown in Table 1.

Their median estimate of the companion animal sector (including horses) contribution to the overall problem of AMR in Australia was 15% [range 0–25%]. (Appendix 3, Table S1).

Table 1. Participant characteristics (n = 22).

Characteristic	Category	n	%
Gender	Female	16	73%
	Male	6	27%
Age	20–29	6	27%
	30–39	10	45%
	40–49	3	14%
	50–59	1	5%
	60–69	2	9%
Postgraduate veterinary qualifications	Yes	5	23%
	No	17	77%
Role	Principal Veterinarian	9	41%
	Associate/Senior Associate	10	45%
	Locum or other	2	9%
Practice location	Metropolitan	10	45%
	Regional	9	41%
	Rural	3	14%
Practice type	Primary/emergency care only	19	86%
	Specialist/referral	1	5%
	Combination of above	2	9%
Animals serviced	Small animals only	19	86%
	Mixed practice	3	14%
Size of practice (veterinary full-time equivalent staff)	2 to 3 veterinary FTEs	6	27%
	4 to 5 veterinary FTEs	11	50%
	more than 5 veterinary FTEs	5	23%
State where practice is located	Victoria	10	45%
	New South Wales	6	27%
	Queensland	2	9%
	South Australia	2	9%
	Tasmania	1	5%
	Western Australia	1	5%
Self-reported interest in AMR and AMS	Low	3	14%
	Moderate	9	41%
	High	10	45%

Interviews

The median interview duration was 90 min (IQR 73-98). Four of the 22 participants were previously known to the interviewer.

Where a theme was raised by more than one participant, non-specific semi-quantitative words such as ‘some’ or ‘multiple’ are used. Enumeration is reserved for responses to the case studies, because these were discussed consistently with every participant. However, no inferences should be drawn from a qualitative study about the prevalence of a phenomenon beyond the sample group.

An overview of interview findings is presented in Figure 2.

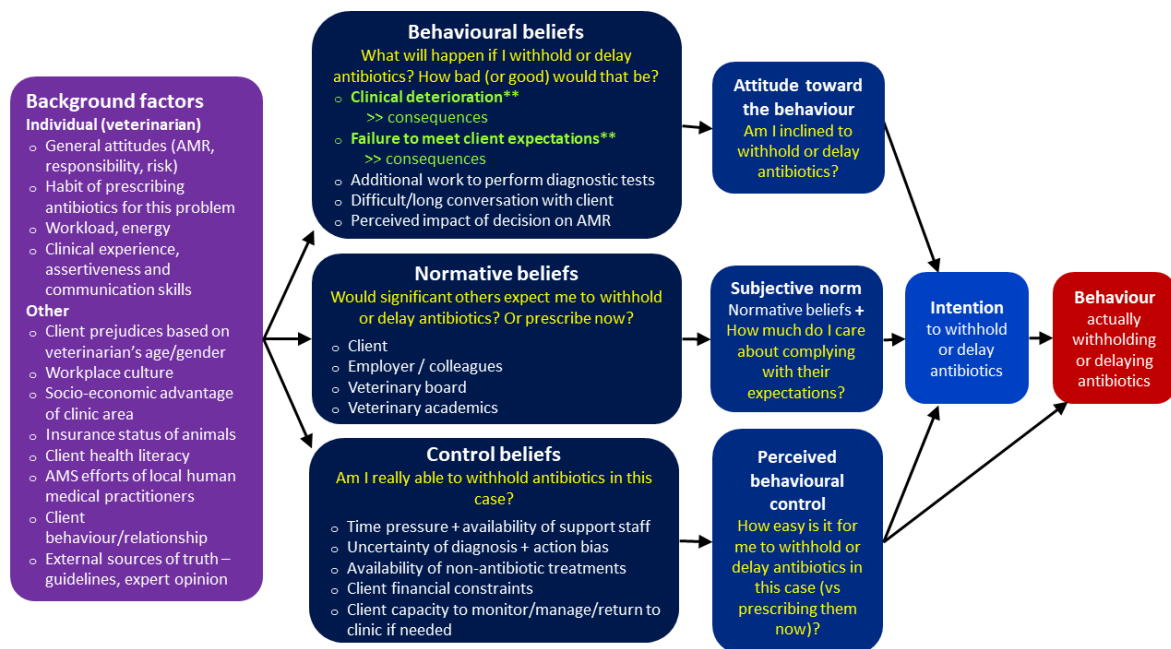


Figure 2. Summary of factors influencing veterinarians' decisions to withhold or delay antimicrobial treatment in the absence of a clear need, using an adaptation of the Theory of Planned Behaviour shown in Figure 1. ** Behavioural beliefs about clinical deterioration and failure to meet owner expectations were key themes and are further explored in Figure 5

Background Factors

Participants identified several important background factors (Figure 3) that influenced a decision to withhold or delay antimicrobial treatment in the absence of a clear clinical indication.

Background Factors	Quote Ref.	Quote— <i>interviewee code, age and gender, practice location, level of self-reported interest in AMR and AMS</i>
Individual		
General attitudes towards antimicrobial use and AMR	a1	I'm terrified by antibiotic resistance. I don't think there is any more pressing concern for human health in our lifetimes ... and I am deeply disappointed in the prescribing behaviour that you see from most human and veterinary practitioners ... the attitudes towards antibiotics are that they're a benign thing... hand out some antibiotics, no harm done ... What are we doing to our patients and ourselves with courses of antibiotics? ... [There's] immense power in the microbiome and immense power with antimicrobials.— <i>Vet P, 35F, metropolitan, high interest</i>
	a2	I do think about [AMR] daily , when I reach for antibiotics... I'm mostly worried about [AMR] for other pets and the fact that I'm not going to be able to treat things easily anymore.— <i>Vet N, 29F, rural, moderate interest</i>
	a3	I would rather lose a client than inadvertently contribute to antimicrobial resistance – well, I'm sure I do contribute to antimicrobial resistance – but I would rather not give an antibiotic for the sake of [retaining a client]...— <i>Vet B, 31M, metropolitan, high interest</i>
	a4	I think that we [veterinarians] are too willy nilly about handing out antibiotics like lollies .— <i>Vet J, 32F, metropolitan, high interest</i>
	a5	So when you're seeing a multi drug-resistant [Staphylococcus aureus] or Pseudomonas-y thing? I don't think it's from the veterinary world , but I think [veterinarians are] just easy targets .— <i>Vet G, 26F, rural, moderate interest</i>
	a6	I think most of the [AMR] problems that we see in humans is doctors' faults , and hospitals' fault and nothing to do with us ...they just use them there willy nilly and they use just hectic stuff .— <i>Vet G, 26F, rural, moderate interest</i>
	a7	[AMR] does scare me a little bit , but I don't feel like I see it enough that I think it's a huge problem in the veterinary industry just yet.... we probably don't do enough cultures because of cost restraints to know how much resistance there is.— <i>Vet M, 28F, regional, low interest</i>

	a8	Vets are not necessarily making these decisions to prescribe because they think it's the best treatment. I think it's sometimes that they're scared, or they can't be bothered, or it's just easier to just go along with what they think the client wants ... People are much more concerned about their day-to-day problems that are immediately in front of them. And antibiotic resistance, probably a little bit like climate change, just seems like this thing that's far off in the future, that ... isn't a problem that we really have to worry about, when we've got angry clients and sick pets right in front of our face, that need us right here and right now.—<i>Vet R, 28F, regional, high interest</i>
	a9	I'm sure a lot of things I use antibiotics on would get better without them ...The challenge is knowing which ones do and [which] don't ... There's some that if I didn't treat would obviously get worse and picking out which ones those are going to be, is really tricky. So potentially, you could reserve antibiotics for things that got really sick, but trying to manage owner expectation, if you're using that kind of philosophy would be ... a lot more challenging than if you're just, 'I've got the animal here. Now let's try and do the right thing by this animal. And forget about the rest of the population whilst I'm fixing this.' ... [If a prescriber] misses someone who really did need those antibiotics, then <i>they're</i> the one who didn't give those antibiotics. So, there's a lot of stress on them, as a consequence of that, as opposed to the resistance thing. It's a much bigger, further away problem.—<i>Vet T, 40M, metropolitan, moderate interest</i>
	a10	I want the animal to get better, I want to fix them. And if there's a 75% chance they'll get better without antibiotics and a 90% chance they'll get better with it, I'd still probably go for the 90% chance.—<i>Vet N, 29F, rural, moderate interest</i>
Habit of prescribing antimicrobials for this problem	a11	I think another thing is probably ... habituation ... that's what we've always given, that's how things are always done ... I have been guilty of just repeating, for the sake of convenience... A lot of vets just get in the habit of, 'Oh, [the dog has] got blood in its stool, we're starting antibiotics immediately.'—<i>Vet B, 31M, metropolitan, high interest</i>
Workload, energy, time	a12	Absolutely, the more overworked you are, the less willpower ... if you're running low on willpower, then you just ... go with what the client wants, if you're absolutely exhausted and you don't have backup.—<i>Vet L, 32M, metropolitan, high interest</i>
	a13	I just don't have the time to read s***. And I can't get access to any articles. Because you need like 'uni-ness' [a connection with a university] subscribing to journals and such.—<i>Vet G, 26F, rural, moderate interest</i>

Clinical experience, assertiveness and communication skills	a14	I've definitely gotten better over my career in terms of not [prescribing antibiotics]... like the cat flu cats that come in, they're just a bit snotty, and you know that they're going to get better , just saying to them that you don't need anything. I think as a young vet, I was very like, they really expect me to do something ...— <i>Vet V, 36F, metropolitan, moderate interest</i>
	a15	I think especially as a new grad, whoever comes in and they want antibiotics , I don't think as a new grad , I probably stood up to [those clients] enough.— <i>Vet M, 28F, regional, low interest</i>
	a16	Over the many years I've worked, I've become much more confident in the way that I talk to people. So, I am much better now being able to explain to people why their cat doesn't need treatment.— <i>Vet V, 36F, metropolitan, moderate interest</i>
	a17	And what I find helps is being more confident and assertive I think, in how we communicate it to clients.— <i>Vet A, 45F, metropolitan, high interest</i>
Other		
Client prejudices based on veterinarian's age/gender	a18	... when you've started to develop grey hairs , what it says is you've been doing this for a long time. So, you tend to get believed more — <i>Vet S, 66M regional, low interest</i>
	a19	Usually all they'll hear is 'Oh, the vet doesn't want to give it antibiotics,' ... and they yell at you. Especially as a young woman ... you already have to work a bit harder for them to trust you... they usually think you're the nurse.— <i>Vet G, 26F, rural, moderate interest</i>
Workplace culture	a20	One of our younger vets ... approached us about would it be possible for us to try to use less antibiotics , particularly in [surgical prophylaxis]? ...we were rapt and it's an example we use for all of our new vets, to say, ' We want you to come to us with ideas ... and any concerns and stuff, because sometimes you're onto something, and we will change .'— <i>Vet U, 39F, regional, low interest</i>
	a21	I think [the attitude of colleagues] makes a big difference... Now I mostly talk to the younger generation who are all completely on board with not using [antibiotics] unrealistically and we all back each other up a lot more.— <i>Vet N, 29F, rural, moderate interest</i>
Socio-economic advantage of clinic area	a22	I'm very fortunate ... I am working in a really high socioeconomic area that is full of people who consider their cat to be their baby , basically... they will just do anything .— <i>Vet V, 36F, metropolitan, moderate interest</i>
Insurance status of animals	a23	... [In] most of the practices I was working at [in England], over 50% of the animals were insured... I'd walk in and go, 'Well, it would be really good to do a blood test. But, you know, I could just put him on antibiotics and get him back in three days and see whether he's improving.' And in England, it used to blow my mind, they'd say, 'Well he's insured , you want to do a blood test, go ahead and do a blood test , or a culture or whatever diagnostic test you wanted.'— <i>Vet X, 54M, regional, high interest</i>

Client health literacy	a24	There's clients where you have to keep things really simple because ... too many scenarios really overwhelms them... And there's others ...they're obviously quite well-versed medically ... or they have a medical background themselves...those ones I definitely do start that conversation about ... 'This is the gold standard, we should do it this way. And there's these risks,' and blah, blah, blah. And some of them are very receptive . So, I do have clients that will be OK with [withholding antibiotics and monitoring the animal]. But I think that the general public is just not there yet .— <i>Vet V, 36F, metropolitan, moderate interest</i>
	a25	[I've never been asked for antibiotics] My clientele ... they're well educated ...I think there'd be a difference in other clinics in [nearby town] where there's less of an understanding of the importance of antibiotics and less of an education about antibiotic use. I think there's still a group of people out there [who request antibiotics] and it might not be to do with socioeconomics either, just education I suppose in general.— <i>Vet Q, 43F, regional, high interest</i>
Antimicrobial stewardship efforts of local human general practitioners	a26	The local doctors [in our town] are very much against antibiotics for antibiotics' sake...[they] are very big on not prescribing unless there is legitimate reason . So, I think there is an underlying level of understanding [among our clients] ... you should only use antibiotics when you really need them .— <i>Vet Q, 43F, regional, high interest</i>
Client behaviour, veterinarian–client relationship	a27	I think, in the past, possibly I've jumped straight to antibiotics because, you know, the client's really frustrated ...— <i>Vet M, 28F, regional, low interest</i>
	a28	[I would consider] How rough a time the client has had at home like if the dog has diarrhoea and they have just been up all night and it's all over the house and they're at their wit's end . And then I will start them on antibiotics.— <i>Vet F, 30F, metropolitan, moderate interest</i>
	a29	Or you just know they're going to be difficult , and you kind of feel that I've got to do something, if there was a pill, maybe " F***offcillin , excuse the language, but it's ... just a capsule full of air and you could just give it to not be in trouble with [the veterinary board]— <i>Vet B, 31M, metropolitan, high interest</i>
	a30	... if it was a client that I knew relatively well ... I might talk to a particularly good client and say, 'Hey... can we try like this [treating without antibiotics]?'— <i>Vet J, 32F, metropolitan, high interest</i>
	a31	[I'm more inclined to try managing without antibiotics] if the owners are not that demanding , and I think they'd be understanding if it didn't clear it up, first time.— <i>Vet N, 29F, rural, moderate interest</i>
External sources of 'truth'	a32	I think there needs to be ... clearer guidelines , especially for someone like me, who doesn't have a lot of experience and looks ... for some sort of evidence to back me so that I know that I'm doing the right thing .— <i>Vet J, 32F, metropolitan, high interest</i>

	a33	So, to convince people, I would often [say] that this [recommendation of no antibiotics] is coming from much higher up , by people [veterinary specialists] who've done much more work in this field and know much more about it... Using more expert opinion, I think is a very powerful thing in practice, because I'm not just saying, this is my judgment or I've just come up with this, there is evidence to suggest this is the case.— <i>Vet X, 54M, regional, high interest</i>
--	-----	--

Figure 3. Background factors influencing the decision to withhold or delay antimicrobial treatment where there was no clear indication, and illustrative quotes. Bold text has been used to highlight key ideas. Grey italics have been used for participant code, age and gender, location of practice and level of interest in AMR and AMS. ***represents redacted obscenity.

Several participants expressed a high degree of concern about antimicrobial resistance, as could be expected of a mostly self-selected cohort. They expressed fear of the consequences of AMR (a1) and a sense that the veterinary profession broadly (a2, a4) and that they personally (a2, a3, a4) bear some responsibility for perpetuating AMR. These attitudes were also reflected in a previous survey of Australian veterinarians, doctors and dentists.³¹ Some participants in our study also reflected on the contribution of antimicrobial use in humans to the broader problem and felt that veterinarians were unfairly blamed for AMR problems in people (a5, a6).

AMR can seem like a distant threat, even though every use of an antimicrobial selects for resistant bacteria, which can persist in the animal for months to years³² and present a risk to veterinary staff, clients and future patients³³. Multiple veterinarians described the trade-off they made between the invisible risk of AMR and their more immediate concerns of sick pets and angry clients (a8, a9). This tension was also described by UK companion animal veterinarians.^{15, 17} Tellingly, one participant who worried that AMR would lead to animal infections she would no longer be able to treat (a2) also indicated that, in a case where it was uncertain whether antimicrobials would be helpful, she was willing to accept the risk of selecting for AMR—and other risks associated with antimicrobial use—for even a minor increase in the probability of clinical resolution, because it was more important to her to ‘fix’ an animal as quickly as possible (a10). This pressure to resolve a problem in a single visit was also described by other participants (b14, c1, n1, n18) as a barrier to withholding antimicrobial treatment. It was also evident in studies of veterinarians in the UK¹⁵ and the Netherlands,¹⁹ and is supported locally by a survey study of Australian pet owners, one-quarter of whom indicated that they would be annoyed if their animal was not fixed the first time and they had to return to the clinic³⁴. However, a search of the medical literature failed to find a similar expectation in human medicine. Further research is warranted to explore the reasons behind this attitude among pet owners, whether it occurs in human patients and whether it can be mitigated by improved communication by prescribers.

Interestingly, only one of the participants (a1) mentioned the direct adverse effects that systemic antimicrobials commonly have on patients, such as nausea, diarrhoea and lingering disruption of the animal’s microbiome, as additional reasons to avoid unnecessary antimicrobial use. One veterinarian even stated that there was no direct, immediate harm from antimicrobials (c6). Reminding veterinarians—and pet owners—of these additional risks may increase their motivation to avoid antimicrobial therapy.

One participant with a low interest in AMR and AMS demonstrated circular reasoning that might explain complacency about AMR among some veterinarians. Because she was not seeing many AMR organisms in her practice—organisms that can only be identified by bacterial culture and susceptibility testing—she felt that AMR was not yet a serious problem in animals. Yet she also

acknowledged that she and her colleagues requested very few culture and susceptibility tests (a7). This suggests that some veterinarians will only recognise the risk of AMR when they observe antimicrobial treatment failure.

Some veterinarians mentioned common clinical scenarios that were previously thought to require antimicrobials, and for which there is now well-publicised evidence that antimicrobials are not indicated, including acute diarrhoea in dogs,³⁵ dental surgeries in systemically well patients and routine desexing surgeries.^{36, 37} Some noted that they themselves—or other veterinarians they knew—persisted in giving antimicrobials in such cases, and that habit (a11) was a contributor to that choice. UK veterinarians also acknowledged the role of habit in their antimicrobial prescribing.¹⁶

High workloads and a related lack of energy (a12) were also recognised as contributing to decisions to prescribe when there was no clear indication, especially in combination with a client who appeared to expect antimicrobials. Increasing veterinarian workloads, partially due to increasing rates of pet ownership during the COVID-19 pandemic, and attrition from the veterinary clinical workforce^{38, 39} may therefore increase inappropriate antimicrobial prescribing. The effect of fatigue was echoed in a Danish study of medical general practitioners, who were 25% more likely to prescribe antimicrobials in their fourth than in their first hour of consulting.⁴⁰ Being time-poor and lacking access to paywalled scientific journals also inhibited veterinarians from staying up to date with current antimicrobial use recommendations (a13). Considering this, researchers hoping to influence veterinary antimicrobial prescribing are likely to have more impact with open-access publishing, and by providing easy-to-digest study summaries for clinicians.

Many of the more experienced veterinarians reflected on the change in their propensity to prescribe antimicrobials between the beginning of their career and the current time, due to the development of confidence and communication skills. Clinical experience and additional training could give veterinarians assurance that certain common illnesses will resolve without antimicrobial treatment (a14). The development of assertiveness and strong communication skills—to explain to an expectant client why antimicrobials are not required—also enabled a decision to withhold or delay prescription of antimicrobial treatment for an animal (a14, a15, a16, a17). These findings echo those of a UK study, which also suggested that communication training for veterinarians could enable AMS¹⁷. However, regardless of confidence and communication skills, the prejudices some clients held about younger (a18, a19) and female (a19) veterinarians made it more difficult to convince them that antimicrobials were not needed.

One veterinarian and practice owner noted that a workplace culture that is receptive to change had been a powerful enabler of avoiding unnecessary antimicrobials. In this practice, actively seeking and fairly evaluating the input of all staff had led to the elimination of routine antimicrobial use for desexing and other clean surgeries (a20), in line with current veterinary antimicrobial use guidelines.⁴¹ Mateus *et al.* in the UK also noted that regular meetings where veterinary staff discuss clinical cases and protocols was an enabler of AMS.¹⁵ Similarly, a supportive workplace culture—where veterinarians had confidence their colleagues would support their decisions (a12)—was noted to enable withholding of antimicrobial treatment.

Several important background factors relating to a practice's clientele were also identified. High socio-economic advantage (a22), pet insurance uptake (a23) and high health literacy (a24, a25) were all enablers of decisions to withhold or delay antimicrobial treatment. These were felt to increase the client's willingness and capacity to pursue (often expensive) diagnostic tests rather than (cheaper) antimicrobial treatment trials, or to undertake conservative management and

monitoring of the animal at home and return to the clinic if needed. One veterinarian in a regional town also acknowledged the positive influence of the local medical general practitioners, who over the years had educated their patients about the importance of avoiding unnecessary antimicrobial treatment. The understanding this had established in the local community had made it easier for the veterinarians to withhold or delay antimicrobial treatment for the same people's pets (a26). That people are applying the information they receive from their own doctors to their pets' health care suggests that the reverse might also be true, and supports collaborative medical–veterinary efforts to provide consistent messages to the public about responsible antimicrobial use, such as the 'Antibiotic Guardian' campaign that started in the UK.⁴²

The relationship between the veterinarian and the client was another key background factor in a decision to withhold antimicrobial treatment. When dealing with a 'difficult' client, it was tempting to avoid confrontation and dispatch them by prescribing a medication that the client perceived to be curative (a29), such as antimicrobials. In contrast, a 'good' client could work with the veterinarian to implement a non-antimicrobial management plan (a30), had realistic expectations of outcomes and was unlikely to become angry if the animal's condition did not immediately improve (a31). Similarly, when the client expressed frustration or exhaustion (a27, a28) from managing the unwell animal at home (e.g., severe diarrhoea, coughing), the veterinarian felt more compelled to take tangible action, and that action was often to give antimicrobials.

Where withholding antimicrobials was supported by evidence-based antimicrobial prescribing guidelines (a32) and/or expert opinion, particularly that of registered veterinary specialists (a33), veterinarians felt more comfortable withholding antimicrobials. Quoting an external source of 'truth' could deflect client pressure to prescribe and could be particularly helpful for less experienced veterinarians (a32). This phenomenon of deferring to external sources was also described in a study of Dutch veterinarians.¹⁹ Guidelines that recommend withholding antimicrobials for a particular condition would also protect the veterinarian if the client were later to lodge a complaint with the veterinary registration board. However, awareness of guidelines was patchy. In Australia, independently-developed veterinary prescribing guidelines had existed for companion animals for a few years prior to the interviews,^{41, 43} but few participants had seen them, despite the presumed bias in this study towards veterinarians interested in AMS. This suggests that more effort is required to distribute and publicise the availability of guidelines for antimicrobial use within the Australian veterinary profession.

Behavioural Beliefs

Behavioural beliefs, i.e., beliefs about the consequences of a behaviour and the implications thereof (Figure 4), featured strongly in a veterinarian's decision to withhold antimicrobials when there was no clear indication. These beliefs were dominated by fear of the animal deteriorating clinically, and the related fear of failing to meet owner expectations.

Behavioural beliefs	Quote ref.	Quote— <i>interviewee code, age and gender, practice location, level of self-reported interest in AMR and AMS</i>
Clinical deterioration + consequences	b1	The main things that you think of when someone leaves and you haven't given them antibiotics, you're like, is it gonna get worse ? Is the client going to ring up tomorrow and abuse me for not giving them the antibiotics?— <i>Vet M, 28F, regional, low interest</i>

	b2	[Once the abscess is draining, the client's] job is to firmly wipe the scab off the abscess at least once or twice a day ... and bring it back in three or four days ... [treatment success] just depends on the competency of the people . Mechanical cleaning is the way, antibiotics are ... no help. I don't see any difference between treating with antibiotics and not, other than the waste of antibiotics .— <i>Vet H, 68M, regional, high interest</i>
	b3	My understanding of the organisms in those types of abscesses is once they're exposed to oxygen, they will die. And so they don't necessarily need antibiotics. [But] I have a really hard time when I can see and smell and 'taste' pus , not to give antibiotics. When I know there's an infection there, I struggle with that... I would give antibiotics.— <i>Vet U, 39F, regional, low interest</i>
	b4	[Sometimes if you don't give antibiotics] you get the cat back after the drainage period and the abscess recurs . Then the owner's really grumpy because then there's another anaesthetic and all of that. So, I'm trying to cover my bum a little bit.— <i>Vet S, 66M regional, low interest</i>
	b5	I don't know that giving [amoxicillin-clavulanate] is the best thing to do, but I've had cat bite abscesses go badly in the past when I haven't given antibiotics , and I would be worried about that happening again.— <i>Vet B, 31M, metropolitan, high interest</i>
	b6	Coughing dogs, I give a lot of them doxycycline and I guess it's kind of covering my bases . A lot of them probably I could just give them meloxicam (anti-inflammatory) or [cortico]steroids—or nothing—and they may get better. But I guess I also do worry if it is a bacterial infection and it gets worse and the dog does get sick, then I'd feel quite bad .— <i>Vet N, 29F, rural, moderate interest</i>
	b7	[Inexperienced veterinarians] are afraid of failure, lacking in confidence in their own judgment, afraid of not being thought of well ... and if they don't do it [prescribe antibiotics], and something goes wrong , [they're afraid that] they're going to be in trouble .— <i>Vet H, 68M, regional, high interest</i>
	b8	I think where we in this clinic are inclined to give antibiotics is if we have a particularly sick animal where we can't see what's wrong and where we are denied the opportunity to work it up .— <i>Vet A, 45F, metropolitan, high interest</i>
	b9	There's the old adage that everyone hears at vet school, ' Nothing should die without a course of antibiotics or a course of [cortico]steroids.' And it's such a throwaway line. But it makes you feel negligent if things ... go very badly and you haven't done what is perceived to be something as simple as giving a course of antibiotics .— <i>Vet Y, 39F, metropolitan, moderate interest</i>
	b10	Yeah, if people come in and I'm like, 'No, it doesn't have a UTI (urinary tract infection), don't do anything, go away,' ... they're often very upset about that. Because they think it's got a problem and they want to do something to fix the problem and paying the consult fee to be told he's fine, can make them grumpy .— <i>Vet N, 29F, rural, moderate interest</i>

Failure to meet owner expectations + consequences

b11	You have [clients saying], 'Oh, I paid X dollars. And I didn't even get anything off the vet! '— <i>Vet C, 33F, metropolitan, moderate interest</i>
b12	I've seen enough stray cats that have been in fights to know that a lot of them will heal [without antibiotics]. But I kind of feel like the owner's brought the cat in for me to fix it , so I want to fix it. I'm trying to give it the best opportunity to heal and ... not giving antibiotics in my mind feels a bit negligent .— <i>Vet T, 40M, metropolitan, moderate interest</i>
b13	With this irritating client, I think maybe this client is going to kick up a stink if I don't do something , or if this does get worse and I didn't [prescribe antibiotics] I will have a crappy day because they'll write a nasty email or something. That is a big factor.— <i>Vet B, 31M, metropolitan, high interest</i>
b14	I guess [you're more likely to prescribe antibiotics] if ... they're the kind [of client] that will always complain , kick up a stink ... ones where you're just like, 'Oh, I know this is going to be a massive fallout if it doesn't get fixed. So it has to be fixed, the first time... if they've got an established history of being difficult , then you're less brave to take risks with their pet.— <i>Vet V, 36F, metropolitan, moderate interest</i>
b15	I'm not going to put myself in a position where I'm gonna get yelled at by a client and impact my mental health for the sake of the greater good of antibiotic resistance, because I just don't have the energy for that. I need to save that for other things. Sometimes it's not worth the crusade.... I'm not going to put my receptionist in the firing line , because I'm on my high horse ... because they're gonna cop it ... there is a bit of that as well and mental health being what is in the veterinary profession.— <i>Vet G, 26F, rural, moderate interest</i>
b16	I know plenty of vets who have gone to the [veterinary] board for more trivial things than [withholding antibiotics] ... there's definitely that fear in the profession. Even in six months, I've seen it. I've seen it and heard it and people go to the board for sillier things than that.— <i>Vet E, 24F, regional, moderate interest</i>
b17	Losing a client is probably one part of it; bad publicity , so potentially not getting other clients , whether that's through Facebook or social media ; stress on staff who are associated with that, would probably be the main [concerns].— <i>Vet T, 40M, metropolitan, moderate interest</i>
b18	... there's always that risk that someone's just going to take something unreasonably and then just go and slaughter you on social media .— <i>Vet V, 36F, metropolitan, moderate interest</i>
b19	I'll probably say look, it probably just needs a couple of days . But if it looks worse tomorrow, give us a call ... and I will set aside some antibiotics And that seems to work a lot of the time. I reckon probably about 60% of the time, they don't come in to get antibiotics the next day. But they've left happy . — <i>Vet M, 28F, regional, low interest</i>

Difficult/long conversation with client + time pressure	b20	Sometimes ... you're running late. And you don't have time to have the conversation with the owner about the fact that the dog really doesn't need it ... sometimes [giving antibiotics] is like... it's an easy way out .— <i>Vet W, 39F, regional, moderate interest</i>
	b21	And sometimes those are battles that I'm like, I don't want to debate this right now. Even though I should. Even though I could talk your ear off about why you don't need antibiotics .— <i>Vet D, 25F, regional, high interest</i>
	b22	Sometimes it's just a case of, I'm going to be the one who's brave enough to actually have this slightly confrontational conversation, which ... is going to be the best thing for the pet even though it's a bit uncomfortable initially.— <i>Vet R, 28F, regional, high interest</i>
Additional work to perform diagnostic tests	b23	... on a Saturday, and I've been overbooked , I'm much more likely to just say, 'OK, let's just try this and get you out of here. And come back if it doesn't get better.' It's just ... you don't have the time to work things up .— <i>Vet V, 36F, metropolitan, moderate interest</i>
Perceived impact on AMR of withholding antimicrobials	b24	I've been burned before where I've told a client to just ride it out ... then they literally come back the next day but to see a different vet because they would like some antibiotics. Because that's what they've gotten before and that's what's worked well for them.— <i>Vet D, 25F, regional, high interest</i>
	b25	... it's all very well that one vet draws a line and says, 'OK, we're not going to [treat that with antibiotics]'. But if no one else has drawn that same line, then....I don't know if pointless is the right word, but I don't see there's a massive benefit in it being a single vet sort of thing. So, if there was going to be change ... I think it has to be industry change, not individual change ... it does feel like on my own, I'm not going to have much impact on [AMR]. And potentially all I'm going to do by trying to do the right thing is make my patients suffer on an individual level.— <i>Vet T, 40M, metropolitan, moderate interest</i>
	b26	But there is that thing that if you don't give them what they want , we have another six clinics within a five-kilometre radius of us.— <i>Vet J, 32F, metropolitan, high interest</i>

Figure 4. Background factors influencing the decision to withhold or delay antimicrobial treatment where there was no clear indication, and illustrative quotes. Bold text has been used to highlight key ideas. Grey italics have been used for participant code, age and gender, location of practice and level of interest in AMR and AMS. There were three main scenarios in which participants described giving systemic antimicrobials when they were not indicated. The first is where the cause of illness was probably or certainly not responsive to antimicrobials, but the client expected the veterinarian to medicate the animal, sometimes specifically with an antimicrobial (b1, b7, b11, b12, b13, b15, a29). Alternatively, it could be where the client was frustrated (a27) or despondent about their animal's condition, such as the client 'at their wit's end' dealing with a dog with diarrhoea (a28), increasing the pressure for the veterinarian to take action to address the problem.

Multiple interviewees described implicit and/or explicit client expectations of antimicrobials, similar to a qualitative study of companion animal veterinarians in the UK.¹⁷ These experiences

are also reflected in a recent study, in which 15% of Australian pet owners indicated that they had explicitly requested antimicrobials from their veterinarian.³⁴ However, a few interviewees in our current study felt that this was becoming less common and attributed this to increasing public understanding of AMR (n5, n6, a25). UK veterinarians also reported increasing public awareness of AMR as an enabler of withholding antimicrobials.^{16, 17} However, studies in both countries have found that public understanding of AMR in pets was still poor overall and knowledge of interspecies transmission of bacteria was low.^{17, 34}

Some veterinarians felt that if they were to withhold antimicrobials, particularly with clients who expected antimicrobials and were known or suspected to be 'difficult' (a29) and demanding (a31), it would lead to a long, possibly adversarial (b20, b21, b22) conversation with the client, requiring time and energy that they rarely had. In such scenarios, many veterinarians felt that they had only two choices: to go bravely into 'battle' with that client (b21) and accept the possible fallout or capitulate. Given that this fallout could include clients verbally abusing them or their colleagues (b1, b15, b17), lodging a complaint about them with the veterinary board (b16), pursuing civil legal action (n12-17) or 'slaughtering' the clinic on social media (b17, b18), with impact on staff mental health and business reputation and revenue, it is clear why veterinarians sometimes felt that withholding antimicrobial treatment was simply 'not worth the crusade' (b15) and occasionally used antimicrobial therapy as an 'easy way out' (b20). There was also a sense that there might be no benefit in withholding antimicrobials, as a determined client could obtain antimicrobials from another veterinarian at the same practice (b24) or take their business to a different practice (a3, b26). Losing dissatisfied clients to another practice was a concern for some veterinarians and it was a bigger risk where there were many other veterinary practices in the local area (b26). However, some veterinarians were willing to stand by their principles, even if it meant losing clients (a3).

The second scenario was a known bacterial infection that could be managed without systemic antimicrobials, but where non-antimicrobial management would be more difficult for the client. There can be a higher risk of treatment failure if antimicrobials are withheld, due to the client failing to execute adequate home management, unrecognized lowered immunity in the animal, or the development of unforeseen infective complications. However, in some cases this risk may be managed by improving client instruction and follow-up, rather than by using systemic antimicrobials. For example, client handouts explaining non-antimicrobial management and automated text messages to check on progress.

One example of this is the cat fight abscess case study discussed with all participants; the draining subcutaneous abscess (without cellulitis) described is not life-threatening and would usually resolve without antimicrobials, provided that the cat has normal immune function and drainage is maintained by the client regularly cleaning the abscess, as recommended by Vet H (b2) and local prescribing guidelines.⁴¹ However, most participants in this study (20/22) opted to give this cat systemic antimicrobials, most commonly amoxicillin-clavulanate for 5 to 7 days (12/22), or cefovecin (5/22), a single long-acting injection with a duration of efficacy of 14 days. These veterinarians were asked whether they would consider getting the owner to manage the wounds instead. Some said that there were rare, highly competent, clients who could be trusted with this task (c11, c12), but for all other clients, they would give antimicrobials to decrease the risk of treatment failure and thereby protect themselves from client dissatisfaction (b4). Some veterinarians used phrases that framed antimicrobials as a form of self-defence, such as 'cover my bum' (b4) or 'cover my bases' (b6). Previous adverse experiences with withholding antimicrobial treatment reinforced this behaviour (b5). Another admitted that, for her, giving antimicrobials was an irrational, almost involuntary, response to the sensory experience of pus (b3).

The third scenario is when the diagnosis was unclear and antimicrobials were given just in case they helped, as a ‘treatment trial’. This was particularly true where there were clinical signs that are associated with a bacterial infection, such as fever, but which could equally be caused by viral infection or even non-infectious conditions. This type of prescribing has also been described in medical intensive care units.⁴⁴

Antimicrobial treatment trials are relatively common in veterinary medicine for a few reasons. The non-verbal nature of the patients—and clients who are not always able to observe their animals—mean that the history and physical examination of an ill cat or dog are often insufficient to reach a diagnosis. At this point, there are three main pathways the veterinarian can take: diagnostic work-up; watch-and-wait; or a treatment trial—commonly, a course of antimicrobials. The latter approach can be appealing when the veterinarian weighs the invisible and seemingly distant consequences of AMR (a8, a9) against the drawbacks of the first two approaches.

Diagnostic work-up is often expensive for the client, except in the unusual instances where the animal is insured, and a definitive diagnosis is sometimes never achieved, despite costly investigations. There are also workflow implications for the clinic. Unlike human patients, who are usually sent away to specialist providers for investigations, investigations on veterinary patients usually occur within one general practice clinic. This can involve additional time and labour—for example, a fractious cat may need to be admitted to hospital, sedated and then handled by multiple staff, simply to obtain a blood or urine sample. Some investigations require specialised equipment, supplies or personnel that must be brought in from elsewhere. Hence, work-up can pose a challenge, particularly in a busy clinic, and a course of antimicrobials can be a way to avoid—or at least postpone—that additional work (b23). Similarly, UK and Dutch veterinarians felt that time pressure and cost to the client were barriers to performing appropriate investigations and enablers of antimicrobial treatment.^{15, 19}

A watch-and-wait approach—which can include a ‘delayed’ antimicrobial prescription—is inexpensive and is commonly the most prudent course of action for an animal with mild, non-specific signs. Some participants said they often used this approach to keep an owner happy despite withholding antimicrobials (b19), but it poses a higher risk of clinical deterioration if a serious bacterial infection is indeed developing (b6, n17). Additionally, this approach sometimes requires the veterinarian—or other clinic staff—to expend time and energy coaching the client to provide supportive care and monitor changes in the animal’s condition. Some veterinarians said that they would feel compelled to call the client days later, in case antimicrobials (or some other treatment) needed to be initiated. When exhausted and under time pressure, this extra work associated with the watch-and-wait option becomes less appealing. Furthermore, the veterinarian must have faith that the client will not perceive watch-and-wait as the veterinarian ‘doing nothing’ (n10, b7) and hence not providing value for the consultation fee (b7, b11). They must also trust that the client has the capacity (a24) to carry out their recommendations, including contacting the clinic in a timely fashion if the animal needs further attention, and will not become irritated about returning to the clinic to collect medication. This trust is not always present (c11, c12).

Where the diagnosis was unclear and an animal had severe clinical signs, veterinarians were also less likely to withhold antimicrobials because the risk/benefit equation had shifted (b8, b9). This kind of ‘Hail Mary’ prescribing—hoping antimicrobials might be life-saving—was particularly appealing when the client was unable or unwilling to spend money on further diagnostic tests (b8).

Two major fears predominated when veterinarians considered withholding antimicrobials: the fear of clinical deterioration (b1, b2, b3, b4, b8, b9, c11) and the fear of failing to meet client expectations (b7, b12, b13, b15, b16, b17, b18, b26), and the downstream consequences of these two outcomes. These two fears—and the factors that heightened those fears—are shown in Figure 5, to further describe the logic and the connections between these central ideas described by interviewees.

The perceived impact of withholding antimicrobials was another important behavioural belief for veterinarians. While some interviewees saw every course of antimicrobials that they avoided as a victory, others saw it as futile, because they believed most other veterinarians were using antimicrobials liberally (b25) and considered their personal contribution to antimicrobial use to be negligible, or because they expected that the client would simply obtain the antimicrobials from another veterinarian (b24, b26). In a study of Australian medical general practitioners, there was also a sense of futility about withholding antimicrobials, but those doctors' reasons were quite different; they saw human hospital and veterinary use of antimicrobials as dwarfing their own sector's contribution.⁴⁵

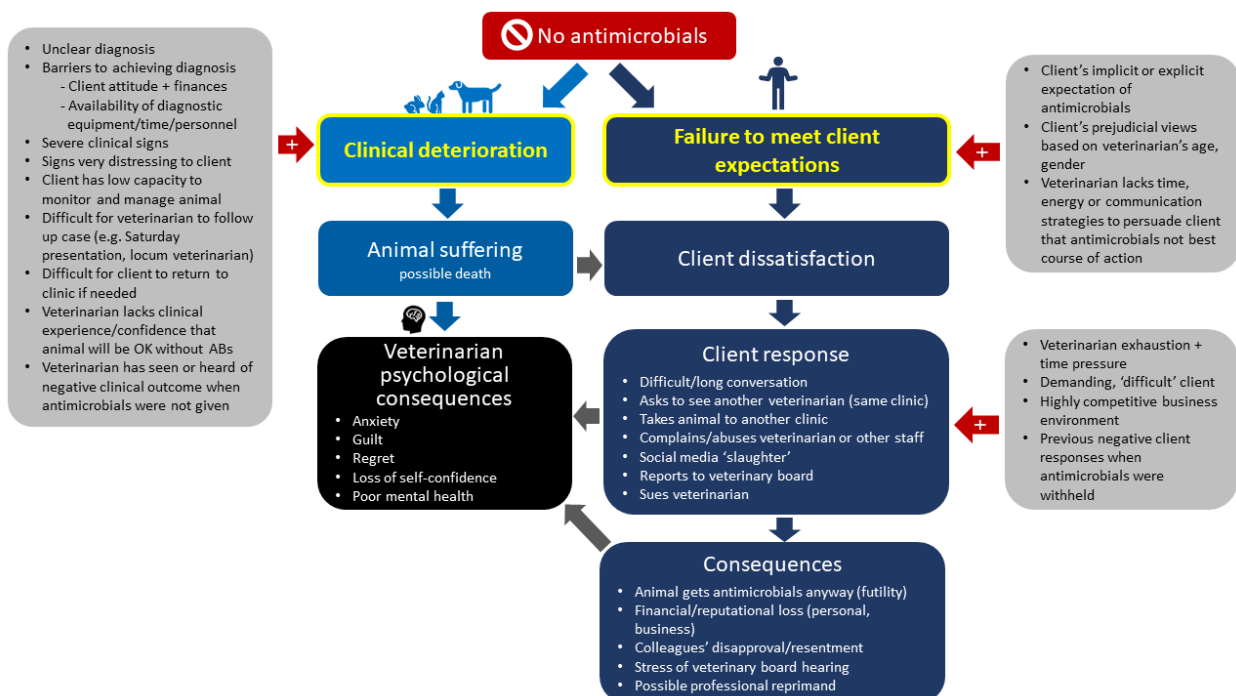


Figure 5. Schema of the dominant behavioural beliefs that interviewees associated with withholding or delaying antimicrobial treatment. Secondary factors that heighten fears are shown in grey.

Normative Beliefs

Interviewees mentioned a range of people whose expectations influenced their decision to withhold antimicrobial treatment (Figure 6). Client expectations were commonly mentioned, but the expectations and modelled behaviours of their employer and colleagues, and the perceived expectations of the veterinary board, were also important. Somewhat surprisingly, the influence of veterinary academics was also mentioned by a few participants.

Normative beliefs	Quote ref.	Quote— <i>interviewee code, age and gender, practice location, level of self-reported interest in AMR and AMS</i>
Client (animal owner)	n1	A lot of [our clients] are elderly. A lot of them are on the pension and a lot of them are also used to ... the old-school way ... 'I used to just come in and they'd give me a pill and it would fix it! '— <i>Vet N, 29F, rural, moderate interest</i>
	n2	... if they've had their cat bite abscess seen nine times before and nine times it's had [an antimicrobial] then they'd be more likely to put in a complaint to you [if you don't prescribe it]... they'll be like, 'Well all those other much more experienced vets use it and ... it's always gone super well when it's had that.' So obviously, when you've been out [in practice] six months it's, you know... you don't want to suggest that your colleagues haven't made the right decision ... if they've used something 10 times before then it makes it hard for you to give a good reason why maybe we shouldn't use it.— <i>Vet E, 24F, regional, moderate interest</i>
	n3	... the owner's like, 'He's had antibiotics for it before and it made it better and I know he just needs antibiotics again, ' and you kind of know that no matter what you suggest, especially if ... he's been to your other colleagues and they've given [antibiotics]... a lot of the time, I go, 'OK. Yep. We'll go with that again.' — <i>Vet W, 39F, regional, moderate interest</i>
	n4	Sometimes even when they book a consult ... they might ask the receptionist , 'What's the vet going to do?' And they might tell them, 'The vet might ... recommend antibiotics, ' and sometimes ... they will come in with an expectation that I'll be dispensing stuff ... Sometimes even I accidentally shoot myself in the foot at the beginning of a consult [by saying to the client], 'We might have to put it on antibiotics, we might not.' And then at the end.... [if] we don't need it, I accidentally already set them up for that, but I don't dispense ... I've got to backtrack on that.— <i>Vet P, 35F, metropolitan, high interest</i>
	n5	I think the general population is starting to get a bit of an understanding of this stuff [AMR] as well ... it doesn't seem to be a massive problem in consults with people wanting antibiotics. Every now and then there'll be something (<i>sic</i>) that wants an antibiotic that I don't think necessarily needs it. I would probably try and give them an alternative , depending on what it was.— <i>Vet T, 40M, metropolitan, moderate interest</i>
	n6	And some clients actually ... are quite conscious of antibiotic resistance and they don't like their dogs being on antibiotics unless they really have to.— <i>Vet C, 33F, metropolitan, moderate interest</i>
Employer	n7	But because of my fear of judgment from my boss and other vets in the clinic, if I didn't put the cat on antibiotics, and then it didn't get better, I would just put it on antibiotics to start with. Even though if it were my own cat, I potentially would be happy to wait and see if it would heal without any antibiotics.— <i>Vet R, 28F, regional, high interest</i>

	n8	... that pressure from the clinic owner . He's a bit old-school ... his version of gold standard medicine ... includes hitting them with antibiotics ... making sure you're meeting that client's expectation .— <i>Vet J, 32F, metropolitan, high interest</i>
	n9	... when I was a new graduate, my first boss always said, ' Never let them go out the door without something . If you do nothing and it comes back to bite you , you're in trouble. If you do something and it comes back to bite you, well, you've got a reserve.' So, I think that was impressed on me as a new graduate to always, always get them out the door with something .— <i>Vet S, 66M regional, low interest</i>
	n10	[My first boss] said... '... [if you don't medicate] the perception of the owner is that you didn't do anything . You should just give it a shot of [amoxicillin-clavulanate] or something, then at least ... the owner would have thought it was you!'— <i>Vet V, 36F, metropolitan, moderate interest</i>
	n11	... yeah, the monetary factor as well; if [vets] are being pushed to make minimum [revenue] , like if you have a cat with FLUTD [a stress-induced urinary disorder that rarely requires antibiotics] and you don't give antibiotics , then you are going to make less money ... for that 20-minute or 15-minute consult. And if your boss is pushing you , that's going to change your decisions. And that's really sad.— <i>Vet Q, 43F, regional, high interest</i>
Colleagues	n12	Definitely previous vets [affect the decision to prescribe—the client] might have gone to a completely different veterinary clinic, they might have seen a locum vet or a different vet [at] this current clinic— play a big role in influencing whether antibiotics get dispensed or not.— <i>Vet D, 25F, regional, high interest</i>
	n13	It's very powerful when a [veterinary dental] specialist says , 'For the last three years I haven't put any of my grade 3 or grade 4 dentals on antibiotics. And I've never had any issues with resolution of infection in the mouth.'— <i>Vet X, 54M, regional, high interest</i>
	n14	...inappropriate use of antibiotics is so widespread ... the vet boards talk about, what would a reasonable colleague think was acceptable? ... [Many vets] think that everybody else does it . And if they <u>don't</u> do it, and something goes wrong, they're going to be in trouble .— <i>Vet H, 68M, regional, high interest</i>
	n15	The nurses are converted . The nurses see how passionate I am about [antimicrobial stewardship]. And also how much it concerns me. And they also see the difference in patient care with us moving away from antibiotic use , and for example, moving towards probiotic use in acute diarrhoea ... and they really like that. I've had "lunch and learns" where I've had people come in and teach them more about the microbiome ...and therefore maybe a little bit more on board with avoiding antibiotics. Of course, the nurses then ... put pressure on the vets to do the right thing.— <i>Vet P, 35F, metropolitan, high interest</i>

Veterinary Board	n16	My colleague went to [the veterinary board] for not giving a hamster antibiotics for a routine desexing, and [they] showed him a Canadian article saying you should be giving antibiotics... that's one of his rationales for giving lots of antibiotics, to avoid [the veterinary board] ...that's a big thing; [the veterinary board] and client expectation and fear and concern about being reprimanded ... — <i>Vet B, 31M, metropolitan, high interest</i>
	n17	If I didn't give the antibiotics, and then it turns out ... the dog actually did have quite a bad infection and say it dies ... what are the consequences of that, and not just, the animal dies , but maybe the animal just becomes a bit sick , and they go to another clinic and the other clinic finds whatever, and then the client reports you to the vet board or sues you. — <i>Vet W, 39F, regional, moderate interest</i>
Veterinary academics	n18	We had a lovely [microbiology] lecturer at uni... And every time I prescribe antibiotics, I have [her] in the back of my head. And... cat bite abscesses are one of those situations where I'm like, ' Sorry, [lecturer]. ' ... that sounds so silly... I feel like I'm conscious of it, but I still do it [prescribe antibiotics] because there's almost like this [client] expectation of, just, 'Fix my cat, I don't want to come back. I just want you to fix it on this occurrence. '— <i>Vet J, 32F, metropolitan, high interest</i>
	n19	... if I'm getting guilt-tripped by the [veterinary] profession or by ... researchers , or by lecturers because I gave a greyhound client three boxes of metronidazole—sometimes I'm just like, you know what, ' Screw you guys, 'cause I'm the frontier. '— <i>Vet G, 26F, rural, moderate interest</i>

Figure 6. Normative beliefs influencing decision to withhold or delay antimicrobial treatment where there is no clear indication, and illustrative quotes. Bold text has been used to highlight key ideas. Grey italics have been used for participant code, age and gender, location of practice and level of interest in AMR and AMS.

As previously discussed, multiple interviewees mentioned that their clients commonly communicated an expectation of receiving antimicrobials for their animal, which made it more difficult to withhold them. Such expectations were often established by other veterinarians who had previously prescribed antimicrobials (n1, n12), especially for the same clinical presentation (n2, n3). In this situation, withholding antimicrobials could be seen as directly contradicting the previous veterinarian(s), which led to psychological discomfort, particularly when the previous veterinarian was more experienced (n2). Veterinarians in the UK also cited this awkwardness as a driver of antimicrobial prescribing.¹⁸ In human hospitals, a similar unwillingness to break professional etiquette by questioning the decisions of others, particularly others of higher status, also enables inappropriate antimicrobial prescribing.^{46, 47}

However, some veterinarians reported that expectations of antimicrobial treatment were uncommon in their clinic clientele (a25, n5). This could be due to historically conservative antimicrobial use by veterinarians at that clinic, the client's level of understanding of AMR (n5), which can in turn be influenced by educational level (a24, a25) or, as mentioned above, by the AMS efforts of local medical general practitioners (a26). One veterinarian described the key role of reception or nursing staff in setting expectations of antimicrobials prior to the consultation (n4).

Interviewees were less likely to withhold antimicrobials if they suspected their employer and

colleagues would judge them negatively for failing to fix the ailment the first time (n7), for not meeting client expectations (n8) or for falling short of revenue targets (n1). Some participants reflected on the lingering influence of an employer they had had early in their career, who had encouraged unnecessary antimicrobial use (n9, n10). Conversely, having veterinary colleagues who valued responsible antimicrobial use (a21) enabled withholding of antimicrobial treatment. Veterinary nurses who understood antimicrobial resistance and were ‘converted’ to the cause (n15) were also cited as powerful enablers, highlighting the valuable role of para-veterinary staff in AMS programs. Interviewees also mentioned that when veterinary specialists, who were viewed with reverence, condoned the withholding of antimicrobial treatment in particular conditions (n13), this helped them to do the same.

Older veterinarians and ‘old-school’ ways of practising veterinary medicine (n1, n8, a21) were mentioned by some younger interviewees in the context of more liberal antimicrobial use, and younger veterinarians were sometimes associated with more conservative use (a20, a21). This was also reported in two UK studies,^{15, 16} but is somewhat contradicted by our finding that veterinarians with more clinical experience and stronger communication skills felt more confident in withholding unnecessary antimicrobials (a14, a15, a16). Indeed, one of the older veterinarians in our study believed that younger veterinarians prescribed more antimicrobials out of fear or a lack of confidence (b7). Notably, while the median age of interviewees was 34 years, the only two participants who indicated that they would not prescribe antimicrobials for the cat fight abscess case were aged 68 (b2) and 43. Quantitative research is needed to establish whether there is a true association between the clinical experience of veterinarians and unnecessary antimicrobial prescribing, and if there is, in which direction it influences prescribing.

Belief that there is widespread liberal (b6) or ‘willy nilly’ (a4) use of antimicrobials by the Australian veterinary profession was a barrier to withholding antimicrobials. Veterinarians cited a few reasons for this: firstly, the perceived likelihood that their withholding of antimicrobials would be futile, because it would have negligible impact on the overall problem (b25), and because the client might just obtain antimicrobials from another veterinarian (b24, b26). Veterinarians also feared the veterinary board (n16, n17) would rule against them if the case deteriorated, because professional negligence is judged by comparison with what ‘a reasonable colleague’ would do. If a veterinarian believes that most of their profession prescribes antimicrobials to dogs and cats at high rates, it follows that withholding antimicrobials is more likely to be viewed by a veterinary board as negligent (b9, b12, n14). Comparison of two recent AMS trials in the UK⁴⁸ and Australia⁴⁹ suggests that overall companion animal antimicrobial prescribing rates in Australia are probably relatively low. However, a central tenet of the TPB—and many other behavioural theories—is that it is a person’s belief about relevant others, rather than the evidence, that shapes behaviour. Indeed, prescribing antimicrobials to avoid the significant stress of a veterinary board hearing in itself—with the potential for professional reprimand—was mentioned by multiple interviewees (n16, b16, a29).

A few veterinarians felt that the academics who had taught them as undergraduates would disapprove of some of their current antimicrobial use. However, the other element of the subjective norm—how much these veterinarians cared about the approval of this group—was low. One indicated that the approval of the client who expected antimicrobials outweighed the academics’ disapproval ‘in the back of [her] head’ (n18). Similarly, another defiantly acknowledged that she was far more strongly motivated by protecting herself and her colleagues from client dissatisfaction than by the approval of veterinary academics (n19).

Control Beliefs

Although a decision to withhold (or prescribe) antimicrobials is always within the control of the veterinarian, there were several situations in which veterinarians perceived that there was no practical alternative to prescribing antimicrobials (Figure 7).

Control beliefs	Quote ref.	Quote— <i>interviewee code, age and gender, practice location, level of self-reported interest in AMR and AMS</i>
Time pressure + availability of support staff	c1	A typical Friday afternoon ... you've been consulting all day ... you always get slammed and the [receptionists] will always try and squeeze something in ... you feel like you're running 10 hours behind. People are getting grumpy ... and a client that's been waiting for 20 minutes, who just wants it fixed . And you just go, 'Here you go, let's try [antibiotics] first .' And so things like offering to do a culture and sensitivity [test], offering to do ... whatever, goes out the window a bit, and you fall back on that, 'Let's do a treatment trial first and see if that fixes it.'— <i>Vet J, 32F, metropolitan, high interest</i>
	c2	[You're more likely to prescribe antibiotics] on a Saturday when you've got less support staff around you to do the tests and things that you're thinking maybe you should be doing, investigating further .— <i>Vet W, 39F, regional, moderate interest</i>
Availability of non-antimicrobial therapeutics	c3	I don't really have too many people asking for antibiotics, I think they just want something and ... with diarrhoea cases ... we've never really had an option [other than metronidazole] to give them, except bland diet. And then recently we got the [probiotic paste]. And since then, I've used less antibiotics just because I have something to give them to go home with , that's <u>like</u> a medication.— <i>Vet F, 30F, metropolitan, moderate interest</i>
	c4	I guess another thing that I used to do—and I've gotten a lot better about—is putting dogs with diarrhoea on metronidazole , because it clears them up, but a lot of them probably would get better, maybe a bit slower without it. And I think owners like being given something , rather than being told it will just pass, just fix its diet... I was using [mixed antibiotic preparation for diarrhoea] for a while, which is horrible as well... then I was putting them on [probiotic paste], which doesn't have antibiotics in it.— <i>Vet N, 29F, rural, moderate interest</i>
Uncertainty of diagnosis + action bias	c5	But often, you don't have [a clear diagnosis]. And you just have to make a decision ... it's not getting better. You have to give it something . Let's try this [antibiotics].— <i>Vet G, 26F, rural, moderate interest</i>
	c6	I guess if there's like a fever of unknown origin ... there's no focus of infection obvious after doing bloods and maybe a scan ... then if the dog or the cat isn't getting better , I would reach for [antibiotics] and say, well, apart from the resistance, they're not going to do the animal any direct, immediate harm , and they might just help it because we don't actually know what's going on here.— <i>Vet C, 33F, metropolitan, moderate interest</i>

Client financial constraints	c7	We've got some fantastic clients, but cost always seems to be a huge issue . And it's not just with diagnostics for a UTI, but it would be for most things, you offer them a choice, and then they go, 'Ooh, cost,' so you offer them that other choice, which is let's try antibiotics ... and it's always option B [antibiotics] first.— <i>Vet J, 32F, metropolitan, high interest</i>
	c8	There have been times in the past that I have gone, let's just try antibiotics if the owner doesn't have money to investigate further. If it's really not obvious what's going on, I will just go on with the [antibiotics].— <i>Vet W, 39F, regional, moderate interest</i>
	c9	Where we are at times going—OK, empirical [antimicrobial] treatment, I'm just going to throw everything at this animal—is usually when the client ... has got zero dollars to do anything, and you feel, 'No, I have to help this animal . And I'll help the clients as well. And then you go, I'm just going to [give antibiotics].'— <i>Vet A, 45F, metropolitan, high interest</i>
	c10	... where the owners don't have money to work things up . So a cat that has chronic nasal discharge, and you're like, 'OK, well, we should really do imaging and a scope and biopsies and stuff,' but they don't have the money, so you're like, 'OK, well, we'll just have to trial antibiotics .'— <i>Vet V, 36F, metropolitan, moderate interest</i>
Client capacity to adequately monitor, manage and return to clinic if needed	c11	There are certainly some clients that I have really high level of trust in [to nurse and monitor their animal], but they're not the norm ... we could certainly try [managing an abscess without antimicrobials] if they feel comfortable to monitor at home and come back in a few days ... [but] a lot of clients have more difficulty in assessing how the animal is going. Sometimes we feel it's in the animal's best interest to overdo it , rather than underdo it, knowing that we might not see them again , and there's been a period of time where they are suffering a lot , that we could have avoided.— <i>Vet T, 40M, metropolitan, moderate interest</i>
	c12	I would be more inclined on my own animals to not give antibiotics at that point, knowing that I can be monitoring them a little more, and maybe draining [the abscess] a little more competently , than an owner might at home.— <i>Vet U, 39F, regional, low interest</i>
	c13	Having worked for so long now, I think [I can identify] clients that will handle things like that [cat fight abscess management at home] and ones that won't. — <i>Vet V, 36F, metropolitan, moderate interest</i>

Figure 7. Control beliefs influencing decision to withhold or delay antimicrobial treatment where there is no clear indication, and illustrative quotes. Bold text has been used to highlight key ideas. Grey italics have been used for participant code, age and gender, location of practice and level of interest in AMR and AMS.

The time that the animal is presented to the clinic can determine whether the veterinarian feels it is feasible to withhold antimicrobials. Both the time pressure in a busy clinic (b20), especially being 'slammed' on Fridays (c1) and Saturdays (b23, c2), and the lack of other clinic staff to assist with investigations (c2), tended to lower a veterinarian's threshold for prescribing antimicrobials. Studies of human antimicrobial prescribing suggest similar links between prescribing and time pressure⁴⁵ and difficulty accessing further investigations.⁵⁰

Similar to the findings of a UK study,¹⁷ the Australian veterinarians interviewed felt that many of their clients had an expectation of receiving medication for a sick animal, giving them a sense that the veterinarian had ‘done something’ to fix the illness (a14, a29, b10, b13, n10) in exchange for the consultation fee. Antimicrobials can satisfy that client expectation, but in illnesses for which there are non-antimicrobial therapies available, the veterinarian can avoid antimicrobials and still give the owner ‘something ... to go home with’ (c3). An example provided by more than one veterinarian was acute diarrhoea in dogs, a common presentation that has often been treated with the antimicrobial metronidazole. In recent years, a probiotic paste has been available on the Australian market that had trial evidence of efficacy in reducing the duration of clinical signs⁵¹. Some veterinarians said that since this product had become available, they had rarely used antimicrobials for acute diarrhoea (c3, c4, n15). Similarly, Hopman et al. reported that Dutch veterinarians cited the availability of alternative therapeutic options in deciding whether to use antimicrobials.¹⁹

When reflecting on situations where they felt they had little choice but to give antimicrobials, interviewees often talked about unclear diagnoses, the animal having been unwell for a prolonged period (c5), especially if severely unwell (c6, b10), and situations where further diagnostics were not feasible (c6, b8), usually due to clients’ financial constraints (c7, c8, c9, c10, n1). Veterinarians felt compelled to take action to help the animal and the owner (c9) and antimicrobials often felt like the only practical option. Furthermore, once a veterinarian had mentioned the option of an antimicrobial treatment trial, it could be difficult to convince the client to do anything else (c7, n4).

Clients perceived to have lower capacity to perform home care—such as regularly cleaning a wound, monitoring relevant changes in their animal, and returning to the clinic in a timely fashion if the condition deteriorated—also sometimes made it seem impossible to withhold antimicrobials (c11, c12), particularly when there was potential for the animal to suffer (c11). However, there were some clients that interviewees felt could be trusted with such tasks, including those with a healthcare background or significant animal husbandry skills. One veterinarian said that as she had gained clinical experience, she felt more able to accurately identify those clients, and hence better able to identify opportunities to withhold antimicrobials more safely (c13).

Suggestions for Curbing Unnecessary Antimicrobial Use in Companion Animals

Possible solutions discussed by interviewees fell into six categories: client education; veterinarian education and training; para-veterinary staff education and training; workplace culture; informational resources; audit and sanctions.

Client education about the benefits of avoiding unnecessary antimicrobials—such as through posters in the clinic waiting room—was suggested by multiple participants, to reduce conflict with clients when withholding antimicrobials (a24, a25, a26). However, others felt that this would have limited or no impact, either because of the amount of other information clients were presented with at the clinic, or an unwillingness of clients to change their beliefs. Nonetheless, this suggestion would be relatively simple to implement and seems worthy of investigation.

Some participants suggested that increased teaching of AMS to veterinary undergraduates would be helpful; others felt that current teaching was already sufficient, but that the real-life challenges of clinical practice, including prescribing behaviour modelled by more experienced veterinarians around the new graduate, sometimes prevented veterinarians from withholding antimicrobials appropriately. Postgraduate education in antimicrobial stewardship was also suggested by some participants, with the proviso that it be delivered in a way that is convenient for busy clinicians and provided free of charge.

Strong communication skills were a clear enabler for withholding unnecessary antimicrobials while keeping clients happy. While some participants had developed these skills organically over years of trial and error, several felt that communication skills training, especially in their first few years after graduation, would have improved their antimicrobial prescribing. This suggestion would be relatively straightforward to implement and seems worthy of further research. Targeted communication skills training has been successfully trialled in general medical practitioners in Germany, and has resulted in significant reduction in inappropriate antimicrobial prescribing for upper respiratory tract infections.⁵²

One veterinarian suggested that client communication training for reception and nursing staff could reduce the number of difficult conversations about antimicrobials. Additionally, providing education for para-veterinary staff, explaining why unnecessary antimicrobial therapy should be avoided, as one participant had done (n15), engaged and motivated them to facilitate judicious antimicrobial use. Two modifiable aspects of practice culture were identified as enablers of appropriate antimicrobial use: inviting staff to suggest evidence-based changes to practice protocols and supporting veterinarians when they have made an appropriate decision to withhold antimicrobials.

A few participants expressed a desire for succinct, evidence-based information on common clinical conditions to provide guidance about when to prescribe antimicrobials and when to withhold them. That these veterinarians were unaware of the Australian Veterinary Prescribing Guidelines for dogs and cats, which provide this information, highlights a need to further publicise their existence. The authors have already commenced work on this task.

A few participants felt that auditing the antimicrobial use of individual veterinarians or veterinary practices, and providing feedback on their use, would be helpful. Social normative prescribing feedback has been successfully applied in other antimicrobial stewardship initiatives^{53, 54} and would be readily implementable in practices that submit data to a central repository, such as VetCompass (UK) and VetCompass Australia. Publicising data on actual veterinary prescribing habits could also reduce the perceptions of Australian companion animal veterinarians that their profession is using antimicrobials liberally and that a single veterinarian's AMS efforts are therefore futile. In fact, rates of antimicrobial use in Australian pets have been declining for some years⁴⁹ and Australian veterinarians have a high degree of concern about AMR.³¹

One participant, who had previously practised under an auditing system with prescriber sanctions in Denmark, felt that this was effective in curbing unnecessary use. However, they also acknowledged the difficulty of executing such an intervention in Australia, as this would require legislative changes and a mechanism to monitor antimicrobial use in animals.

Further Discussion

To our knowledge, this study is the first to reveal the pivotal role of client capacity in the choice to withhold antimicrobials. Clients who were perceived as motivated and capable (of undertaking non-antimicrobial management and monitoring) enabled veterinarians to appropriately withhold antimicrobial treatment. This finding suggests the potential for AMS interventions targeting pet owner skills and motivation.

This study also documents for the first time the roles of clients' gender and age prejudices, veterinary workplace culture and para-veterinary staff in appropriate use of antimicrobials. Veterinarians who felt supported by their colleagues and who felt their workplaces were open to change were empowered to withhold antimicrobial treatment. Para-veterinary staff could either undermine or support AMS efforts through their conversations with clients and with the

veterinarians themselves. This underlines the importance of involving receptionists, veterinary nurses and practice managers in antimicrobial stewardship initiatives. Cultivating a supportive and respectful workplace culture, where young and female veterinarians are publicly valued, could help to tackle clients' gender and age prejudices and reduce unnecessary prescribing.

The influence of social media on veterinary decision-making, or, more precisely, the threat of negative comments on the practice's social media page, is another new finding. This is also the first study that we are aware of to link the antimicrobial stewardship messages of human physicians with the behaviour of their patients as veterinary clients, suggesting that a united public education campaign about antimicrobials could yield benefits to all sectors.

A major strength of this study was the candour of the interviewees. This was likely aided by the interviewer's role as a fellow veterinarian, which established trust and empathy with participants, and her ability to suggest realistic variations on scenarios to draw out veterinarians' beliefs. Empathic interpretation of the interview transcripts was also enhanced by the authors' lived experiences. Additionally, although the authors had expected some findings to be specific to the local context, the themes either echoed findings of previous UK and Dutch studies or were novel themes that are likely to exist in companion animal medicine in many other countries. Another strength is the application of a widely used theoretical framework to the thematic analysis, allowing for simpler comparison with other qualitative study findings. A limitation is that only three of the 22 participants expressed a low interest in AMR and AMS, while ten stated that they had a high interest in AMR and AMS. Thus, solutions suggested by participants to reduce inappropriate prescribing may be more suited to veterinarians who are already somewhat engaged with AMS, and less suitable for those with low interest.

Conclusions

Many veterinarians are motivated to use antimicrobials only when they are necessary, as they are worried about the consequences of AMR. However, these concerns can be outweighed by behavioural beliefs, especially fears of clinical deterioration and client dissatisfaction if antimicrobials are withheld or delayed. These fears can be compounded by diagnostic uncertainty and time pressure, as well as a range of client factors, including client expectations of receiving medication, financial constraints, a poor veterinarian–client relationship and doubts about the client's capacity to nurse and monitor their animal. Prescribing antimicrobials often gives veterinarians a sense of safety; conversely, withholding or delaying antimicrobial treatment can feel like an act of bravery.

Access to evidence-based prescribing guidelines, a supportive and change-ready workplace culture, para-veterinary staff who are engaged in judicious antimicrobial use, and strong communication skills were all perceived to encourage appropriate withholding of antimicrobial treatment. These enablers can be incorporated into veterinary undergraduate and continuing education. Uptake of pet insurance and availability of alternative, non-antimicrobial therapeutic products also enabled antimicrobial withholding.

Veterinary antimicrobial stewardship initiatives could benefit from consideration of these complex influences on a veterinarian's decision to withhold or delay antimicrobial use, and from the suggestions made by veterinarians in this study to reduce unnecessary antimicrobial use, such as social normative feedback on their prescribing, client AMS education and veterinarian communication skills training.

Author Contributions: Conceptualization, R.S., L.H., K.B. and G.B.; methodology, R.S.; supervision, L.H., K.B. and G.B.; formal analysis, R.S. and A.S.; data curation, R.S.; writing—

original draft preparation, R.S.; writing—review and editing, L.H., A.S., G.B., K.B. and R.S.; visualization, R.S. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by National Health and Medical Research Council Australia, grant number CRE1079625 (National Centre for Antimicrobial Stewardship). L.H. is funded by the Australian Research Council through the Discovery Early Career Research Award program. R.S. and A. S. hold Australian Government Postgraduate Award scholarships.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee of The University of Melbourne (protocol code 1955762, date of approval 13 March 2020).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The raw data are not publicly available due to restrictions of this project's ethical approval.

Acknowledgments: We gratefully acknowledge fellow veterinary postgraduate students, Kellie Thomas and Suzanna Richards, who accompanied and assisted R.S. in learning about qualitative research techniques.

Conflicts of Interest: The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

References

1. McManus MC. Mechanisms of bacterial resistance to antimicrobial agents. *Am J Health Syst Pharm* 1997;54:1420-1433; quiz 1444-1426.
2. Lipsitch M, Samore MH. Antimicrobial use and antimicrobial resistance: a population perspective. *Emerg Infect Dis* 2002;8:347-354.
3. Gibson JS, Morton JM, Cobbold RN et al. Multidrug-resistant *E. coli* and enterobacter extraintestinal infection in 37 dogs. *J Vet Intern Med* 2008;22:844-850.
4. van Cleef BA, van Benthem BH, Verkade EJ et al. Dynamics of methicillin-resistant *Staphylococcus aureus* and methicillin-susceptible *Staphylococcus aureus* carriage in pig farmers: a prospective cohort study. *Clin Microbiol Infect* 2014;20:O764-771.
5. Bosch T, Verkade E, van Luit M et al. Transmission and persistence of livestock-associated methicillin-resistant *Staphylococcus aureus* among veterinarians and their household members. *Appl Environ Microbiol* 2015;81:124-129.
6. Agga GE, Cook KL, Netthisinghe AMP et al. Persistence of antibiotic resistance genes in beef cattle backgrounding environment over two years after cessation of operation. *PLoS One* 2019;14:e0212510.
7. Pouwels KB, Hopkins S, Llewelyn MJ et al. Duration of antibiotic treatment for common infections in English primary care: cross sectional analysis and comparison with guidelines. *Br Med J* 2019;364:l440.
8. Weese JS, Cruz A. Retrospective study of perioperative antimicrobial use practices in horses undergoing elective arthroscopic surgery at a veterinary teaching hospital. *Can Vet J* 2009;50:185-188.
9. Hardefeldt LY, Browning GF, Thursky KA et al. Cross-sectional study of antimicrobials used for surgical prophylaxis by bovine veterinary practitioners in Australia. *Vet Rec* 2017;181:426.

10. Vaughn VM, Flanders SA, Snyder A et al. Excess antibiotic treatment duration and adverse events in patients hospitalized with pneumonia: a multihospital cohort study. *Ann Intern Med* 2019;171:153-163.
11. Touboul-Lundgren P, Jensen S, Drai J, Lindbaek M. Identification of cultural determinants of antibiotic use cited in primary care in Europe: a mixed research synthesis study of integrated design "Culture is all around us". *BMC Public Health* 2015;15:908.
12. Currie K, King C, Nuttall T, Smith M, Flowers P. Expert consensus regarding drivers of antimicrobial stewardship in companion animal veterinary practice: a Delphi study. *Vet Rec* 2018;182:691.
13. Servia-Dopazo M, Taracido-Trunk M, Figueiras A. Non-clinical factors determining the prescription of antibiotics by veterinarians: a systematic review. *Antibiotics (Basel)* 2021;10:133.
14. Degeling C, Rock M. Qualitative research for One Health: from methodological principles to impactful applications. *Front Vet Sci* 2020;7:70.
15. Mateus AL, Brodbelt DC, Barber N, Stark KD. Qualitative study of factors associated with antimicrobial usage in seven small animal veterinary practices in the UK. *Prev Vet Med* 2014;117:68-78.
16. King C, Smith M, Currie K et al. Exploring the behavioural drivers of veterinary surgeon antibiotic prescribing: a qualitative study of companion animal veterinary surgeons in the UK. *BMC Vet Res* 2018;14:332.
17. Smith M, King C, Davis M et al. Pet owner and vet interactions: exploring the drivers of AMR. *Antimicrob Resist Infect Control* 2018;7:46.
18. Thompson AC, Chandler CIR, Mateus ALP et al. What drives antimicrobial prescribing for companion animals? A mixed-methods study of UK veterinary clinics. *Prev Vet Med* 2020;183:105117.
19. Hopman NEM, Hulscher MEJL, Graveland H et al. Factors influencing antimicrobial prescribing by Dutch companion animal veterinarians: A qualitative study. *Prev Vet Med* 2018;158:106-113.
20. Business Wire. UK Pet Insurance Market 2019: Consumer Research Report. <https://www.businesswire.com/news/home/20190910005520/en/United-Kingdom-Pet-Insurance-Market-2019-Consumer-Research-Report---ResearchAndMarkets.com>. 2019. Retrieved:25/05/2022
21. Engel P, Mihm U. Six things you need to know about pet insurance. <https://www.choice.com.au/money/insurance/pet/articles/six-things-you-need-to-know-about-pet-insurance>. 2021. Retrieved:21 June 2022
22. Hardefeldt LY, Gilkerson JR, Billman-Jacobe H et al. Barriers to and enablers of implementing antimicrobial stewardship programs in veterinary practices. *J Vet Intern Med* 2018;32:1092-1099.
23. Ajzen I. The theory of planned behavior. *Organizational Behavior and Human Decision Processes* 1991;50:179-211.
24. Warreman EB, Lambregts MMC, Wouters RHP et al. Determinants of in-hospital antibiotic prescription behaviour: a systematic review and formation of a comprehensive framework. *Clin Microbiol Infect* 2019;25:538-545.
25. Walker AE, Grimshaw JM, Armstrong EM. Salient beliefs and intentions to prescribe antibiotics for patients with a sore throat. *Br J Health Psychol* 2001;6:347-360.

26. Sable MR, Schwartz LR, Kelly PJ, Lisbon E, Hall MA. Using the theory of reasoned action to explain physician intention to prescribe emergency contraception. *Perspectives on Sexual and Reproductive Health* 2006;38:20-27.
27. Rashidian A, Russell I. General practitioners' intentions and prescribing for asthma: using the theory of planned behavior to explain guideline implementation. *Int J Prev Med* 2012;3:17-28.
28. Talkhan H, Stewart D, McIntosh T et al. The use of theory in the development and evaluation of behaviour change interventions to improve antimicrobial prescribing: a systematic review. *J Antimicrob Chemother* 2020;75:2394-2410.
29. Alradini F, Bepari A, AlNasser BH, AlGheshem EF, AlGhamdi WK. Perceptions of primary health care physicians about the prescription of antibiotics in Saudi Arabia: Based on the model of Theory of planned behaviour. *Saudi Pharm J* 2021;29:1416-1425.
30. Ajzen I. The theory of planned behaviour: reactions and reflections. *Psychology and Health* 2011;26:1113-1127.
31. Zhuo A, Labbate M, Norris JM 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:e020439.
32. Jernberg C, Lofmark S, Edlund C, Jansson JK. Long-term ecological impacts of antibiotic administration on the human intestinal microbiota. *ISME J* 2007;1:56-66.
33. Crespo-Piazuelo D, Lawlor PG. Livestock-associated methicillin-resistant *Staphylococcus aureus* (LA-MRSA) prevalence in humans in close contact with animals and measures to reduce on-farm colonisation. *Irish Veterinary Journal* 2021;74:21.
34. Scarborough R, Hardefeldt L, Browning G, Bailey K. Pet Owners and Antibiotics: Knowledge, Opinions, Expectations, and Communication Preferences. *Antibiotics* 2021;10.
35. Unterer S, Strohmeyer K, Kruse BD, Sauter-Louis C, Hartmann K. Treatment of aseptic dogs with hemorrhagic gastroenteritis with amoxicillin/clavulanic acid: a prospective blinded study. *J Vet Intern Med* 2011;25:973-979.
36. Australian Infectious Diseases Advisory Panel (AIDAP). Antibiotic Prescribing: Detailed Guidelines. <https://animalmedicinesaustralia.org.au/wp-content/uploads/2019/11/AIDAP-Australian-Infectious-Diseases-Advisory-Panel-and-Antibiotic-Prescribing-Detailed-Guidelines-.pdf>. 2013. Retrieved:25/05/2022
37. British Small Animal Veterinary Association. PROTECT ME: BSAVA/SAMSoc Guide to Responsible Use of Antibacterials. https://www.bsavalibrary.com/content/chapter/10.22233/9781910443644.chap6_1. 2018. Retrieved:03/05/2022
38. Findlay J. As pet ownership skyrockets during pandemic, a national vet shortage puts pressure on clinics and pets at risk. <https://www.abc.net.au/news/2020-12-26/vet-shortage-puts-pressure-on-clinics,-puts-pets-at-risk/13009562>. 2020. Retrieved:25 May 2022
39. Rafferty S. Shortage of vets nationally in 'demanding and exhausting' job. <https://www.abc.net.au/news/2021-05-10/vet-shortage-causing-exhaustion-prompts-cry-for-government-help/100121134>. 2021. Retrieved:25 May 2022
40. Linder JA, Doctor JN, Friedberg MW et al. Time of day and the decision to prescribe antibiotics. *JAMA Intern Med* 2014;174:2029-2031.

41. The University of Melbourne. Australian Veterinary Prescribing Guidelines, Dogs and Cats (version 2). <https://vetantibiotics.fvas.unimelb.edu.au/about/resources>. 2019. Retrieved:25 May 2022
42. Bhattacharya A, Hopkins S, Sallis A, Budd EL, Ashiru-Oredope D. A process evaluation of the UK-wide Antibiotic Guardian campaign: developing engagement on antimicrobial resistance. *Journal of Public Health (Oxf)* 2017;39:e40-e47.
43. The University of Melbourne. Australian Veterinary Prescribing Guidelines, Dogs and Cats (version 1). <https://vetantibiotics.fvas.unimelb.edu.au>. 2017. Retrieved:19 June 2019
44. Pandolfo AM, Horne R, Jani Y et al. Understanding decisions about antibiotic prescribing in ICU: an application of the Necessity Concerns Framework. *BMJ Qual Saf* 2022;31:199-210.
45. Fletcher-Lartey S, Yee M, Gaarslev C, Khan R. Why do general practitioners prescribe antibiotics for upper respiratory tract infections to meet patient expectations: a mixed methods study. *BMJ Open* 2016;6:e012244.
46. Broom A, Kirby E, Gibson AF, Post JJ, Broom J. Myth, manners, and medical ritual: defensive medicine and the fetish of antibiotics. *Qual Health Res* 2017;27:1994-2005.
47. Charani E, Castro-Sanchez E, Sevdalis N et al. Understanding the determinants of antimicrobial prescribing within hospitals: the role of “prescribing etiquette”. *Clinical Infectious Diseases* 2013;57:188-196.
48. Singleton DA, Rayner A, Brant B et al. A randomised controlled trial to reduce highest priority critically important antimicrobial prescription in companion animals. *Nat Commun* 2021;12:1593.
49. Hardefeldt LY, Hur B, Richards S et al. Antimicrobial stewardship in companion animal practice: an implementation trial in 135 general practice veterinary clinics. *JAC Antimicrob Resist* 2022;4:dla015.
50. Huibers L, Vestergaard CH, Keizer E et al. Variation of GP antibiotic prescribing tendency for contacts with out-of-hours primary care in Denmark - a cross-sectional register-based study. *Scand J Prim Health Care* 2022;40:227-236.
51. Nixon SL, Rose L, Muller AT. Efficacy of an orally administered anti-diarrheal probiotic paste (Pro-Kolin Advanced) in dogs with acute diarrhea: A randomized, placebo-controlled, double-blinded clinical study. *J Vet Intern Med* 2019;33:1286-1294.
52. Strumann C, Steinhäuser J, Emcke T, Sonnichsen A, Goetz K. Communication training and the prescribing pattern of antibiotic prescription in primary health care. *PLoS One* 2020;15:e0233345.
53. Bradley DT, Allen SE, Quinn H, Bradley B, Dolan M. Social norm feedback reduces primary care antibiotic prescribing in a regression discontinuity study. *J Antimicrob Chemother* 2019;74:2797-2802.
54. Hallsworth M, Chadborn T, Sallis A et al. Provision of social norm feedback to high prescribers of antibiotics in general practice: a pragmatic national randomised controlled trial. *The Lancet* 2016;387:1743-1752.

Chapter 6: Seeking simplicity, navigating complexity: How veterinarians select an antimicrobial drug, dose and duration for companion animals

A version of this paper has been published in the Journal of Veterinary Internal Medicine (2024);

doi: 10.1111/jvim.17197

Ri O. Scarborough^{a,b}, Kirsten E. Bailey ^{a,b}, Anna E. Sri^{a,b}, Glenn F. Browning ^{a,b} and Laura Y. Hardefeldt^{a,b}

^a Asia-Pacific Centre for Animal Health, Melbourne Veterinary School, Faculty of Science, The University of Melbourne, Parkville, VIC 3010, Australia

^b National Centre for Antimicrobial Stewardship, Peter Doherty Institute of Infection and Immunity, Melbourne, VIC 3000, Australia

Abbreviations:

AMR = antimicrobial resistance

AMS = antimicrobial stewardship

CA = companion animal

PO = per os

TMS = trimethoprim-sulfonamide combination

amoxiclav = amoxicillin-clavulanate

vet = veterinarian

Acknowledgments: Funding provided by the National Health and Medical Research Council of Australia, grant number CRE1079625 (National Centre for Antimicrobial Stewardship). Laura Y. Hardefeldt is funded by the Australian Research Council through the Discovery Early Career Research Award program. R.O.S. and A.E.S. hold Australian Government Research Training Program scholarships. These findings have been presented, in part, as part of a webinar series for Antimicrobial Awareness Week by the National Centre for Antimicrobial Stewardship (Australia). We acknowledge the interviewed veterinarians, who gave generously of their time.

Conflicts of Interest: Authors declare no conflict of interest.

Off-label Antimicrobial Declaration: Authors declare no off-label use of antimicrobials.

Human Ethics Approval Declaration: Approved by The University of Melbourne Human Research Ethics Committee, Approval number 1955762.1.

Abstract

Background

Minimizing harm from antimicrobials requires use of the narrowest spectrum drug, at an effective dose for the minimum effective duration. Many prescribers are not currently following these guidelines. To address suboptimal antimicrobial use, the underlying reasons must be understood.

Objectives

To identify factors influencing choices of antimicrobial drug, dose and duration for companion animals.

Subjects

Twenty-two veterinarians treating companion animals in Australia. Diversity of participants was deliberately sought.

Methods

Semi-structured interviews were conducted online. Two case studies were discussed, then a range of broader questions was posed. Transcripts were analyzed thematically, using an inductive approach.

Results

Few participants chose guideline-concordant management for the case studies. Prescribing choices were influenced by a complex array of factors associated with the clinical case, pet owner, drug, veterinarian, veterinary colleagues, and external factors. Key factors driving broad-spectrum antimicrobial use included a sense of safety, habit, ease of administering the drug (especially in cats), pharmaceutical marketing and the self-perpetuating 'dispensary cycle'. Many participants were concerned about antimicrobial resistance, but insufficiently informed about how to minimize this risk. Several participants believed that longer durations of treatment and ensuring patients finish a pre-determined course would decrease the risk of antimicrobial resistance and improve clinical outcomes.

Conclusions and clinical importance

Veterinarians are engaged with the concept of antimicrobial stewardship, but face numerous practical barriers and require more information. In particular, improved education is needed on enhancing patient safety by minimizing both spectrum of activity and duration of treatment, and dispelling myths about 'finishing the course'.

Introduction

Antimicrobial stewardship (AMS) has been described as a coherent set of actions that promote using antimicrobials responsibly.¹ It has two main objectives: 1) to eliminate unnecessary use of antimicrobials; and, 2) when antimicrobials are required, to maximize the benefits of treatment while minimizing harm, both to the treated patient and the broader community. These harms include drug reactions, dysbiosis, and the selection of antimicrobial resistance (AMR) determinants, in both the treated pathogen(s) and the patient's commensal flora, which can spread to other bacteria and other animals. To minimize these harms, prescribers should use a clinically and microbiologically suitable antimicrobial of the narrowest spectrum of activity or lowest possible importance rating, at an effective dose, for the shortest effective duration. However, this approach is not always followed in practice.

There is evidence that habitual, social, practical and structural factors can influence human and animal prescribers' antimicrobial choices as strongly as biological considerations.²⁻⁸ Understanding all influences on veterinary antimicrobial decisions is critical when designing interventions to improve the appropriateness of prescribing. Some influences are likely to be consistent, such as the role of habit, whereas others can be context-specific. For example, substantial differences exist between countries in veterinary education,⁹ the regulation, prescription and sale of antimicrobials,¹⁰ the availability of specific drugs and formulations,¹¹ cultural attitudes towards antimicrobials,¹² community health literacy¹³ and uptake of pet insurance,¹⁴ all of which can affect prescribing decisions.

Qualitative research studies with companion animal (CA) veterinarians in the United Kingdom¹⁵⁻¹⁸ and the Netherlands¹⁹ have examined factors influencing antimicrobial prescribing as a whole (i.e. both the decision to prescribe antimicrobials, as well as the choice of antimicrobial drug, dose and duration). Although in practice these decisions are made almost simultaneously, it is useful to examine them as discrete events, because there are distinct factors relevant to one, but not the other. We have previously published an analysis of the interviews conducted for the study described here that examined the factors influencing the initial decision to prescribe antimicrobials or not.²⁰ The aim of our current study was to use a phenomenological approach to understand how veterinarians make decisions about drug selection, dose and duration of treatment.

Methods

The method used has been published previously.²⁰ Briefly, one author, a veterinarian (R.S.), conducted semi-structured interviews with 22 veterinarians in Australia in 2020.

Positionality statement: R.S. identifies as an Australian-born and Australian-educated female veterinarian who had held clinical roles in mixed practice and companion animal practices and was now studying for a PhD in Veterinary Medicine. This positionality was explained to the 18/22 participants who had not previously met R.S.; the others knew her from their veterinary undergraduate studies. pharma

Most participants were recruited through convenience sampling using veterinary social media groups. A few additional participants were then purposively sampled to ensure a wider range of demographics and workplace types. Each interview included two case studies: a cat with a simple SC abscess, and a dog with a sporadic bacterial lower urinary tract infection. Participants outlined their preferred investigation and management for each case. The interview also explored a broad range of topics related to antimicrobial use. The interview guide has been published

previously²⁰ and is included in Appendix 3, Document S2. The project was approved by The University of Melbourne Human Research Ethics Committee (Project ID: 1955762).

In Australia, antimicrobial importance ratings used in veterinary and human medicine are defined by the Australian Strategic and Technical Advisory Group on Antimicrobial Resistance (ASTAG), categorizing each drug as of high, medium or low importance.²¹ Other jurisdictions may have their own national importance ratings systems or use the World Health Organization²², World Organization for Animal Health²³ importance ratings, or both.

Interviews were conducted and audio-recorded using Zoom Cloud Meetings (San Jose, USA). Transcripts created using Otter.ai (Mountain View, USA) were manually corrected by the interviewer. Thematic analysis was performed inductively by R.S. to develop a draft codebook of themes (hereafter referred to as ‘factors’) using NVivo (Version 12, QSR International, Burlington, USA). Two researchers (RS, AS) then independently coded the same two interviews, discussed discrepancies and refined the codebook, which is Table 1. The remaining 20 interviews coded solely by RS.

Results

Participant characteristics

The demographics of the participants have been described previously.²⁰ In summary, the participants were mostly working exclusively with companion animals (19/22), were predominantly female (16/22) and covered a broad age range (24 to 68 years). Participant age generally correlated with years of clinical experience.

The interviews lasted a median of 90 minutes (interquartile range 73-98).

Case studies

The approaches to management of the two case studies by the veterinarians are presented in Figure 1. For the female dog with sporadic bacterial cystitis, local²⁴ and international²⁵ guidelines recommend low-importance amoxicillin or trimethoprim-sulfonamide (TMS) for 3 to 5 days only. When discussing this case, five of the 22 participants selected an antimicrobial drug concordant with the local guidelines²⁴ (amoxicillin or TMS), but only one also selected a guideline-concordant duration of treatment (3-5 days). Most participants (13/22) selected medium-importance amoxicillin-clavulanate for 7-21 days and four selected high-importance enrofloxacin for 3-10 days. It should be noted that empirical amoxicillin-clavulanate is considered acceptable in the international guidelines when amoxicillin without clavulanate is not readily available²⁵ but no guidelines recommend empirical enrofloxacin.

		Local antimicrobial importance ratings of selected drug							
		n/a	Low importance			Medium importance		High importance	
		No antimicrobial therapy	Amoxicillin	Doxycycline	Trimethoprim-sulfonamide (TMS)	Cephalexin	Amoxicillin-clavulanate	Enrofloxacin	Cefovecin
Dog with sporadic bacterial cystitis (bacilli)	Number of participants	-	4 veterinarians*	-	1 veterinarian*	-	13 veterinarians	4 veterinarians	-
	Duration range	-	7-14 days		3 days*		7-21 days	3-10 days	
Cat with fight abscess, surgically drained	Number of participants	2 veterinarians*	1 veterinarian*	1 veterinarian	-	1 veterinarian	12 veterinarians	-	5 veterinarians
	Duration range	-	duration not collected	7 days		duration not collected	5-7 days		14+ days (single long-acting injection)

* local guideline-concordant management

Figure 1: Management selected by participants for the two case studies

Local guidelines²⁴ recommend that an uncomplicated cat fight abscess should be managed surgically, without systemic antimicrobials. Only two of the 22 veterinarians selected this management. If antimicrobials were considered necessary (e.g. because of systemic illness, which was implied in the case study), guidelines recommend low-importance amoxicillin for 5-10 days. Of the 20 who chose to use antimicrobials, only one selected amoxicillin. Again, most (12/20) selected medium-importance amoxicillin-clavulanate and 25% (5/20) selected long-acting (14-day duration), high-importance cefovecin.

Although our study design and small sample size prohibit generalizations from these data, they are consistent with prescribing patterns in large-scale quantitative studies of Australian veterinary prescribing,²⁶⁻²⁸ which have shown that veterinarians frequently use both higher importance drugs and longer durations of treatment than guidelines recommend.

Semi-structured interviews

A wide range of factors influenced participants' choices of antimicrobial drug, dose and duration for dogs and cats. An overview of these factors is shown in Table 1. Illustrative quotations for the listed factors are provided in subsequent tables, and referred to by their quotation codes (e.g. C1) within the text.

Table 1: Overview of factors influencing veterinarians' choices of antimicrobial drug, dose and duration

Case factors	Veterinarian factors
• Clinical features of case • Likely pathogen(s) • Animal temperament and environment • Potential for direct adverse effects	Selecting drug and dose: • Knowledge and past experiences • Concern about AMR • Access to continuing veterinary education (CVE) and relevant, reliable prescribing resources • Communication skills, confidence, relationship with owner • Energy and emotional state • Habit and familiarity Selecting duration: • Knowledge and past experiences, awareness of duration guidelines • Fear of relapse • Uncertainty about relationship between treatment duration and AMR risk • Beliefs about 'finishing the course' • Attitudes to other approaches to duration of therapy
Antimicrobial drug factors	
• Ease of dosing (size/volume, route, divisibility, palatability, duration of action) • Cost to pet owner • Spectrum of activity • Penetration of affected tissue • Non-antibacterial effects	Veterinary practice and colleague factors • The 'dispensary cycle': colleagues' prescribing habits and 'what's on the shelf' • Influence of veterinary colleagues • Influence of broader veterinary community • Influence of veterinary specialists • Financial considerations • Clinic charging policies • Prescribing resources in the clinic • Clinic culture • Time pressure • Capacity to follow up with owner
Pet owner factors	
• Capability, opportunity and motivation to give oral medications • Financial constraints • Relationship with veterinarian • Expectations of receiving a particular medication • Understanding of AMR	External factors • Antimicrobial label information • Information provided in culture and susceptibility reports • Pharmaceutical company marketing

Individual case factors

'If it's bright and happy and not systemically unwell, I'd be a lot more light-handed.'

Veterinarians mentioned several case factors they considered when selecting an antimicrobial drug (Table 2). Severe clinical signs (C1, O11), particular illnesses such as peritonitis (C2), and more uncertainty about the pathogens (C2) prompted veterinarians to select broader-spectrum antimicrobials, multiple antimicrobials, or both, to 'cover all bases' (C3). Relapse or recurrence of infection was cited as a reason to use both a higher-importance or broader-spectrum antimicrobial (C4) and a longer duration of treatment (C1, C4) than for an initial presentation. Where available, information about the pathogen, such as bacterial morphology (C5) or culture and susceptibility results (C6), also was considered.

Table 2: Case factors (C) influencing veterinarians' choice of antimicrobial drug, dose and duration in companion animals

Factor	Quotation code	Quotation, participant code and demographics
Clinical features of case, expected pathogen(s)	C1	If it's been ... on antibiotics and relapsed , or something that's really severe , I think [I'd give a longer course of antimicrobials]. Probably also just the dog's or cat's clinical status ; if it's bright and happy and not systemically unwell, I'd be a lot more light-handed , whereas the dog that I had with pneumonia ... was quite flat ... Veterinarian R, 28F*, regional CA practice, high interest in AMR/AMS
	C2	I would tend to use a broader-spectrum [antimicrobial] for a [gastroenteritis] issue or peritonitis issue because ... it could be anything . I mean, it could be E. coli, could be [Staphylococcus], [Streptococcus]. So you're going to use a broad-spectrum [antimicrobial]. If it's a skin thing , you can be a bit more selective because it's going to be a [Staphylococcus] or a [Streptococcus] mostly. So, I will tend to narrow my choice of spectrum. Veterinarian G, 26F, rural mixed practice, moderate interest in AMR/AMS
	C3	Some colleagues will say, 'Let's stick it on [enrofloxacin], metronidazole and amoxiclav just to cover all bases .' Which is not something I would tend to do, unless I have some kind of culture, or unless something was about to die and the owners didn't have money and it was the only thing I could think of. Veterinarian C, 33F, metropolitan CA practice, moderate interest in AMR/AMS
	C4	Cats that have had frequent urinary tract infections, like the older cats - if I've been seeing one for its third UTI in the last six months - I might reach for enrofloxacin straight away, and do a longer course . Veterinarian F, 30F, metropolitan CA practice, moderate interest in AMR/AMS

Information about the bacteria	C5	[The antimicrobial I would choose for a UTI] depends whether I've got cocci or whether I've got rods . I run a lot on the morphology of what I've got. So, if I've just got cocci, then then I'd be using [amoxicillin-clavulanate] before I'd go anywhere else... [For a UTI with rods] my first antibiotic of choice ... would be enrofloxacin. Veterinarian S, 66M, regional CA practice, low interest in AMR/AMS
	C6	If I got [culture and susceptibility test] results back, then I would probably swap over [from initial empirical amoxicillin-clavulanate] depending on what that comes back as. Veterinarian D, 25F, regional CA practice, high interest in AMR/AMS
Animal temperament and environment	C7	I tend to reserve [long-acting cefovecin] if it's like a really, really fractious animal...when I have a lot more aggressive dogs that kind of screws up me being able to dole out oral antibiotics at all. Veterinarian D, 25F, regional CA practice, high interest in AMR/AMS
	C8	[Whether I use long-acting cefovecin] will really be decided by the cat's behavior like whether it's going to stress the cat more than anything to try and medicate it twice a day. Veterinarian C, 33F, metropolitan CA practice, moderate interest in AMR/AMS
	C9	If [the owner] said, "No, he's an outdoor cat , there's no chance I'll be able to catch him twice a day, I would go with [long-acting cefovecin]." Veterinarian C, 33F, metropolitan CA practice, moderate interest in AMR/AMS
Potential for direct adverse effects	C10	I tend to be a bit less gung-ho about giving antibiotics to younger animals and certainly [I'm more selective in] the types of antibiotics I'm giving... both [to reduce the disruption to] ... normal flora, so gut, skin, whatever. But also other direct effects like enrofloxacin on [growing] bone and joints. Veterinarian T, 40M, metropolitan CA practice, moderate interest in AMR/AMS
	C11	Sometimes we do [keep stock of TMS], not much. I don't want to cause dry eye . I use it every now and then for urinary tract infections, but I find the dose a bit awkward with the tablets. And I think you normally buy like a bottle of 200 or something...I don't use them much. Veterinarian N, 29F, rural CA practice, moderate interest in AMR/AMS

**Age in years and gender; F, female; M, male. CA, companion animal. Bold text added to highlight key phrases.*

The animal's temperament and environment were important, particularly for cats that were fractious (C7, C8) or free roaming (C9). These factors made PO administration of medications more difficult for owners, prompting the use of long-acting cefovecin injections.

Contraindications were considered, such as the adverse effects of fluoroquinolones on growing animals (C10). The risk of adverse effects of TMS (C11, V7) in dogs was a concern for some veterinarians; they seemed unaware that this risk could be decreased by using short durations of treatment.

Antimicrobial drug factors

'It just has to get to the place that I'm trying to get to ... then you just choose based on a few other things like cost, ease of administration, volume of administration...'

Factors relating to the antimicrobial drugs themselves were very important in veterinarians' choices (Table 3). Practical considerations were paramount; the ease of achieving the correct per kilogram dose rate was mentioned by multiple veterinarians as a strong influence on the drug prescribed (A1, A2, A3, A7, A10, C11). Patient body weights in companion animal practice can vary markedly, from a 100 g newborn kitten to a 100 kg adult giant breed dog. Veterinarians described challenges at both ends of the weight spectrum, whether because of the need to split tablets into fractions (A1, A2) or needing several tablets to make up a single dose (A11). Capsules were noted to be difficult to divide (A10) for smaller animals. Lower-volume veterinary practices struggled to maintain an inventory of antimicrobials in a wide range of dose sizes, particularly when supplier minimum order quantities were large (C11).

Table 3: Antimicrobial drug (A) factors influencing veterinarians' choices of antimicrobial drug, dose and duration in companion animals

Factor	Quotation code	Quotation, participant code and demographics
Ease of dosing (formulation, size/volume, route, divisibility, palatability, duration of action)	A1	Sometimes [your preferred antimicrobials] are not available to you or what you have on hand ... [or available] in certain sizes. So, metronidazole tablets, the smallest we have is 200 milligrams, and if I've got a little kitten or puppy that needs something like that, it's really hard to cut a tablet into eighths , otherwise it's got to be intravenous and ... you have to hospitalize them to do that... things like that can be really hard. <i>Veterinarian E, 24F*, regional CA practice, moderate interest in AMR/AMS</i>
	A2	What's the easiest way I can divide this tablet and not give them too much ? ... [If I need to give 300 milligrams] ... Okay, let's give a 500 milligram tablet and divide it...[into] three quarters , things like that ... do play on my mind. I do get clients that, especially if they're old , they struggle to divide tablets up and ... I do try to divide it for them, but then it often crumbles ... So things like that do come into play. <i>Veterinarian D, 25F, regional CA practice, high interest in AMR/AMS</i>
	A3	I would probably choose amoxicillin-clavulanate as my first-line [empirical treatment for the dog UTI]. Because I'm suspecting <i>E. coli</i> , I guess. And it's cheap and easy to give and the ... tablet sizing is quite easy. So, it's generally my first go-to antibiotic for everything . <i>Veterinarian G, 26F, rural mixed practice, moderate interest in AMR/AMS</i>
	A4	Palatability is a big thing. Pretty much the only thing I can give as a liquid is [amoxicillin-clavulanate] palatable drops. You can get [enrofloxacin] but you can't give [enrofloxacin] to cats. So that limits things as well. And if you go and get something compounded , it is hellishly expensive ... and could take five days to come in, and you need it now... If there were more liquid formulations... that'd be nice. <i>Veterinarian M, 28F, regional CA practice, low interest in AMR/AMS</i>

	A5	Most clients are hopeless at medicating their cats with tablets, in particular. Even liquids as well.... the only medications that I would say that our clients consistently, successfully give to cats are probably the transdermals and pastes and things ... flavored pastes like doxycycline they're a bit more successful with. But in terms of your tablets and liquids, it's pretty hit and miss . It's mostly miss! [laughs] <i>Veterinarian T, 40M, metropolitan CA practice, moderate interest in AMR/AMS</i>
	A6	TMS is a difficult one, because obviously, it's a good one to use as a first-line [empirical antimicrobial]. But it is also very difficult to dose in cats. It's difficult to administer because it tastes like shit ... So I don't really use it ... unless I absolutely have to. <i>Veterinarian V, 36F, metropolitan CA practice, moderate interest in AMR/AMS</i>
	A7	If there's not an easy size, flavoring , or whatever, it's going to be a lot harder for vets to use those [medications]. [Pharmaceutical manufacturer] did something a couple years ago, all their tablets were hideous tasting ... generic ... their cephalexin ... tablets... were horrible and trying to get them into animals was a nightmare! At some point, they did flavor them and that's made a massive difference to how much we can now easily use those drugs. <i>Veterinarian T, 40M, metropolitan CA practice, moderate interest in AMR/AMS</i>
	A8	If it is a cat that isn't going to be easily handled , obviously I will go down the track of [a long-acting cefovecin injection] ... and I wouldn't think twice about it. <i>Veterinarian J, 32F, metropolitan CA practice, high interest in AMR/AMS</i>
	A9	Everyone wants simplicity , you don't want to struggle with your cat to put things down [its throat]. You start cursing your vet if you get scratched and bitten , so I think there should be something easier ...If there was something like [long-acting cefovecin] but it wasn't [cefovecin] ... maybe an injection of a longer-acting penicillin or a longer-acting doxycycline... or a gel that you could put under the skin, that would be good. <i>Veterinarian B, 31M, metropolitan CA practice, high interest in AMR/AMS</i>
Cost to pet owner	A10	... as long as it's a responsible choice then probably, [I consider] cost to the client and ... the formulation of the tablet we have on the shelf, like, Is it a tasty tablet? ... Or is this a capsule that they can't break in half? ... Things like that. <i>Veterinarian C, 33F, metropolitan CA practice, moderate interest in AMR/AMS</i>
	A11	Cost does come into it ... There are dogs, especially large ones that I would love to put on cephalexin because the amoxiclav dose, they'd have to eat two or three tablets twice a day . It's not feasible . But the cephalexin is extremely expensive for the client ... I definitely have that as a conundrum . <i>Veterinarian D, 25F, regional CA practice, high interest in AMR/AMS</i>

	A12	Sometimes you say, 'Well, I think clindamycin will work really well here, but it's four times the price of amoxiclav. This person has no money . I'm going to give them the amoxiclav.' ... [Cost] is probably a bigger factor than it should be ... I rarely use [long-acting cefovecin] in a dog, just because it's really expensive . <i>Veterinarian M, 28F, regional CA practice, low interest in AMR/AMS</i>
Spectrum of activity	A13	I do kind of try and have a list of possible bacteria and then pick a spectrum from that. So, in reptiles [enrofloxacin] is actually quite good because it's often a Gram-negative [pathogen]. <i>Veterinarian G, 26F, rural mixed practice, moderate interest in AMR/AMS</i>
Penetration of affected tissue	A14	[I think] more about penetration and less about spectrum [of activity] because I don't know exactly what bacteria I'm treating ...then you just choose based on a few other things like cost, ease of administration, volume of administration . <i>Veterinarian G, 26F, rural mixed practice, moderate interest in AMR/AMS</i>
Non-antibacterial effects	A15	I probably wouldn't use anything other than metronidazole for diarrhea . Mostly I use metronidazole because it has that sort of anti-inflammatory type effect. I can give it IV. It's easy to send home on and it's cheap . <i>Veterinarian G, 26F, rural mixed practice, moderate interest in AMR/AMS</i>
	A16	Well [we use] that one [metronidazole] for ... inflammatory bowel disease ... [to reduce] inflammation in guts and also doxycycline for eyes is the other one... where I'm not actually massively worried about the infection... It's something that ... I've been advised to do by specialists and ... it seems to work, so we do it. <i>Veterinarian T, 40M, metropolitan CA practice, moderate interest in AMR/AMS</i>

*Age in years and gender; F, female; M, male. CA, companion animal. Bold text added to highlight key phrases.

The palatability of PO antimicrobial formulations was another prominent practical consideration (A4, A7), especially for cats. Palatability was cited as a reason to use amoxicillin-clavulanate, which is available as a palatable liquid (A5), and doxycycline, which is available in a flavored paste for cats (A4), over other options. Poor palatability was mentioned as a reason not to comply with antimicrobial use guidelines. For example, TMS is recommended as an empirical treatment for sporadic urinary tract infections in dogs and cats, but was felt to be impractical in cats because of its bitter flavor (A6).

Dosing route and frequency were important determinants of drug selection. Most systemic antimicrobial regimens used in companion animal outpatient practice require at least once daily PO dosing (most commonly twice daily) for at least 3 days. Only one antimicrobial (cefovecin) is currently available as a single, long-acting injection that lasts for this duration.

Hence, where a combination of animal temperament (C7, C8, O1), environment (C9, O2) and owner factors (O1, O2, O3) pointed to difficulties with PO administration (A9), the 'simplicity' of cefovecin was appealing to some participants, and more likely to outweigh any concerns about

AMR risk (O1, O3). Some veterinarians would use this option without a second thought (A8), whereas others would ‘struggle’ with it (D12). One practice had stopped stocking cefovecin, and the staff had developed innovative ways to assist pet owners who could not administer antimicrobials PO (P19). Participants expressed a wish that pharmaceutical companies would develop more user-friendly formulations of low-importance antimicrobials (A9), such as long-acting injections, palatable pastes and liquids, and transdermal medications, as well as topical treatments for otitis externa that do not contain antibacterial drugs (P22).

The cost of the antimicrobial to the owner was mentioned frequently (A3, A4, A10, A15). Veterinarians said they had sometimes not prescribed their preferred antimicrobial drug, to minimize cost (A11, A12).

The antimicrobial’s spectrum of activity (A13) and the ability of the drug to reach the affected tissue (A14) were mentioned by veterinarians as part of their choice. Non-antibacterial effects, such as immunomodulation, also played a role in drug choices (A15, A16).

Owner factors

‘I don’t want to save the world from antibiotic resistance, but cause an old lady to break a hip!’

A range of owner factors were important in veterinary antimicrobial choices (Table 4). The owner’s capability, opportunity, and motivation to administer medication to their animal were important factors in the veterinarian’s choice of antimicrobial agent. Owners who were disabled or frail (O1, O3), too busy or simply ‘blasé’ (O2), or couldn’t catch their outdoor cat (C9) caused some veterinarians to offer an injection of cefovecin, even when their preferred choice was a PO antimicrobial. Veterinarians felt this choice was justified to ensure the animal received a ‘complete’ course (D10, D11).

Table 4: Pet owner (O) factors that influence veterinarians' choice of antimicrobial drug, dose and duration in companion animals

Factor	Quotation code	Quotation, participant code and demographics
Capability, opportunity and motivation to give oral medications	O1	I only tend to use [long-acting cefovecin] if it's a really, really, really fractious animal, and it would benefit this animal to be on antibiotics rather than missing a bajillion doses or having that owner’s head bitten off . Or it's a client that's quite disabled or has difficulty tableting a dog or cat that's otherwise fine to tablet... If I have an old arthritic lady where it's a pain for her to get to the clinic I'll be like, ‘Look, we do have [long-acting cefovecin]. I don't like using it because [it] encourages resistance . It has its pros and cons and it is quite expensive . If you are okay to go ahead with that, then we can.’ Veterinarian D, 25F*, regional CA practice, high interest in AMR/AMS
	O2	If the client is afraid of handling the cat or if they're busy and if they seem like they're not going to remember , they're too blasé or whatever, then my feeling would be, ‘Well at least he has this [long-acting cefovecin] in his system .’ Veterinarian C, 33F, metropolitan CA practice, moderate interest in AMR/AMS

	O3	Which is the lesser of two evils ... the risk of me creating some antibiotic resistance in this German Shepherd, or this old lady falling over and breaking her hip [trying to give the dog antimicrobial tablets]? ... A 90 year-old lady with a German Shepherd, I might say, the safest option is [long-acting cefovecin]... I don't want to save the world from antibiotic resistance, but cause an old lady to break a hip! ... I try and work out ... whatever [antibiotic will give] the best outcome for that particular patient and client, and somewhere on the list, the world . Veterinarian T, 40M, metropolitan CA practice, moderate interest in AMR/AMS
	O4	Three days [of antimicrobial treatment] for most people is not that difficult ... There are many things I've sent home on longer courses that don't get the full course , as much as we try and tell them it's important . I know that, because ... they'll come back and say, 'Oh, I've still got these tablets leftover from the last course...' ... Three to five days would be the perfect window ... the majority [of owners] would be OK up to a week . But beyond that, I'm skeptical of how many actually [continue giving antimicrobials]. Veterinarian T, 40M, metropolitan CA practice, moderate interest in AMR/AMS
	O5	I mean, I'm useless at taking a multivitamin! And I suspect that if I can put a little bit of the fear of God into an owner about antimicrobial resistance , that they can probably follow those instructions for three to five days . I suspect any longer than that ... they are going to forget or they're going to have other commitments that impair them, or the animal is going to become savvy to tablets in a meatball. Veterinarian P, 35F, metropolitan CA practice, high interest in AMR/AMS
Financial constraints	O6	My clients are a little bit more cost-constrained.... and have much larger dogs ... whereas when I was in [my first job], they were basically...Cavoodle, city-type [dog breeds]; I didn't have to worry about having to dose 1000 milligrams of [cephalexin] or something ... Cost does influence my prescribing a lot more than I care to acknowledge. When I think about it, I can't use any of those [antimicrobials] because a client can't afford that ... if I don't give this – not necessarily the antibiotic that the client wants – but if I pick the cheaper of the two, that's the only way they're going to afford to do it . Otherwise, they're just not going to [treat] it, and they're not going to euthanize it. So, they're just gonna leave it to suffer . And ... it's definitely something I [feel] responsibility for. Veterinarian D, 25F, regional CA practice, high interest in AMR/AMS
	O7	I'd say maybe one [owner] every few months, will just say that they can't [tablet their cat] and then I will have no qualms in giving [long-acting cefovecin] a go. But most of them, if you say [long-acting cefovecin is] going to be double the cost of tablets , then they'll try [the tablets]. Veterinarian F, 30F, metropolitan CA practice, moderate interest in AMR/AMS

	O8	... there's a massive cost difference as well [between a long-acting cefovecin injection and amoxicillin-clavulanate tablets] and for most clients, that's adequate [to convince them]. In our setting anyway, cost is a reasonably good deterrent . Veterinarian T, 40M, metropolitan CA practice, moderate interest in AMR/AMS
	O9	Occasionally an owner will want something [an antimicrobial] liquid , and I'll give it to them. But it's so expensive that I say, well, if you can get the tablets down , it's gonna cost you \$5. If you want the liquid, it's gonna cost you \$30, please yourself! Veterinarian H, 68M, regional mixed practice, high interest in AMR/AMS
Relationship with veterinarian	O10	[If the owner said they would prefer not to give tablets] I'd probably tell them to suck it up and do it! [laughter] ... I guess I need to preface that with, my clients are incredibly compliant and really good at things. We have an incredible clientele ... compared to other clinics locally, my clients are very, very good. Veterinarian Q, 43F, regional CA practice, high interest in AMR/AMS
	O11	I might have chosen a heavier-duty antibiotic than ... necessary. The reasoning that goes through my head in those instances is ... 'It's just a really sick animal. And this [antimicrobial] will probably do it, but I just feel safer if I hit it with something a bit harder .' It's probably more ... the case of a difficult client that you've had trouble with communicating with and you feel like you're still not really on the same page, and maybe there's a touch of worry that they're going to come back ... they're going to be pissed off and all that sort of thing. So let's make absolutely sure . Veterinarian U, 39F, regional mixed practice, low interest in AMR/AMS
Expectations of receiving a particular medication	O12	I didn't think [the cat] needed any [antibiotics] at all. And [the owner] was still like, 'No, my wife said he has to have some ,' and I said, 'All right, I'll give you some [amoxicillin-clavulanate].' And he's like, 'No, no, it has to be an injectable or she'll be very angry with me.' There's that expectation, I've had [this] antibiotic before; I want it again ... They had an abscess done six months ago and it got [long-acting cefovecin], and so [my colleagues] were like, 'Just give it again,' because if for some reason it didn't go well, it would come back to bite me in the butt... [My colleagues] use that drug quite a lot so it's harder for me to say , 'I don't think it's the best option here,' because then they'll be like, 'Well, all those other much more experienced vets use it and ... it's always gone super well when it's had that.' So obviously, when you've been [in practice for] six months it's, you know... Veterinarian E, 24F, regional CA practice, moderate interest in AMR/AMS
	O13	[Clients] can definitely ... feel that we're not listening to ...not necessarily demands , but concerns about trying any other way of tableting. Because their previous experience ... [giving antimicrobial tablets] just didn't work , so, 'Just go straight to the [long-acting cefovecin], I don't want to have to fluff around

		and then come back to you...' Veterinarian D, 25F, regional CA practice, high interest in AMR/AMS
	O14	God, if I don't give them what they want, they're going to scream at me . They might not directly scream at me, but they'll scream at someone . Veterinarian D, 25F, regional CA practice, high interest in AMR/AMS
	O15	Part of that [decision] is client expectation as well. If you give a client, say, a week of [antibiotics] and the dog needed two weeks, then they'll be annoyed about having to come back , pay a recheck fee , pay for more antibiotics ... And they might make that clear to you as well; 'I just want this thing sorted and I don't want to have to keep coming back!' Then I'm going to be more inclined to give them a course that [I'm] fairly confident that is going to really get on top of that infection. Veterinarian C, 33F, metropolitan CA practice, moderate interest in AMR/AMS
Understanding of AMR	O16	We tend to avoid using [long-acting cefovecin] where possible ... because of [antimicrobial] resistance , which most of our clients have heard of in some form they kind of know that word. So, we would definitely recommend ... that we stick to either a liquid form or a tablet form [of another antimicrobial]. And hide it in food, that sort of thing. Veterinarian U, 39F, regional mixed practice, low interest in AMR/AMS

**Age in years and gender; F, female; M, male. CA, companion animal. Bold text added to highlight key phrases.*

Some participants felt that 5 to 7 days was the upper limit for the duration most pet owners could reliably dose their animal, either because of memory (O4, O5) or time (O5) limitations, or because the animal would become more avoidant (O5). Owners admitting to having leftover antimicrobial doses (O4) was evidence of non-completion of previous antimicrobial courses.

Owner financial constraints interacted with the differing costs of antimicrobials (discussed in the previous section) to guide drug choice (O6, O7, O8, O9). When financially constrained owners also had large dogs, requiring a higher antimicrobial dose, the effect was compounded (O6). Cost constraints could be so severe that the veterinarian feared the owner might choose no treatment at all, leading to animal welfare concerns (O6). Conversely, sometimes the expense of an antimicrobial drug helped the veterinarian convince a pet owner to accept a cheaper alternative (O7, O8, O9), which may be less convenient, but more appropriate.

A trusting, friendly relationship with a 'good' client may assist in persuading the owner to give PO antimicrobials rather than giving a more convenient, long-acting injection (O10). Conversely, a difficult or distrustful relationship encouraged defensive prescribing, which could mean using a broader-spectrum antimicrobial than necessary (O11, O14) or a longer duration of treatment, or both (P19).

Some veterinarians described the difficulty of dealing with explicit owner expectations or requests for a long-acting antimicrobial injection rather than a PO formulation (O12, O13, O14), particularly when the owner had seen the injection used for a similar presentation (O12, O13). Less experienced veterinarians were sometimes reluctant to appear to the owner to contradict the previous drug choice of a more senior veterinarian (O12), preferring instead to repeat their colleague's selection.

In addition to influencing the choice of drug, owner expectations could influence the duration of treatment chosen. If the owner expressed unwillingness to return for a revisit, the veterinarian might select a longer course (O13, O15).

An owner's pre-existing understanding of AMR could assist with avoiding cefovecin use (O16), allowing a more productive discussion of the reasons to opt for a PO medication instead.

Veterinarian factors

Selecting drug and dose

'I probably overuse [amoxicillin-clavulanate] because it seems safe. Like you can use it in pregnant dogs. You can use it in young dogs. And I feel like it covers 90% of problems.'

Many factors relating to the veterinarian were important in their choice of antimicrobial drug and dose (Table 5a).

Frequent empirical use of broad-spectrum antimicrobial treatment, particularly amoxicillin-clavulanate, was described by multiple participants (V1, V2, V3) to 'cover all bases' (V4), with one participant unable to see any reason to select a narrower spectrum antimicrobial (V3). Broad-spectrum treatment gave veterinarians a sense of safety (V1, V2, D7), reinforced by treatment success (V1, V2, V9) and low rates of overt adverse effects (V2). Safety and treatment success became especially important when the veterinarian felt vulnerable, such as during a 'run of bad clients who were grumpy' (V5).

Table 5a: Veterinarian (V) factors influencing choice of antimicrobial drug and dose in companion animals

Factor	Quotation code	Quotation, <i>participant code and demographics</i>
Knowledge and past experience	V1	I probably overuse [amoxicillin-clavulanate] because it seems safe . Like you can use it in pregnant dogs. You can use it in young dogs. And I feel like it covers 90% of problems. <i>Veterinarian M, 28F*, regional CA practice, low interest in AMR/AMS</i>
	V2	[Amoxicillin-clavulanate] is user-friendly, broad spectrum . Feels kind of safe ... I think you're like most likely to have a benefit using something broad-spectrum like that ... I rarely see any side effects , it's hard to overdose - if they do have too much, if the owner got the dose wrong, you get a [gastrointestinal] upset, that's about it! <i>Veterinarian E, 24F, regional CA practice, moderate interest in AMR/AMS</i>
	V3	I think that if I can get a better activity with the combination [amoxicillin-clavulanate] , then why am I staying with straight amoxicillin? <i>Veterinarian S, 66M, regional CA practice, low interest in AMR/AMS</i>
	V4	In that first year [of clinical practice], I would put so many cases on cephalexin plus metronidazole at the same time because I thought that that would be broad spectrum and sort of cover all my bases ...I remember doing that willy nilly ... <i>Veterinarian F, 30F, metropolitan CA practice, moderate interest in AMR/AMS</i> .

	V5	I'm sort of aware that [amoxicillin-clavulanate] is probably higher than I necessarily need for most urinary tract infections. But I guess I've found that it always clears them... If I've had a run of bad clients who were grumpy because things didn't work. I'm like, 'Nup...I'm gonna go with the [antimicrobial regimen] that's always worked for me. ' <i>Veterinarian N, 29F, rural CA practice, moderate interest in AMR/AMS</i>
	V6	Generally, when I see rods [bacilli] in the urine ... I'm probably going to reach for [enrofloxacin], rightly or wrongly, just because I haven't had much luck with [amoxicillin-clavulanate] when there's rods involved. So, based on past experience , I'd probably go for [enrofloxacin], unless it was a dog under 12 months [of age] . <i>Veterinarian M, 28F, regional CA practice, low interest in AMR/AMS</i>
	V7	Back in my real-world general practice days, probably [my first choice for a bacillary urinary tract infection] was TMS. Because it was cheap . So, for the clients who can't afford a culture and sensitivity, they can afford TMS. And it worked . And you don't have to worry if it's an intact male dog and probably TMS was my go-to in [those] days. And now, I have become unreasonably nervous [about using TMS] because of a handful of cases that have had side effects. <i>Veterinarian Y, 39F, metropolitan CA practice, moderate interest in AMR/AMS</i>
	V18	I think probably from university , they've kind of drilled it into us , 'Don't ever use [enrofloxacin] unless you have a culture or it's a nasty prostatitis or something like that.' So there's a bit of a fear element of 'Ooh, [enrofloxacin]! <i>Veterinarian C, 33F, metropolitan CA practice, moderate interest in AMR/AMS</i>
	V9	I would generally use what I thought has the highest likelihood of success, that's necessary , if that makes sense. So even though I'm aware that [enrofloxacin] would probably work quite well, I wouldn't jump to that or any of the fluoroquinolones because it's unlikely it needs that. I tend to reserve those for more difficult cases . So [amoxicillin-clavulanate] and cephalexin, I know that most UTIs would respond to one or the other of those. The only reasons I might look at alternatives in terms of something stronger - for want of a better word - would be if it was a dosing issue . <i>Veterinarian T, 40M, metropolitan CA practice, moderate interest in AMR/AMS</i>
Concern about AMR	V10	Do I consider resistance with it? Not consciously ... I'm certainly not thinking, if I use this, I might create a resistance issue. <i>Veterinarian T, 40M, metropolitan CA practice, moderate interest in AMR/AMS</i>

	V11	Then you have [enrofloxacin], but you don't really want to be using that... I try and make that the last option ...from vet school, it's all drummed into you "Don't be using [enrofloxacin] unless you have to." From a resistance point of view, that's just something ingrained in me...With cats it's more difficult . [Long-acting cefovecin] gets a fair bit of use . <i>Veterinarian E, 24F, regional CA practice, moderate interest in AMR/AMS</i>
Access to continuing veterinary education (CVE) and prescribing resources	V12	I had slipped across [from using amoxicillin] to using amoxicillin-clavulanate. And ... this CVE course I did... said that there was no particular advantage to the clavulanate , because the probability of it working as a first-line treatment [in cystitis] was just as good for amoxicillin as it was for the mixture and ... I got the courage to go back to just using amoxicillin for cystitis, in the face of my colleagues that were using [amoxicillin-clavulanate]. <i>Veterinarian H, 68M, regional mixed practice, high interest in AMR/AMS</i>
	V13	I try to use the [University of Melbourne] website [which has antimicrobial prescribing guidelines for common conditions]. Sometimes I won't, or can't follow it exactly for whatever reason, but I do try. Especially if it's [a condition] that I haven't seen a lot of , that's not stock-standard, I will look up ... what I'm supposed to be doing ... <i>Veterinarian R, 28F, regional CA practice, high interest in AMR/AMS</i>
	V14	VIN [US website] and the BSAVA [UK] textbooks are probably the things that I use the most in clinic when I need an answer relatively quickly. If I've got a little bit of time up my sleeve, I often go home and [look up] online sources , most of them are either American or European . And that's probably where I get the bulk of my information. The other [source] that I go to in clinic is other vets ... especially if it's something that needs [treatment] to be started straight away. <i>Veterinarian J, 32F, metropolitan CA practice, high interest in AMR/AMS</i>
	V15	I want to be better . But I just don't have the time to read ... And I can't get into any [paywalled journal] articles. Because you need, like, 'uni-ness' [a connection to a university] for subscribing to journals and such ... So, I pretty much base [my antimicrobial prescribing] on VIN [US website] or the Merck Manual ... But there's no journal articles . <i>Veterinarian G, 26F, rural mixed practice, moderate interest in AMR/AMS</i>
	V16	I just want guidance! ... It's a little bit overwhelming ...just give me a dose! For example ... in Plumb's [Veterinary Drug Handbook] ... every time I look up doxycycline, I'm like, 'You're not giving me a direct answer as to what I need to do here. You're giving me five different doses and different ways of dosing.' And I'm like, can I do either and it'll be okay? <i>Veterinarian D, 25F, regional CA practice, high interest in AMR/AMS</i>

	V17	I guess probably accessibility of the information as well ... we have information overload when it comes to publications. And it's fundamentally because we have such a breadth of knowledge that we need to maintain . <i>Veterinarian L, 32M, metropolitan CA practice, high interest in AMR/AMS</i>
Communication skills, confidence, relationship with client	V18	I didn't also realize how much of it's just ... being able to communicate that to clients , why they need to do things a certain way, why they have to dose it twice a day ... that definitely influences my decision [about which antibiotic to use]. <i>Veterinarian D, 25F, regional CA practice, high interest in AMR/AMS</i>
	V19	We usually just tell [owners] that they have to suck it up and do it [give oral antibiotics to their cats]! [laughs] There's just not a lot of room for argument . <i>Veterinarian Y, 39F, metropolitan CA practice, moderate interest in AMR/AMS</i>
	V20	I think there's probably more confident , more outgoing people out there who would have probably spoken up , like, 'This is not what I was taught,' or 'I'd rather not use it.' But ... for new grads , you always get worried that you're doing the wrong thing . <i>Veterinarian D, 25F, regional CA practice, high interest in AMR/AMS</i>
	V21	If it's a client where we have written on their file "very difficult", I don't have the emotional, physical or mental energy to ... debate this with this person. As long as I've said my spiel as to why I don't like prescribing [long-acting cefovecin] when you can probably tablet this animal, then fine. But ... I do it more to cover my own ass than really to practice good antibiotic stewardship. <i>Veterinarian D, 25F, regional CA practice, high interest in AMR/AMS</i>
Energy and emotional state	V22	I'm sure you will see at the start of the vet's shift , there is less pattern recognition and the further you get towards the end of it, you're just eergh [tired sound], I think that plays a role. <i>Veterinarian A, 45F, metropolitan CA practice, high interest in AMR/AMS</i>
	V23	When I'm really stressed , and I've got a lot going on and I just want to get that case out of the way , I'm more likely to go to the [amoxicillin-clavulanate] . But when I don't have that much on my plate and I can talk to [the owner] and I think, 'No I'm going to be a responsible vet today.' ... and then I feel quite good about myself because I'm contributing less to antibiotic resistance. <i>Veterinarian N, 29F, rural CA practice, moderate interest in AMR/AMS</i>
Habit and familiarity	V24	I suppose [I'd choose] something that I'm used to or something I know the dose off the top of my head , especially if it's a busy, busy, evening clinic, I'm like, 'Okay, let's just put them on cephalexin... 20 mg per kg.' Yeah, being honest about it, probably convenience for me as well. <i>Veterinarian C, 33F, metropolitan CA practice, moderate interest in AMR/AMS</i>

	V25	With so many vets, anything with diarrhea gets metronidazole because that's what they've always done! <i>Veterinarian P, 35F, metropolitan CA practice, high interest in AMR/AMS</i>
	V26	Habit! Habit, habit, habit! And it's hard to break it. You get complacent in your habits and you just get stuck in that thing. It's worked and the patient's alive! <i>Veterinarian B, 31M, metropolitan CA practice, high interest in AMR/AMS</i>
	V27	I think that's the primary thing is that it's something that you know , and you're comfortable with. <i>Veterinarian S, 66M, regional CA practice, low interest in AMR/AMS</i>

*Age in years and gender; F, female; M, male. CA, companion animal. Bold text added to highlight key phrases

Conversely, even a single experience of treatment failure (V6) or serious adverse effects (V7) with a particular antimicrobial could make a veterinarian 'unreasonably nervous' (V7) and disproportionately influence their long-term prescribing habits.

Although many participants were unaware of antimicrobial importance ratings and some said they did not consciously consider AMR risk when selecting an antimicrobial (V10), many conveyed concern about AMR (V11, V23, D7) and a sense of an antimicrobial hierarchy, using words such as 'stronger' (V9) or 'heavier-duty' (O11) to describe higher importance antimicrobials that they generally avoided prescribing. Fluoroquinolones were frequently mentioned in this category because of the high risk of AMR (V8, V9, V11), that had been 'drilled' into them at university (V8, V11). A few participants also mentioned cefovecin in this category, but awareness of AMR risk from this drug was less prominent than for fluoroquinolones, and therefore more easily outweighed by the practicality of a long-acting injection (V11).

For some participants, continuing veterinary education had shaped their antimicrobial drug choices (V12), as had awareness of antimicrobial prescribing resources, including guidelines (V13). However, several participants were using resources from other countries (V14, V15), which can be less relevant because of differences in the drugs available, the prevalence of different pathogens and AMR patterns.

Veterinarians also noted problems with the clarity and reliability of published antimicrobial dosages (V16), compounded by a sense of 'information overload' (V17) and the inaccessibility of pay-walled scientific literature (V15).

Veterinarians with strong client communication skills (V18) and confidence (V19, V20) felt more able to resist client pressure to prescribe a particular antimicrobial, but an exhausted veterinarian dealing with a 'difficult' owner (V21) was more likely to capitulate. Veterinarians also recognized that tiredness and stress caused them to default to suboptimal antimicrobial drug choices that demanded less cognitive energy (V22, V23, V24). Participants recognized that habit played an important role (P2, P10, V25, V26, V27) in their drug choices, particularly in stressful situations.

Selecting duration of therapy

'Am I treating it for long enough? Or am I treating it for too long? And where is the problem [of AMR] coming from? Is it treating too long, or not long enough?'

Veterinarians felt treatment durations (Table 5b) were sometimes picked ‘out of the air’ (D1), based on past experience (D2) or colleagues’ suggestions. Many were unaware of any prescribing guidelines on duration and some were concerned about the lack of veterinary evidence for treatment durations (D1). Fear of relapse encouraged longer durations; one participant felt safer treating a sporadic urinary tract infection for 2 to 3 weeks, despite a colleague drawing their attention to evidence that 5 days would suffice (D4). Another noted that if a particular treatment duration had proven effective, it could become ‘just what you do,’ with little impetus to shorten it (D3).

Table 5b: Veterinarian factors influencing choice of antimicrobial treatment duration (D) in companion animals

Factor	Quotation code	Quotation, participant code and demographics
Knowledge and past experience, awareness of guidelines	D1	I do just kind of make it up a bit. And ...I find it very hard to work out durations of things because there's no guidelines (<i>sic</i>) ... I feel like people are just picking numbers out of the air or based on, like, one study... but [researchers] haven't worked out what a minimum and what a maximum [duration] is. <i>Veterinarian G, 26F*, rural mixed practice, moderate interest in AMR/AMS</i>
	D2	I find you suddenly hear from humans [trials], “We’re going much higher dose for only 3 days” and you go, is that something we need to adopt here? ... I find it a bit hard to know, how long is enough? ... I would say some of that is experience-based and just something I say, I think this is going to be all right with 5 days [of antibiotics], I think this is going to be all right with 7 days, I think this one will be all right with 10 days. That is not very scientific! <i>Veterinarian A, 45F, metropolitan CA practice, high interest in AMR/AMS</i>
	D3	I think a lot of it is anecdotal experience. You know, you've seen enough cases and they survived when you... treated them with four to six weeks’ of therapy. So that's just what you do . Rather than thinking, would one week be effective? <i>Veterinarian Y, 39F, metropolitan CA practice, moderate interest in AMR/AMS</i>
Fear of relapse	D4	I was taught three weeks for urinary [tract infections], but ... one of our vets has said ... they don't need that long...I have gone as short as two weeks with some, [but] I haven't gone as short as five days, which is what she was suggesting ... But I'm not game enough to go to five days... that just doesn't seem long enough . Usually I'll either go a two- or three-week course . I guess for a first episode, maybe a two-week course. <i>Veterinarian T, 40M, metropolitan CA practice, moderate interest in AMR/AMS</i>
	D5	I do have times where I probably do push the antibiotics longer than what may be strictly necessary, just as a safety net . <i>Veterinarian V, 36F, metropolitan CA practice, moderate interest in AMR/AMS</i>
Uncertainty about relationship	D6	I don't know... you certainly don't want to underdose but ... do you create resistance by having short durations ? <i>Veterinarian G, 26F, rural mixed practice, moderate interest in AMR/AMS</i>

between treatment duration and AMR risk	D7	Am I treating it for long enough ? Or am I treating it for too long ? And where is the problem [of AMR] coming from? Is it treating too long or not long enough? <i>Veterinarian W, 39F, regional CA practice, moderate interest in AMR/AMS</i>
Concern about finishing the course	D8	... with any antibiotic use, I do want them to finish the course of whatever I give them. It's pretty pointless giving a course of tablets if it's only going to get three days of them. So I would rather give a [long-acting cefovecin] injection to a difficult animal, even though it may not be necessary for whatever the infection is, at least knowing that it's getting the full course of that. <i>Veterinarian T, 40M, metropolitan CA practice, moderate interest in AMR/AMS</i>
	D9	[Using a broad-spectrum antimicrobial] does make me feel a bit more secure , but it also makes me worry ... am I putting too much pressure on here? ... Resistance doesn't just miraculously occur... there has to be a certain duration of pressure ... I go, 'OK, I'm dispensing a broad spectrum than maybe is necessary , but I'll go the right dose and I'll go for a duration that I think is going to be effective, and then I'll very, very much encourage the people to finish the course . <i>Veterinarian A, 45F, metropolitan CA practice, high interest in AMR/AMS</i>
	D10	[Long-acting cefovecin] is so user-friendly . It's really good . Cats are so hard to tablet , you can't sort of hide it in a piece of meat and things like that...it's one injection that last seven (<i>sic</i>) days, it works for skin infections, it works for urinary tract infections, it's got a lot of uses ...What's the point of giving them ten days' worth of tablets , if the owners aren't even going to do it ?... And what's fair on the animal ? ... I think a lot of people find suggestions on antimicrobial usage don't really fit with what you can realistically ... get the client to comply with. <i>Veterinarian E, 24F, regional CA practice, moderate interest in AMR/AMS</i>
	D11	If half the tablets are going to end up in the dog and half the tablets aren't , I feel like that's worse [than giving long-acting cefovecin]. <i>Veterinarian N, 29F, rural CA practice, moderate interest in AMR/AMS</i>
	D12	I still have a real problem in my head about using long-acting cephalosporins in cats. But then I look at little old ladies that get scratched to bits by their cats and think, there's the human issue with that and compliance issues with that animal. Are we better off just giving one injection and knowing it's been done ? I really struggle with that. That's the biggest dilemma that I really have in small animal practice, is use of the long-acting antibiotics. <i>Veterinarian Q, 43F, regional CA practice, high interest in AMR/AMS</i>

Attitudes to other approaches to duration of therapy	D13	[When] the bacteria are winning the fight, the balance is in their favour. If we do something to tip it back the other way, the immune system's going to take over and sort it out. [When we give antibiotics] we're just giving the [patient] a bit of an advantage in the fight, to tip the balance back ... I think over the years I've used antibiotics too long . We had it sort of drummed into us that you had to complete the course . And I think probably used them too long. And of recent times I've tended to try and contract it down to some rational basis. <i>Veterinarian H, 68M, regional mixed practice, high interest in AMR/AMS</i>
	D14	So probably [I'd treat the UTI for] five to seven days. But recently, we've been moving towards only treating while the symptoms are there . So ... once the signs have stopped - when the pollakiuria, stranguria and hematuria ... resolves - [the owner] can probably just stop the antimicrobials ... they don't have to complete the course necessarily...probably just to be on the safe side, I'd say give another dose [after clinical signs resolve], just to be sure. <i>Veterinarian V, 36F, metropolitan CA practice, moderate interest in AMR/AMS</i>
	D15	The assumption there... is that the symptoms are directly related to the level of infection ... my worry would be ... not actually completely resolving the infection . So, it's still there at some subclinical level. And then as soon as we stop the antibiotics, it's going to come back again... My only other concern with that would be the reliance on the owner to appreciate what is a resolution of symptoms, which some clients I think would be amazing at, and some would be terrible at ... So that would be my other concern with it would be how reliable the owner is as a judge of those things. <i>Veterinarian T, 40M, metropolitan CA practice, moderate interest in AMR/AMS</i>

*Age in years and gender; F, female; M, male. CA, companion animal. Bold text added to highlight key phrases.

Some veterinarians expressed uncertainty about whether under- or over-treating an infection contributed more to AMR (D6, D7). However, many believed that erring on the side of longer durations (D5) and ensuring a patient finished all planned antimicrobial doses, even if they seemed better, was important (D9, D10, O2, O4). This approach was believed to decrease the risk of relapse (D5, D15) and of leaving behind AMR bacterial subpopulations (D6). Concern about owner compliance and 'finishing the course' was the primary justification veterinarians gave for using long-acting cefovecin injections when there was any doubt about the owner's capability to administer PO medications (C9, D6, D10, D11). Another driver was concern for owner safety, particularly with frail owners who might get 'scratched to bits' giving tablets to their cats (D12).

A few participants were aware of recommendations to minimize antimicrobial treatment duration and had adopted a 'shorter is better' approach (D13), sometimes using clinical sign resolution as a guide (D14). However, one expressed concern about such an approach in outpatients because of variability in owners' observational skills (D15). Veterinarians who viewed antimicrobials as assisting the animal's immune system to 'tip the balance' in favor of the patient (D13) appeared more comfortable with shorter durations.

Practice and colleague factors

'I know I should use a narrow-spectrum drug ... but in reality, I would probably use amoxiclav, because that's what we've got on the shelf.'

Practice culture and colleagues substantially influence antimicrobial prescribing decisions (Table 6). A veterinarian's current co-workers strongly influence their antimicrobial drug selection, often by a mechanism we call the 'dispensary cycle' (Figure 2). In many countries, veterinarians both prescribe and dispense medication, incurring costs for holding inventory of various antimicrobials and pressure to use them before expiration (P1). Our interviews indicated that the prescribing habits of veterinarians in a practice determine which antimicrobials are routinely kept in their dispensary (P1). In turn, the available drugs determine what veterinarians will prescribe (P1, P2, P3, P4, P5) and shape the habits of new graduates and locum veterinarians (P6, P5). This cycle amplifies the use of more popular drugs and limits less popular choices.

Table 6: Practice and colleague (**P**) factors influencing veterinarians' choice of antimicrobial drug, dose and duration in companion animals

Factor	Quotation code	Quotation, participant code and demographics
The 'dispensary cycle': colleagues' prescribing habits and 'what's on the shelf'	P1	[Amoxicillin] I have used at times, but we don't always have that there. It's usually only if I have ordered it in for something else and if I happen to have some there I need to get rid of , I might use that, but otherwise it's amoxiclav or cephalixin based on, they're on the shelf, and they normally work ... I did certainly use [TMS] a lot more probably in my first 10 years of practice, when I was in mixed practice. And that was predominantly because it was on the shelf . We just don't keep it on the shelf [now] really ... that's the main reason we're not using it . Veterinarian T, 40M*, metropolitan CA practice, moderate interest in AMR/AMS
	P2	When I first started out, I probably did use just amoxicillin quite a lot more than what I do now ... the main reason I don't use [amoxicillin] so much these days is that I kind of ... forget that it exists and, you know, amoxiclav is so good for everything! [laughs] ... I know where the amoxiclav is on the shelf . I know it's always there. I know that I probably should choose something like amoxicillin . Veterinarian W, 39F, regional CA practice, moderate interest in AMR/AMS
	P3	I know I should use a narrow-spectrum drug like amoxicillin without the clavulanate ... but in reality, I would probably use amoxiclav because that's what we've got on the shelf . Veterinarian R, 28F, regional CA practice, high interest in AMR/AMS
	P4	Most of the places I've worked at have not had amoxicillin very accessible ... so usually [I use] amoxiclav ... I think amoxicillin is a better choice but it's not as available. We don't stock it in our clinic. We just don't have the ability to have a massive inventory . And we use amoxiclav so much . It's not ideal, but that is the reality. Veterinarian V, 36F, metropolitan CA practice, moderate interest in AMR/AMS

	P5	I've got a locum ... that is really struggling to just use [amoxicillin]. 'I just want to use amoxiclav. I just like it!' I'm like, 'It's not necessary.' ... I think it's where you get used to doing something ... particularly for locums where they're moving between different clinics , they'll probably pick out a few things that they know will be there and will use them. <i>Veterinarian Q, 43F, regional CA practice, high interest in AMR/AMS</i>
	P6	I think a lot of medicine ... is habit-based. You've got a 10-minute consult; you don't have time to do this stuff properly. And then the [new graduate] vets do what the other vets in their clinic do . And the cycle continues. <i>Veterinarian P, 35F, metropolitan CA practice, high interest in AMR/AMS</i>
	P7	I haven't seen any reduction in the effectiveness of amoxicillin ... it wasn't really until I got a new graduate [veterinarian] and they started wanting [amoxicillin-clavulanate], that I ordered it. And then it was easier to grab that. But then I started ... saying, '... there's been no shift [in susceptibility to amoxicillin] – so why are we using the clavulanate ?' And actually a couple of them have started shifting in my direction... we're ordering a lot more amoxicillin now and ... much less clavulanate. <i>Veterinarian H, 68M, regional mixed practice, high interest in AMR/AMS</i>
	P8	The first clinic I worked at we just wouldn't order [long-acting cefovecin] because they did the maths and they worked out they wouldn't use the bottle [before its expiry date]. So we just weren't allowed to order it in. <i>Veterinarian M, 28F, regional CA practice, low interest in AMR/AMS</i>
Influence of veterinary colleagues	P9	I think my early decision-making when it came to antibiotic prescription was more based on what my senior vets were telling me and less based on what I was taught at university. ...my indoctrination to it was, you know, just use this drug and nothing else . So ... whoever taught me or whoever I [worked] with in my first clinic , does play a big role in terms of what I'm comfortable with using ... regardless of what I might have been taught at [university] <i>Veterinarian D, 25F*, regional CA practice, high interest in AMR/AMS</i>
	P10	Most of that, I must admit, stemmed from my first ever job after [university], where you just gave whatever antibiotics your boss recommended for that particular case. And if it worked , that's my go-to for future cases . <i>Veterinarian U, 39F, regional mixed practice, low interest in AMR/AMS</i>
Influence of broader veterinary community	P11	And it wasn't until, in the [group for Australian veterinarians] on Facebook somebody was like, "Oh, I'm using [long-acting cefovecin], shame on me ," and there's all the comments about it, that I realized that actually, it's one of those drugs that you should be limiting to just very specific cases. <i>Veterinarian W, 39F, regional CA practice, moderate interest in AMR/AMS</i>

Influence of veterinary specialists	P12	When I see that the specialist has sent me a summary of things, I'm like, what other drugs can I use for future cases? And I think that is because I have an inherent trust that they know way more than I do. And they know what they're doing . <i>Veterinarian D, 25F, regional CA practice, high interest in AMR/AMS</i>
	P13	With skin infections, you're going to get a clinical cure in seven to 10 days. But the dermatologists have hammered into me : 'thou shalt treat for 10 days past clinical cure ', hence, three weeks ... it's just been hammered into me that that's what you are to do. So that's what I do... [Veterinary specialists] know far more than I will ever know. <i>Veterinarian S, 66M, regional CA practice, low interest in AMR/AMS</i>
	P14	Maybe [I'd] talk to [veterinary] specialists and see what they're saying, but I don't give prima facie god-like belief to what they say ... they only see the weird stuff . They're not seeing the everyday stuff! <i>Veterinarian H, 68M, regional mixed practice, high interest in AMR/AMS</i>
Financial considerations	P15	If anything, I probably, subconsciously or consciously, worry more about prices of things being too much . I'm not really thinking, 'I'm gonna put this on a course of clindamycin or marbofloxacin because that's more expensive than [enrofloxacin] so we can make a bit more money on that.' So, no, I can honestly say that that's not a consideration ... to make more money . <i>Veterinarian T, 40M, metropolitan CA practice, moderate interest in AMR/AMS</i>
	P16	To be honest, sometimes if I'm choosing between two, I'll ...see, how much is that going to cost? ... Sometimes, especially if it's a big dog, I think, 'Oh my God, that's a lot of money ,' and ... go for the cheaper one ... So, I don't really think about what profit it's going to make for the clinic. <i>Veterinarian W, 39F, regional CA practice, moderate interest in AMR/AMS</i>
Clinic charging policies	P17	I didn't realize as a new grad how much money really plays a role in my decision-making. And that differs from clinic to clinic, because it just depends on what prices they set, what's their dispensing fee , things like that. <i>Veterinarian D, 25F, regional CA practice, high interest in AMR/AMS</i>
	P18	The cool thing about a three-day course of [antimicrobial] is it's once a day, so we can do one dose then and there. [If an owner can't tablet] I can be like, 'Bring the dog in for two more days, my nurses will give a tablet free of charge .' <i>Veterinarian P, 35F, metropolitan CA practice, high interest in AMR/AMS</i>
	P19	If you give a client, say, a week of something and the dog needed two weeks, then they'll be annoyed about having to come back , pay a recheck fee , pay for more antibiotics ... they don't want to come back. And they might make that clear to you as well... then you're going to be more inclined to kind of give them a course that you're fairly confident that is going to really get on top of that infection . <i>Veterinarian C, 33F, metropolitan CA practice, moderate interest in AMR/AMS</i>

Prescribing resources in the clinic	P20	I have seen in some clinics, they'll have ... a big [antimicrobial prescribing guidelines] poster ... where it says you've got a prostatic abscess, these are your options or you've got a skin condition, do it at this dose, and you've got these options. So, I think it's out there. I just don't know that we use it as much as we should . <i>Veterinarian M, 28F, regional CA practice, low interest in AMR/AMS</i>
Clinic culture	P21	And ... we've got lots of different treats and I've got information [resources for clients] on the fear-free tableting techniques , how to pill your cat or your dog... The other thing I do - I've got a couple of real asshole cats, thankfully I've got beautiful clients and they will bring their cats in for just a daily injection of amoxicillin ... and it's two seconds. Sometimes we just go out to their car and do it in the car park . We will make it easy , if we can, for people. <i>Veterinarian P, 35F, metropolitan CA practice, high interest in AMR/AMS</i>
	P22	I really wanted to treat ear infections appropriately and we were having a lot of yeast ear infections coming in that didn't have any bacteria. I asked my boss if we could get [anti-fungal] just to kill the yeast and mix that with [corticosteroid] so that we didn't have to use any antibiotics at all . He was open to that and immediately got it in. And we were able to get all these dogs off antibiotics and on a yeast-only drop. <i>Veterinarian R, 28F, regional CA practice, high interest in AMR/AMS</i>
Time pressure	P23	The time and financial pressures that [general practice veterinarians] face are extremely challenging. They're often in a position where they just need to quickly and cheaply make the problem go away ... It's an unfortunate reality ... they deal with difficult clients every 10 or 15 minutes, who have \$40 or \$50 to make the problem go away. <i>Veterinarian Y, 39F, metropolitan CA practice, moderate interest in AMR/AMS</i>
	P24	I've had 20-minute and 30-minute consultation times ... so I've never felt as much time pressure as I'm sure some other vets ... I think that's part of the reason why I've been able to communicate [with owners] the way that I have ... but I honestly don't know what my [antimicrobial prescribing] behavior ... would be like, even despite my knowledge and my values , if I was really burnt out and had worked a lot of hours and seen a huge volume of clients ... if I was pushed to that level of desperation . <i>Veterinarian R, 28F, regional CA practice, high interest in AMR/AMS</i>
Capacity to follow-up with owner	P25	[When I prescribe antibiotics, I will] call or get reception to call the owner the next day to make sure that there's been an immediate and impressive response . <i>Veterinarian P, 35F, metropolitan CA practice, high interest in AMR/AMS</i>

*Age in years and gender; F, female; M, male. CA, companion animal. Bold text added to highlight key phrases.

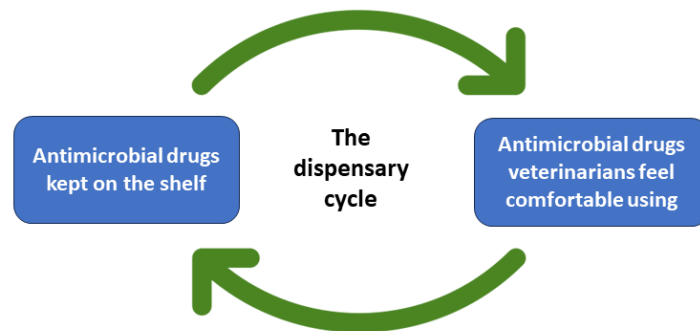


Figure 5: The dispensary cycle, which increases the use of commonly used antimicrobials and decreases the use of less commonly used antimicrobials

The dispensary cycle was best illustrated by the perpetuation of broad-spectrum amoxicillin-clavulanate use, which was available in every participant's practice, whereas narrower-spectrum amoxicillin was rarely stocked (P1, P2, P3, P4, P5), hence rarely used, and sometimes forgotten about entirely as an option (P2). This situation occurred despite several veterinarians acknowledging that in many instances they should opt for amoxicillin instead of amoxicillin-clavulanate (P2, P3, P4). One experienced veterinarian noted he had 'slipped' into using amoxicillin-clavulanate instead of amoxicillin because of his younger colleagues' preferences for the combination (V12) and was now trying to reverse that trend (P7), in the interests of AMS.

In other instances, the dispensary cycle could favor AMS. One veterinarian mentioned that a trend of dwindling cefovecin use in their practices resulted in disposal of unused, expired product, prompting a policy to stop ordering the high-importance antimicrobial (P8).

More experienced colleagues, particularly those at a new graduate's first workplace, also had a direct influence on prescribing, directing which antimicrobials to use, even if the choice was at odds with what they had learned at university (P9). This early influence could have long-lasting impact on drug selection (P9, P10).

Signals from the broader veterinary community also played a role in drug choice. For one participant, other veterinarians' comments on a social media group caused her to decrease her use of long-acting cefovecin (P11).

Veterinary specialists strongly influenced the antimicrobial choices of some general practice participants (A16) who felt that specialists 'know way more than I do' (P12, P13). One experienced general practice veterinarian described this as a 'god-like belief' in specialists (P14); another used biblical language to describe specialists' advice on antimicrobial duration (P13).

Participants' antimicrobial choices were not motivated by financial gain. Indeed, they were conscious of selecting a drug that minimized costs for owners (O6, O7, O8, O9), rather than improving clinic profits (P15, P16), even if they owned the practice (P15). Clinic charging policies also affected drug choice and duration. Fees for medication dispensing (P17), nurses administering medication to animals (P18), and veterinary re-examination (P19) were identified as potential or actual barriers to optimal antimicrobial use.

Displaying antimicrobial prescribing guidelines (P20) in a practice and providing owners with information on topics such as administering medications to cats (P21) and common infections

that do not need antimicrobials were felt to help decrease suboptimal antimicrobial use. Clinic culture played an important role, with clinic leaders who were open to change (P22) and teams engaged in AMS (P21) empowering veterinarians to make more considered prescribing choices. Conversely, time pressure on consultations (P6, P23, P24) and owner financial limitations (P23) encouraged inappropriate antimicrobial use.

The capacity of the practice to communicate with pet owners was another influential factor. When a veterinary practice could follow up with owners soon after starting antimicrobial treatment, veterinarians felt confident using narrower spectrum antimicrobials (P25), knowing they could modify treatment in a timely fashion, if the initial choice proved ineffective.

External factors

'I think part of the problem is we are ... reliant on our [drug company] reps... they come over with cake and pizza and they have this talk about a new drug ... it's a factor!'

Several external factors influenced veterinary antimicrobial prescribing choices (Table 7). Outdated or insufficient dosage information on some antimicrobial drug labels in Australia was a problem cited by veterinarians (E1, E2). Other participants were unaware that label doses could not always be relied upon to be clinically effective.

Table 7: External (E) factors influencing veterinarians' choice of antimicrobial drug, dose and duration in companion animals

Factor	Quotation code	Quotation, <i>participant code and demographics</i>
Antimicrobial label information	E1	I completely ignore the dosing directions on packets . Because they say 12.5 to 13.5 milligrams per kilogram [for amoxiclav], and my understanding is that [with the label dose] you ... don't get as good penetration ...and the spectrum actually increases as you increase your dose, so you get better anaerobic and Gram-negative [bacterial] coverage at the higher doses . <i>Veterinarian P, 35F*, metropolitan CA practice, high interest in AMR/AMS</i>
	E2	I do tend to go more off the dosages on the bottles , although there's some drugs [for which the label dose rates] are just plain wrong . <i>Veterinarian U, 39F, regional mixed practice, low interest in AMR/AMS</i>
	E3	I guess some of the vets in my clinic have the opinion that, 'Well, [long-acting cefovecin has] been registered for this use , so ... we're going to use it as we need to.' ... It's how you justify its use to yourself, I think, when you know it's probably not what we should be using, they're like, 'Well, it shouldn't be available to us if we aren't supposed to use it,' sort of thing. <i>Veterinarian E, 24F, regional CA practice, moderate interest in AMR/AMS</i>

Information in culture and susceptibility reports	E4	That's exactly it ... [When I get a culture and susceptibility report with lots of susceptible results], I don't know which antibiotic to choose. It might be great for that infection, but I might be carpet-bombing the gut and causing a resistance that I have no idea of. <i>Veterinarian B, 31M, metropolitan CA practice, high interest in AMR/AMS</i>
Pharmaceutical company marketing	E5	I think part of the problem is we are ... reliant on our [drug company] reps... they come over with cake and pizza and they have this talk about a new drug ... it's a factor! I mean, how convenient is that [long-acting cefovecin] with a fractious cat ? You don't have to worry about it! I think ... we need to approach our relationships with those external stakeholders in a much more stringent way, because it is big money , it's Big Pharma ... I remember seeing [a drug company presentation] about [long-acting cefovecin] overseas, and it was like, ' It's good for skin, good for teeth, good for urine! ' [laughter], so ... you have to look at who is providing that resource. <i>Veterinarian B, 31M, metropolitan CA practice, high interest in AMR/AMS</i>
	E6	[Long-acting cefovecin] ... that is one that is certainly used without the necessary thought...I think the [brand] name is no mistake ... that's clever marketing . And I think the convenience is over-sold . <i>Veterinarian Y, 39F, metropolitan CA practice, moderate interest in AMR/AMS</i>
	E7	I always thought that [long-acting cefovecin] was just a ... super handy , super convenient form of antibiotic. And you could pretty much use it for anything , especially in cats, like UTIs or abscesses and everything ... was marketed as a really convenient drug ... but the info about it being one of those that you should reserve ... that never really was publicized . <i>Veterinarian W, 39F, regional CA practice, moderate interest in AMR/AMS</i>
	E8	But if I see [a guideline] produced by the [pharmaceutical] company ... then I wonder how many times [that company's drug] is going to be suggested as first-line treatment? <i>Veterinarian F, 30F, metropolitan CA practice, moderate interest in AMR/AMS</i>
	E9	No organization that has a vested interest in the sales of drugs should be allowed to provide guidelines for them. Not for drugs that will have an impact on the whole of society ... We're talking about critical medications that we will run out of. <i>Veterinarian L, 32M, metropolitan CA practice, high interest in AMR/AMS</i>

*Age in years and gender; F, female; M, male. Bold text added to highlight key phrases.

A drug's registration for a species and indication was interpreted by some veterinarians as an official endorsement of that application, with the attitude that 'it shouldn't be available to us if we aren't supposed to use it' (E3).

Where microbiological culture and susceptibility testing was used, some participants felt the reports provided insufficient guidance, especially when a bacterium was susceptible to multiple antimicrobials (E4).

Veterinarians recognized that pharmaceutical companies influenced their antimicrobial choices. Pharmaceutical representatives routinely visit clinics to promote their products (E5). Veterinarians felt that clever branding and marketing (E6, E7) encouraged them to use antimicrobials less appropriately. One set of antimicrobial use guidelines funded by a pharmaceutical company was viewed with skepticism by some participants (E8, E9), whereas others were unaware of the funding source.

Discussion

Our study highlighted many factors that influence companion animal veterinarians' selection of antimicrobial drug, dose and duration, many of which are unrelated to the animal and its clinical presentation. Some factors are amenable to intervention, to minimize suboptimal antimicrobial use.

With respect to personal and social factors, we found that two erroneous beliefs held by some veterinarians are a substantial barrier to AMS: that a pre-determined duration of antimicrobial treatment must be followed; and that a longer duration of treatment reduces the risk of AMR because it is more likely to eliminate resistant pathogen subpopulations. Current evidence shows that shorter durations are generally as effective as longer durations and are less likely to cause adverse effects and select for AMR.^{29, 30} Nevertheless, the 'finish the course' mantra persists, leading to unnecessarily long durations of treatment and overuse of long-acting cefovecin injections. A stronger emphasis in veterinary education on minimizing antimicrobial treatment durations is needed. Additionally, because much of the evidence for shorter-duration antimicrobial treatment is from trials in human patients,³¹⁻³⁴ more animal trials to establish typical minimum effective durations would likely help convince veterinarians to adopt shorter regimens.

Although many of our participants expressed concern about AMR, they had inadequate awareness of prescribing guidelines, as shown by their case study responses, and tended to favour empirical use of medium- to high-importance, broad-spectrum antimicrobials, similar to their counterparts in the United Kingdom.¹⁸ This practice was partly driven by a sense of safety with broader spectrum drugs, because they 'cover' more pathogens, and perpetuated by what we have termed the 'dispensary cycle'. The resulting (almost complete) replacement of amoxicillin with broader-spectrum amoxicillin-clavulanate on the shelves of Australian small animal practices²⁷ is not supported by local bacterial susceptibility patterns³⁵ nor local prescribing guidelines, which recommend amoxicillin without clavulanate for several common infections.²⁴ Practices aiming to promote appropriate antimicrobial use therefore should ensure they provide locally relevant prescribing guidelines and that all guideline-recommended antimicrobials are reliably available.

Veterinary colleagues markedly influenced our participants' antimicrobial choices. Notably, veterinary specialist advice had a powerful effect on general practitioner veterinarians and senior veterinarians had a long-lasting influence on new graduate colleagues, the latter of which has been recognized previously.^{18, 19, 36} To support AMS, we suggest that veterinary specialists be involved in delivering AMS education relevant to their subspecialty. We also suggest that

veterinary schools equip new graduates with strategies for non-confrontational discussions with colleagues about different treatment approaches.

The veterinarian-client relationship also impacted antimicrobial choices. Our previously published analysis of the decision to prescribe or withhold antimicrobials found that veterinarians were more inclined to prescribe if the pet owner was ‘difficult’.²⁰ Our current analysis further demonstrated that a distrustful relationship with a pet owner can also lead veterinarians to defensively prescribe both broader-spectrum antimicrobials and longer durations of treatment than they might otherwise select. Building trust between clients and veterinarians within a practice may thus unexpectedly improve AMS.

At a clinic level, routine follow-up with owners of pets after they have begun a course of antimicrobials enabled lower importance antimicrobial drug choices. We suggest that automated phone calls, emails or text messaging may allow clinics to implement this practice at relatively low cost. Clinic videos and leaflets that assist pet owners with administering PO medications to cats were suggested by participants to decrease reliance on long-acting cefovecin injections. A recent global survey of cat owners showed that only half had been provided with information on how to administer PO medication at home and almost all of them found the information useful.³⁷ To our knowledge, such resources have not been included in past companion animal AMS trials³⁸⁻⁴⁰ and may be worth including in future trials.

More broadly, participants saw a role for pharmaceutical companies, drug regulatory authorities and veterinary microbiology laboratories in steering them towards better antimicrobial choices. The importance of the available antimicrobial formulations, in particular their ease of administration has been repeatedly highlighted by others.^{15, 18, 19, 41, 42} Our study suggests pharmaceutical companies could contribute to AMS by developing formulations of lower-importance antimicrobials, such as amoxicillin and TMS, that are more convenient to administer. Particular attention should be given to palatability and making it simple to achieve appropriate dose rates for a wide range of patient sizes. There might also be a place for increased scrutiny of antimicrobial marketing practices. Some veterinarians in our study felt that pharmaceutical company-sponsored information resources were encouraging suboptimal antimicrobial choices, a concern that has previously been expressed by veterinarians in the United Kingdom.⁴³

Some veterinarians felt that drug regulatory authorities should play a stronger role in encouraging AMS, by not registering or restricting access to some antimicrobials. French government efforts to curb unnecessary use of high-importance antimicrobials, such as cefovecin, by requiring antimicrobial susceptibility results before prescribing,⁴⁴ may be an example for other countries to follow. A cross-sectional survey of Australian veterinarians suggests such a move would be widely supported by the profession.⁴⁵ Furthermore, drug regulators should ensure that registered label antimicrobial doses are kept up-to-date, to avoid the confusion caused by outdated, subtherapeutic label doses⁴⁶ for amoxicillin and amoxicillin-clavulanate in dogs and cats.

Our participants also identified that many culture and susceptibility reports contain no AMS guidance, and simply list all tested drugs in alphabetical order. We suggest that veterinary microbiology laboratories could better support clinicians by adopting ‘cascade reporting’, i.e. suppressing selected susceptibility results (e.g. for high-importance antimicrobials) and arranging the remaining results in order of AMS preference. This type of reporting is well established in human hospitals.⁴⁷ Another potential solution is to group susceptibility results by the drugs’ antimicrobial importance ratings and explain that lower-importance drugs should be used preferentially. This traffic-light reporting approach has been adopted by veterinary

diagnostic laboratories at the University of Melbourne (see Appendix 4, document S1) and the University of Sydney, but its effect on prescribing has not been evaluated.

One limitation of our qualitative study was recruitment bias. Because most participants self-selected in response to social media posts that mentioned antimicrobial use, it is not surprising that a large proportion (10/22) reported a high interest in AMR and AMS and only a small proportion of participants had low interest (3/22). Purposively recruiting more veterinarians who were disinterested in AMS may have uncovered additional themes. Another limitation is that some findings will not be relevant in situations where veterinary antimicrobials are dispensed by a third party, rather than the veterinary practice itself. A strength of the study was the frankness shown by participating veterinarians. As all interviews were conducted by a veterinarian, participants could assume that the interviewer understood the challenges and complexity of their work. Interpretation of the interview data was enhanced by the fact that all authors are veterinarians with clinical experience.

Conclusion

Our study adds to the understanding of prescriber decisions about antimicrobial drug, dose, and duration of treatment. It identifies important reasons why many veterinarians continue to use antimicrobials of higher importance or for longer durations than necessary or both. These include ease of administration, difficult relationships with clients, the perceived safety of broad-spectrum choices, the ‘what’s on the shelf’ dispensary cycle and the belief that finishing a pre-determined course is central to responsible antimicrobial use. It also supports several findings from previous qualitative studies undertaken in the United Kingdom and the Netherlands.

Our study also suggests the potential value of practical measures to enhance antimicrobial stewardship in veterinary practice, such as improving veterinary education on the importance of minimizing treatment duration, enhancing antimicrobial susceptibility reports, providing more guidance to cat owners on giving PO medications and implementing routine, post-consultation follow-up messages.

References

1. Dyar O, Huttner B, Schouten J, Pulcini C. What is antimicrobial stewardship? *Clinical Microbiology and Infection* 2017;23:793-798.
2. Broom A, Kirby E, Gibson AF, Post JJ, Broom J. Myth, manners, and medical ritual: defensive medicine and the fetish of antibiotics. *Qual Health Res* 2017;27:1994-2005.
3. De Souza V, MacFarlane A, Murphy AW et al. A qualitative study of factors influencing antimicrobial prescribing by non-consultant hospital doctors. *J Antimicrob Chemother* 2006;58:840-843.
4. Speksnijder DC, Jaarsma ADC, van der Gugten AC, Verheij TJM, Wagenaar JA. Determinants Associated with Veterinary Antimicrobial Prescribing in Farm Animals in the Netherlands: A Qualitative Study. *Zoonoses Public Health* 2015;62:39-51.
5. Broom J, Broom A, Kirby E. The drivers of antimicrobial use across institutions, stakeholders and economic settings: a paradigm shift is required for effective optimization. *J Antimicrob Chemother* 2019;74:2803-2809.

6. Coyne LA, Latham SM, Williams NJ et al. Understanding the culture of antimicrobial prescribing in agriculture: a qualitative study of UK pig veterinary surgeons. *J Antimicrob Chemother* 2016;71:3300-3312.
7. Papoutsis C, Mattick K, Pearson M et al. Social and professional influences on antimicrobial prescribing for doctors-in-training: a realist review. *J Antimicrob Chemother* 2017;72:2418-2430.
8. Ilerano C, Thursky K, Peel T et al. Influences on surgical antimicrobial prophylaxis decision making by surgical craft groups, anaesthetists, pharmacists and nurses in public and private hospitals. *PLoS One* 2019;14:e0225011.
9. Espinosa-Gongora C, Jessen LR, Dyar OJ et al. Towards a Better and Harmonized Education in Antimicrobial Stewardship in European Veterinary Curricula. *Antibiotics* 2021;10:364.
10. Mutua F, Sharma G, Grace D et al. A review of animal health and drug use practices in India, and their possible link to antimicrobial resistance. *Antimicrobial Resistance & Infection Control* 2020;9:1-13.
11. Bywater R. Identification and surveillance of antimicrobial resistance dissemination in animal production. *Poult Sci* 2005;84:644-648.
12. Borg MA. National cultural dimensions as drivers of inappropriate ambulatory care consumption of antibiotics in Europe and their relevance to awareness campaigns. *J Antimicrob Chemother* 2011;67:763-767.
13. Sørensen K, Pelikan JM, Röthlin F et al. Health literacy in Europe: comparative results of the European health literacy survey (HLS-EU). *Eur J Public Health* 2015;25:1053-1058.
14. Springer S, Lund TB, Grimm H et al. Comparing veterinarians' attitudes to and the potential influence of pet health insurance in Austria, Denmark and the UK. *Veterinary Record* 2022;190:e1266.
15. King C, Smith M, Currie K et al. Exploring the behavioural drivers of veterinary surgeon antibiotic prescribing: a qualitative study of companion animal veterinary surgeons in the UK. *BMC Vet Res* 2018;14:332.
16. Tompson AC, Chandler CIR, Mateus ALP et al. What drives antimicrobial prescribing for companion animals? A mixed-methods study of UK veterinary clinics. *Prev Vet Med* 2020;183:105-117.
17. Smith M, King C, Davis M et al. Pet owner and vet interactions: exploring the drivers of AMR. *Antimicrob Resist Infect Control* 2018;7:46.
18. Mateus AL, Brodbelt DC, Barber N, Stark KD. Qualitative study of factors associated with antimicrobial usage in seven small animal veterinary practices in the UK. *Prev Vet Med* 2014;117:68-78.
19. Hopman NE, Hulscher ME, Graveland H et al. Factors influencing antimicrobial prescribing by Dutch companion animal veterinarians: A qualitative study. *Prev Vet Med* 2018;158:106-113.
20. Scarborough RO, Sri AE, Browning GF, Hardefeldt LY, Bailey KE. 'Brave enough': A qualitative study of veterinary decisions to withhold or delay antimicrobial treatment in pets. *Antibiotics* 2023;12:540.
21. Australian Strategic and Technical Advisory Group on Antimicrobial Resistance (ASTAG). Importance ratings and summary of antibacterial uses in human and animal health in Australia.

www.amr.gov.au/resources/importance-ratings-and-summary-antibacterial-uses-human-and-animal-health-australia. 2018. Retrieved:18 Feb 2023

22. World Health Organization (WHO). WHO List of Medically Important Antimicrobials: a risk management tool for mitigating antimicrobial resistance due to non-human use.

www.who.int/news/item/08-02-2024-who-medically-important-antimicrobial-list-2024. 2024.

Retrieved:14 Feb 2024

23. World Organisation for Animal Health (WOAH). OIE List of Antimicrobial Agents of Veterinary Importance. www.woah.org/app/uploads/2021/06/a-oie-list-antimicrobials-june2021.pdf. 2021.

Retrieved:18/02/2023

24. The University of Melbourne. Australian Veterinary Prescribing Guidelines, Dogs and Cats (version 2). <https://vetantibiotics.science.unimelb.edu.au/about/resources/>. 2019. Retrieved:25 May 2022

25. Weese JS, Blondeau J, Boothe D et al. International Society for Companion Animal Infectious Diseases (ISCAID) guidelines for the diagnosis and management of bacterial urinary tract infections in dogs and cats. *Veterinary Journal* 2019;247:8-25.

26. Hur B, Hardefeldt LY, Verspoor KM, Baldwin T, Gilkerson JR. Evaluating the dose, indication and agreement with guidelines of antimicrobial use in companion animal practice with natural language processing. *JAC-Antimicrobial Resistance* 2022;4.

27. Hur BA, Hardefeldt LY, Verspoor KM, Baldwin T, Gilkerson JR. 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:e0230049.

28. Hardefeldt L, Hur B, Verspoor K et al. Use of cefovecin in dogs and cats attending first-opinion veterinary practices in Australia. *Veterinary Record* 2020;187:e95-e95.

29. Llewelyn MJ, Fitzpatrick JM, Darwin E et al. The antibiotic course has had its day. *Br Med J* 2017;358:j3418.

30. Spellberg B. The new antibiotic mantra—"Shorter is better". *JAMA Internal Medicine* 2016;176:1254-1255.

31. Grant J, Le Saux N. Duration of antibiotic therapy for common infections. *Journal of the Association of Medical Microbiology and Infectious Disease Canada* 2021;6:181-197.

32. Michael M, Hodson EM, Craig JC, Martin S, Moyer VA. Short compared with standard duration of antibiotic treatment for urinary tract infection: a systematic review of randomised controlled trials. *Archives of Disease in Childhood* 2002;87:118-123.

33. Falagas ME, Avgeri SG, Matthaïou DK, Dimopoulos G, Siempos II. Short- versus long-duration antimicrobial treatment for exacerbations of chronic bronchitis: a meta-analysis. *J Antimicrob Chemother* 2008;62:442-450.

34. Hanretty AM, Gallagher JC. Shortened Courses of Antibiotics for Bacterial Infections: A Systematic Review of Randomized Controlled Trials. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy* 2018;38:674-687.

35. Scarborough R, Browning GF, Hardefeldt LY, Galgut BI, Marenda MS, Bailey KE. Clavulanate and cephalosporins: what is the cost of convenience? *Australian Veterinary Practitioner* 2023;53:209-219.

36. Hardefeldt LY, Gilkerson JR, Billman-Jacobe H et al. Barriers to and enablers of implementing antimicrobial stewardship programs in veterinary practices. *J Vet Intern Med* 2018;32:1092-1099.
37. Taylor S, Caney S, Bessant C, Gunn-Moore D. Online survey of owners' experiences of medicating their cats at home. *Journal of Feline Medicine and Surgery* 2022;24:1283-1293.
38. Hardefeldt LY, Hur B, Richards S et al. Antimicrobial stewardship in companion animal practice: an implementation trial in 135 general practice veterinary clinics. *JAC-Antimicrobial Resistance* 2022;4:dla015.
39. Singleton DA, Rayner A, Brant B et al. A randomised controlled trial to reduce highest priority critically important antimicrobial prescription in companion animals. *Nature Communications* 2021;12.
40. Hopman NEM, Portengen L, Hulscher MEJL et al. Implementation and evaluation of an antimicrobial stewardship programme in companion animal clinics: A stepped-wedge design intervention study. *PLoS One* 2019;14:e0225124.
41. Servia-Dopazo M, Taracido-Trunk M, Figueiras A. Non-clinical factors determining the prescription of antibiotics by veterinarians: a systematic review. *Antibiotics (Basel)* 2021;10:133.
42. De Briyne N, Atkinson J, Pokludov L, Borriello SP, Price S. Factors influencing antibiotic prescribing habits and use of sensitivity testing amongst veterinarians in Europe. *Veterinary Record* 2013;173:475-481.
43. Tompson AC, Mateus ALP, Brodbelt DC, Chandler CIR. Understanding antibiotic use in companion animals: a literature review identifying avenues for future efforts. *Frontiers in Veterinary Science* 2021;8.
44. Bourély C, Fortané N, Calavas D, Leblond A, Gay É. Why do veterinarians ask for antimicrobial susceptibility testing? A qualitative study exploring determinants and evaluating the impact of antibiotic reduction policy. *Prev Vet Med* 2018;159:123-134.
45. Sri A, Bailey KE, Gilkerson JR, Browning GF, Hardefeldt LY. Attitudes towards Use of High-Importance Antimicrobials—A Cross-Sectional Study of Australian Veterinarians. *Antibiotics* 2022;11:1589.
46. Hardefeldt L, Gilkerson J, Billman-Jacobe H et al. Antimicrobial labelling in Australia: a threat to antimicrobial stewardship? *Aus Vet J* 2018;96:151-154.
47. Al-Tawfiq JA, Momattin H, Al-Habboubi F, Dancer SJ. Restrictive reporting of selected antimicrobial susceptibilities influences clinical prescribing. *J Infect Public Health* 2015;8:234-241.

Chapter 7: General discussion

This body of research explored reasons underlying antimicrobial use in Australian companion animals that is non-concordant with guidelines, with a view to developing evidence-based AMS interventions.

The first paper, *Use of local antibiogram data and antimicrobial importance ratings to select optimal empirical therapies for urinary tract infections in dogs and cats*, explored the potential microbiological reasons for veterinarians to deviate from Australian and international guidelines, using the common diagnosis of urinary tract infections as an exemplar. More than 6,000 AST results from 2015 to 2019, predominantly from dogs and cats presenting to first-opinion veterinarians across Victoria, formed the largest collection of Australian veterinary antibiograms published to date. This paper has been cited 47 times since its publication in late 2020, reflecting significant interest in the results.

These antibiograms showed the prevalence of AMR in urinary pathogens was lower than had been seen in previous Australian studies, which had been mostly based on smaller datasets with a higher proportion of cases from veterinary specialist and referral practices. Rates of resistance to most antimicrobials in this study were also lower than in many international studies. While the differences could be partially explained by variation in laboratory techniques and reporting, it seems likely that there is also genuine geographical variation in AMR.

Despite challenges with non-veterinary and non-urinary breakpoints used by the laboratory, the findings demonstrated that the Australian AMU guideline recommendations for empirical treatment - amoxicillin or TMS – should be highly effective for sporadic urinary tract infections in Victorian general practice. In only 4% of UTI cases from which AST results were obtained was the use of medium-importance amoxicillin-clavulanate justified, while the use of high-importance enrofloxacin was only required in 0.6% of cases, and no cases required the use of cefovecin. As AST is usually only requested for refractory cases that have already received antimicrobials, the susceptibility of urinary pathogens to the antimicrobials recommended in the guidelines is likely to be even higher at first presentation, so the need for medium- and high-importance antimicrobials will be lower than these findings suggest. Thus, there is no microbiological justification for the historical pattern of antimicrobial use in the treatment of UTIs in dogs in Australia (~70% amoxicillin-clavulanate, ~10% cephalexin and ~10% enrofloxacin) or cats (~45% cefovecin, 45% amoxicillin-clavulanate).^{1, unpublished data}

Additional analyses performed showed that empirical antimicrobial selection for treatment of this common condition can be refined by determining the morphology of the bacteria responsible – amoxicillin being the superior choice for infections with cocci and TMS the better choice for bacilli or mixed infections. As urine sediment microscopy is routinely performed on cases of suspected UTI in Australia, this insight is immediately implementable without any change to veterinary workflows. It has been widely shared with practising veterinarians through oral presentations at several veterinary conferences and an infographic published online.² It has also supported further postgraduate research, forming the basis of a decision support tool used in a clinical trial implemented by another PhD student.³

A subsequently published antibiogram of commercial veterinary laboratory data from Queensland showed very similar results to my study, with 97% of isolates from dog and cat urinary tract infections susceptible to at least one low-importance antimicrobial and only 0.6% of cases caused by organisms that justified the use of high-importance enrofloxacin.⁴ Another

study from the University of Sydney found that dog urinary tract pathogens had lower susceptibility to amoxicillin than both my study and the Queensland study,⁵ but those samples came mostly from a veterinary teaching hospital, rather than first-opinion veterinary practices, so it was likely that the UTI cases in this study were more complex, and caused by organisms with higher levels of resistance than those seen in routine general veterinary practice. It would be useful to perform an analysis of commercial veterinary laboratory data from New South Wales. This would provide additional confidence that the Victorian results are applicable in first-opinion veterinary practices across the Eastern seaboard of Australia, where the majority of the pet population resides. Separating C&S results from first-opinion practices and other practices would be useful in all future studies of clinical samples.

The second paper, *Clavulanate and cephalosporins: what is the cost of convenience?*, focused on the mismatch between veterinarians' apparent preference for amoxicillin-clavulanate and cefovecin and microbiological results. A smaller, more recent collection of Victorian AST results (from the same laboratory as the first paper) confirmed that dog and cat urinary tract isolates remained highly susceptible to amoxicillin and TMS in 2020-21. In this analysis, I additionally showed that amoxicillin-clavulanate only provided a benefit over amoxicillin alone in 10% of all culture-positive cases, and the organisms isolated from the majority of these 10% of cases were also susceptible to TMS, which would be microbiologically preferred over amoxicillin-clavulanate.

I subsequently conducted an online poll of veterinarians, in the Facebook group Australian Veterinarian Network, asking what proportion of the infections in dogs and cats that they successfully treated with amoxicillin-clavulanate they would expect to respond to amoxicillin alone. Almost two-thirds of the 143 respondents said 80% or less, with one-quarter estimating 50% or less, whereas the AST data in my study suggested that the actual proportion would be close to 90%. While this was a small, informal poll, it reflects a real and common perception that the clavulanate combination is often needed to treat infections in companion animals. Challenging veterinarians' beliefs about the proportion of infections caused by beta-lactamase producing bacteria (and hence warrant use of amoxicillin-clavulanate) would therefore be a good target for AMS interventions.

As with the first study, none of the isolates from swabs or the urinary tract in this second study had patterns of resistance that justified the use of cefovecin; all cefovecin-susceptible isolates were also susceptible to lower importance antimicrobials. Interestingly, I was unable to find other instances where cumulative antibiograms included the proportion of isolates that could be treated with a low-importance antimicrobial, and the proportions that required a medium-importance or high-importance antimicrobial, because of resistance to all tested lower-importance antimicrobials. This appears to be a useful approach that could be incorporated into the summarisation of antibiograms, for both medical and veterinary pathogens, to support communication with clinicians about empirical antimicrobial selection, provided that contributing laboratories use comparable methodologies and reporting.

These first two papers combined provide robust quantitative evidence that common pathogens of companion animals in Australia are highly susceptible to low-importance antimicrobials, including those recommended in guidelines for urinary tract infections. The frequent use of medium-importance amoxicillin-clavulanate and high-importance cefovecin in practice, therefore, must be driven by factors other than microbiology.

The third paper began an exploration of social factors that influence both the decision to use antimicrobials, and the choice of drug, dose and duration.

The study, *Pet owners and antibiotics: knowledge, opinions, expectations, and communication preferences*, established that some pet owners do indeed expect antimicrobials, representing a genuine challenge for veterinarians when a pet has no indication that requires AMU. It also found there was **low public understanding of One Health AMR dynamics**, even among human health professionals, with implications for veterinary-client communication.

This survey of more than 500 pet owners found that 25% had, at some point, been surprised, frustrated or disappointed when their pet was not given antibiotics. Furthermore, despite expected desirability bias in responses, 15% admitted to explicitly requesting antibiotics for their pet. Another 2% had hinted that they wanted antibiotics and 8% said they did not express their preference in any way. These findings are similar to those of a small 2019 US study,⁶ but both studies contrast somewhat with a UK qualitative study, which appeared to suggest that unnecessary antimicrobial use is driven by the veterinarian's perception of what the client expects, rather than the client's actual expectations.⁷

This study also found that when pet owners expect their animal to receive antibiotics, they are usually still satisfied with the consultation if no antibiotics are prescribed. The way that the reasoning for this course of action is communicated appears to be important; pet owners responded to hearing about reassuring clinical signs and published evidence to support this decision and appreciated a focus on relieving discomfort for the animal. When considering a more convenient long-acting injectable treatment, compared with a less convenient course of oral antibiotics, pet owners responded well to messages about the oral antibiotic drug being the 'best match' for the bacteria involved, and reducing the risk of adverse effects and potential AMR in their pet, specifically. However, messages about AMR spreading beyond the treated pet, or AMR as a global public health issue, failed to resonate. This is at least partly explained by the respondents limited understanding of AMR; even though the survey respondents were skewed, in being more educated than the average population, only a minority (39% overall; 46% of those with a health science background) agreed that bacteria can be transferred from pets to their owners, and even fewer (29% overall; 34% of those with a health science background) agreed that bacteria can be transferred from owners to pets. This finding demonstrates a significant gap in the understanding of the public – and even that of human health professionals – about zoonotic and anthroozoonotic risks. This presents a challenge to coordinated One Health AMS efforts. Qualitative research with Australian pet owners would help to better understand how they conceptualise AMR risks for their pets and themselves, and how veterinarians can more effectively communicate with them about the risks of AMU.

This paper has been cited 29 times since its publication and stimulated a subsequent survey of more than 900 US pet owners, using many of the same survey questions, with permission from this author. An interesting difference between the two studies was that a much larger proportion of the US pet owners (17%) than Australian pet owners (5%) said that if the veterinarian said that antibiotics probably wouldn't help, they would want some anyway, 'just in case'.⁸ This finding was also reflected in an earlier US study of pet owners.⁶ Additional studies are needed to confirm this difference, but it is plausible that Australian pet owners are truly more aware of the risks of AMU than their American counterparts.

The fourth and fifth published studies included in this thesis explain how real and perceived client expectations, and a range of other factors, contribute to the two types of suboptimal AMU: unnecessary AMU and suboptimal choices of necessary AMU. Both studies were based on 22 in-depth interviews with veterinarians who treat companion animals in

Australia. Two carefully chosen case studies (vignettes) were discussed early in each interview: a cat with an uncomplicated cat fight abscess (for which local guidelines recommend no antimicrobials) and a canine sporadic bacterial cystitis (for which local guidelines recommend amoxicillin or TMS). Few veterinarians chose guideline-concordant management for the case studies.

The interviewer's declared positionality as a formerly practising Australian veterinarian allowed rapid rapport and mutual understanding, encouraging participants to be open about their thought processes.

The first of these phenomenological studies, *'Brave enough': a qualitative study of veterinary decisions to withhold or delay antimicrobial treatment in pets*, focused on unnecessary AMU. Themes relating to the decision to prescribe antimicrobials (when there was doubtful or no benefit) were generated in an initial inductive analysis and then mapped deductively to the Theory of Planned Behaviour. The central themes were two intertwined behavioural beliefs: the fear of clinical deterioration and the fear of client dissatisfaction if antibiotics were not given. These fears were heightened by a series of other factors, including 'difficult' or aggressive client behaviour, an unsupportive workplace culture, the inexperience of the veterinarian and lack of time and energy to discuss with the client why antibiotics were not a good idea.

Many findings of this study aligned with qualitative research in the Netherlands⁹ and UK¹⁰, showing the influence of time pressure, availability of non-antimicrobial treatments, lack of confidence and communication skills, force of habit, prescribing norms within the practice, and avoiding contradicting colleagues on decisions to prescribe antibiotics that were unnecessary. The narrowed focus on unnecessary AMU, rather than all suboptimal AMU - allowed a clearer picture of this behaviour to be obtained, and the use of an established theoretical framework facilitated comparisons with prescribing research from other contexts. Some novel findings from this study included the importance in decision making of: the fear of dissatisfied clients criticising the practice on social media; the role of client prejudice against younger and female veterinarians in driving unnecessary prescribing; the capacity of the client to adequately monitor their pet at home; and reception staff establishing client expectations of antibiotics. Another interesting finding was that in a small regional town, the attitude of local medical practitioners to human AMU had an influence on client attitudes to animal AMU at the veterinary practice. Encouragingly, some important factors contributing to unnecessary AMU are modifiable at a practice level. For example, time pressure on consultations, ensuring that reception staff do not foreshadow AMU when booking consultations, creating a culture of continuous improvement in the practice, and actively supporting younger veterinarians in their clinical decisions are all measures that can be implemented in veterinary practices. These should be included, where possible, in future veterinary AMS interventions. Targeted communication skills training for veterinary undergraduates and new graduates, to help them communicate effectively with clients and colleagues about AMS, would also probably help reduce unnecessary AMU.

Suboptimal choice of drug, dose and duration was explored in the fifth publication, *Seeking simplicity, navigating complexity: How veterinarians select an antimicrobial drug, dose, and duration for companion animals*. This study revealed, for the first time, that a single, apocryphal belief lies at the heart of many suboptimal drug and duration choices, namely that an animal must complete a pre-determined duration of antibiotic treatment, because this will supposedly reduce the risk of leaving behind resistant isolates. This core belief was a powerful driver for the use of long-acting cefovecin injections. Cefovecin was generally not the preferred antimicrobial agent of veterinarians, but they used it because the delivery method and 14-day

duration guaranteed that the animal finished the course. This guarantee – along with the ease of administration - were particularly important if the animal was fractious, free-roaming or the owner seemed incapable of administering oral medications. To tackle inappropriate cefovecin use, it is therefore critical to challenge two underlying prescriber beliefs; that finishing the course reduces the risk of AMR and that in common infections, longer durations are more effective than shorter durations. If a somewhat longer-acting (e.g. 4-day duration) injectable amoxicillin were to become available, this would also likely help to reduce cefovecin use, providing a better alternative for situations where oral antimicrobials are not feasible, including for aggressive animals.

Similarly, a belief that antibiotics must completely clear an infection - that is, leave no remaining pathogens - lest these cause a relapse, encouraged veterinarians to prescribe longer courses of treatment. One veterinarian interviewee, who favoured shorter durations, noted that many of his colleagues seemed to have forgotten that successful antibiotic treatment only needed to 'tip the balance' in favour of the animal's immune system.

'Tipping the balance' and 'shorter is better' could be useful ways of communicating with veterinary students and clinicians about optimal durations of antimicrobial treatment. Since this study, both have been incorporated into the teaching of veterinary undergraduates at The University of Melbourne and are anecdotally effective. I also discussed these ideas on a 2022 *Vet Vault* Podcast episode entitled *Antibiotic Mythbusting*¹¹, that has reached an audience of more than 3000 veterinary clinicians across Australia and internationally. Like 'Not All Bugs Need Drugs', these simple phrases could also be incorporated into future AMS resources for veterinary clinicians.

This study also revealed several reasons why amoxicillin-clavulanate remains overused in companion animals, while amoxicillin is underused. Many veterinarians reported a sense of safety from using a broader-spectrum agent such as amoxicillin-clavulanate and reported comfort when they were very familiar with a drug's effectiveness, dose rate and adverse effect profile. One interviewee could see no point in using amoxicillin alone if amoxicillin-clavulanate could achieve the same things and more. Others admitted to having forgotten that amoxicillin exists without clavulanate. The reason for this was also clear: the antimicrobials veterinarians prescribe daily are those that are kept in stock at their clinic, and what is 'on the shelf' in turn determines what veterinarians in the clinic will prescribe, because they prefer to avoid a special order for one patient. This self-perpetuating 'dispensary cycle' has long favoured broad-spectrum amoxicillin-clavulanate and explains why displaying AMU guidelines and discussing AMS in a practice are unlikely to drive change, unless the guideline-recommended drugs are already on the shelf. Ordering those drugs in anticipation of their use, in a range of formulations and sizes, is a critical step that should be incorporated into future AMS initiatives.

The interviewed veterinarians offered a range of suggestions to help improve antimicrobial prescribing in companion animal practice, including public education campaigns, government subsidies for AST, and audit and feedback on their antimicrobial prescribing.

Conclusion

This body of research used quantitative methods to demonstrate the mismatch between pathogen susceptibility and antimicrobial use in Australian companion animal practice and qualitative methods to understand the many non-clinical reasons for the mismatch. These include pet owner factors, veterinarian factors, practice factors and broader context factors.

Qualitative research with Australian pet owners would be a useful next step to better understand the findings of the pet owner survey, such as why some pet owners still want antimicrobials even when the veterinarian does not recommend them, and what would make them more comfortable with a 'no prescription' consultation.

Additional large-scale Australian antibiograms from clinical samples are also much needed to guide rational empirical choices. A trial of routine audit and feedback on the rate of AMU– the proportion of encounters that result in AMU - and the proportion of low-, medium- and high-importance drugs used, would also be informative and is possible at a clinic level using VetCompass Australia data. Work has begun on an online dashboard for this purpose. Further analyses of drug choices by clinical indication, and durations of treatment, would help to evaluate the impact of the Australian veterinary prescribing guidelines and other AMS efforts over the last several years. Recent improvements in large language models are likely to facilitate such explorations of guideline concordance.

Key recommendations arising from this work include the need to:

- Update future dog and cat cystitis treatment guidelines to recommend in-clinic urine cytology to choose between empirical amoxicillin (for cocci) or TMS (for bacilli or a mixture of bacterial morphologies)
- Publish further cumulative antibiogram data, ideally from veterinary general practice samples only, to build a clearer picture of pathogen susceptibility patterns that reflect general practice cases. Antibiogram data should be regularly updated to detect any changes in pathogen susceptibility patterns.
- Incorporate antimicrobial importance ratings into cumulative antibiograms and report the proportion of isolates susceptible to relevant low-importance antimicrobials, those requiring a medium-importance antimicrobial and those justifying the use of a high-importance antimicrobial
- Encourage pharmaceutical companies to develop longer-acting injectable formulations of low-importance antimicrobials, such as amoxicillin
- Develop interventions to challenge the perceptions of veterinarians about the prevalence of beta-lactamase producing pathogens in Australian companion animals, and thus the need for the routine use of the amoxicillin-clavulanate combination
- Develop interventions to combat the beliefs of veterinarians about 'finishing the course' to reduce the risk of AMR and encourage a 'shorter is better' mentality
- Encourage practices to order stocks of guideline-recommended drugs at the same time that guidelines are introduced
- Involve paraveterinary staff in AMS interventions, and ensure communication with clients does not create expectations of AMU
- Provide AMS-focused communication skills training for veterinary undergraduates and graduates, highlighting evidence-based strategies to use with clients who expect antimicrobials, e.g. focusing on the risks of AMU to their pet specifically

An outcome of the studies described in this thesis is that some of these recommendations are already being implemented in Australian veterinary practices and veterinary undergraduate teaching.

References

1. Hardefeldt LY, Selinger J, Stevenson MA 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;225:34-39.
2. The University of Melbourne. Australian Veterinary Prescribing Resources. <https://science.unimelb.edu.au/avpg/resources>. Retrieved:15/10/2025
3. Hii AW, Gilkerson JR, Bailey KE et al. Outcomes from an intervention study implementing fee-free culture and susceptibility urine testing in dogs and cats. *Veterinary Record* 2025:e5500.
4. Mack C, Gibson JS, Meler E et al. Antimicrobial susceptibility patterns of aerobic bacteria isolated from canine urinary samples in South East Queensland, 2013 to 2018. *Aus Vet J* 2024.
5. Wei AY, Thompson MF, Worthing KA et al. Frequency and antimicrobial susceptibility profiles of bacterial species isolated from canine and feline urine samples in Sydney, Australia, 2012-2021. *Veterinary Microbiology* 2025:110541.
6. Redding LE, Cole SD. Pet owners' knowledge of and attitudes toward the judicious use of antimicrobials for companion animals. *Journal of the American Veterinary Medical Association* 2019;254:626-635.
7. Smith M, King C, Davis M et al. Pet owner and vet interactions: exploring the drivers of AMR. *Antimicrob Resist Infect Control* 2018;7:46.
8. Frey E, Kedrowicz A, Hedgpeth MW. Decision making on antimicrobial use: Cat and dog owners' knowledge and preferences for veterinary communication. *Veterinary Record* 2024;194:no-no.
9. Hopman NE, Hulscher ME, Graveland H et al. Factors influencing antimicrobial prescribing by Dutch companion animal veterinarians: A qualitative study. *Prev Vet Med* 2018;158:106-113.
10. Mateus AL, Brodbelt DC, Barber N, Stark KD. Qualitative study of factors associated with antimicrobial usage in seven small animal veterinary practices in the UK. *Prev Vet Med* 2014;117:68-78.
11. Hiemstra HP, Gerard. The Vet Vault. *Episode #60: Antibiotic Mythbusting with Dr Ri Scarborough*, thevetvault.com, 2022.

Appendix 1: Supplementary materials for Chapter 2

Use of Local Antibigram Data and Antimicrobial Importance Ratings to Select Optimal Empirical Therapies for Urinary Tract Infections in Dogs and Cats

Dog Breed	Age (whole years completed)																		Total	
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17		18
Labrador Retriever	21	8	8	13	9	3	4	8	19	21	20	38	31	34	32	14	3	1		287
Pug	1	7	6	19	16	11	14	18	23	17	21	23	16	7	4	4		1		208
Golden Retriever	23	3	14	6	5	6	7	6	7	10	10	22	18	12	18	8	2	1		178
Border Collie	9	2	5	2	12	8	6	14	10	23	24	19	11	14	6	4	2	1		172
Cavalier King Charles Spaniel		1	3	3	5	8	6	7	30	20	17	18	11	9	15	2	1			156
Maltese Cross	1		2	6	3	1	5	11	10	12	23	16	16	12	12	11	3	3	1	148
Poodle Cross	6	1	9		6	3	2	7	8	11	9	7	12	7	3	3	2	1	1	98
Miniature Schnauzer	5	1	2	7	7	3	6	5	14	6	7	5	10	8	2			1		89
Staffordshire Bull Terrier		1	5	3	1	2	3	4	9	5	9	11	10	8	12	2	2			87
Cocker Spaniel			2	3	6	1	1	9	7	9	5	10	11	7	6	3	1	1		82
Cavalier King Charles Spaniel Cross	1	4	1	1	2	4	7	10	8	9	5	8	2	6	3		1			72
Jack Russell Terrier	2	1	6	5	1	3	2	1	3	5	4	5	2	11	8	6	3	4		72
Beagle	1		1				2	1	3	5	3	7	4	14	11	9	2			63
Kelpie Cross	2	1	1	3	1	2	1	6	3	4	4	7	8	8	6	3	3			63
French Bulldog	17	10	5	4	7	3	5	3	3		4									61

Only breeds that contributed >60 samples are included. Darker cells represent higher frequencies.

Figure S1: Frequency of samples by dog breed and age

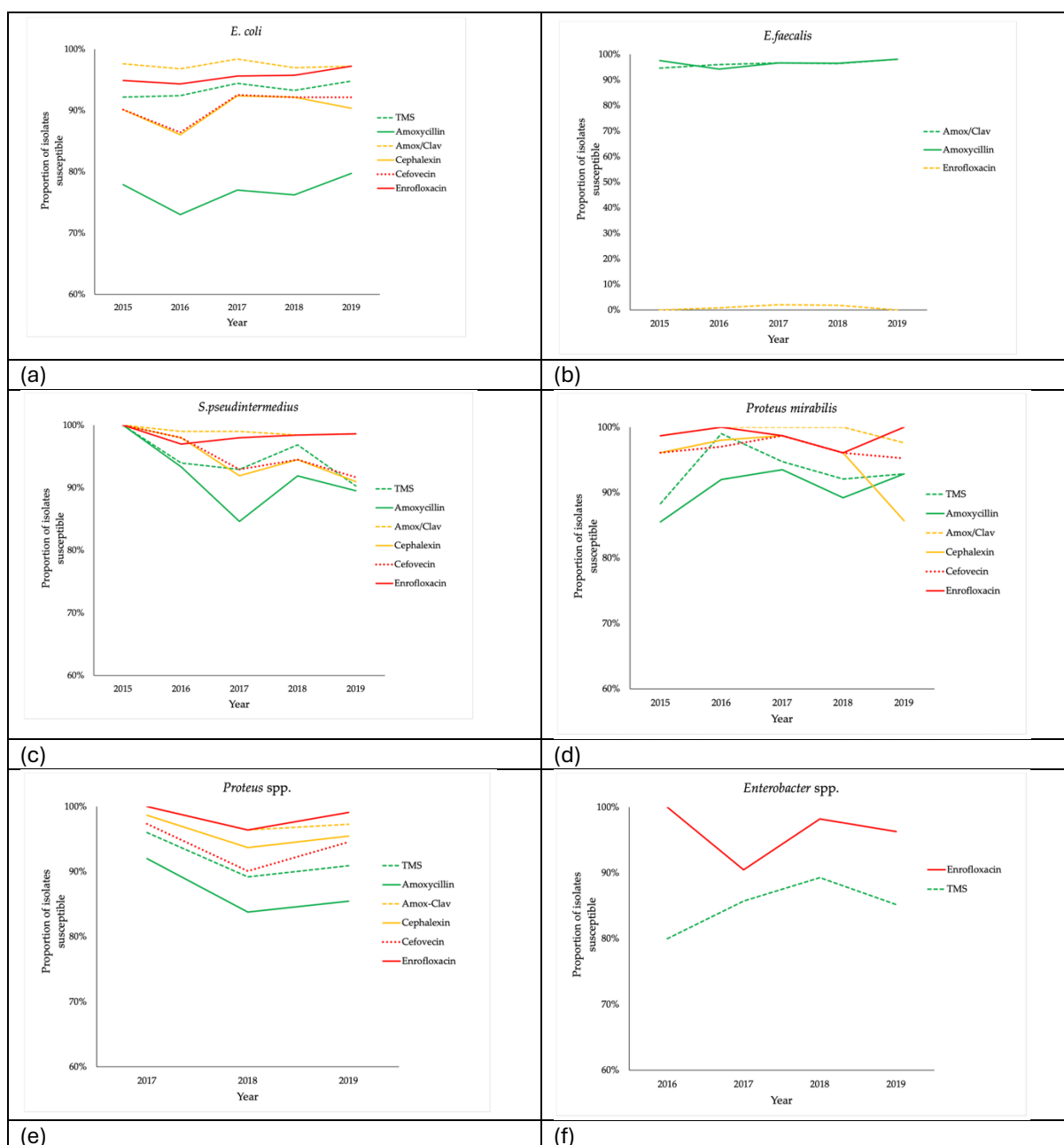


Figure S2 a-f: Changes in susceptibility over time for the most common species/genera.

a) *E. coli*; b) *Enterococcus faecalis*; c) *Staphylococcus pseudintermedius*; d) *Proteus mirabilis*; e) *Proteus* spp. (not otherwise specified); f) *Enterobacter* spp.

Amox-Clav = amoxicillin clavulanate; TMS = trimethoprim-sulfonamide. Chart colors represent local antimicrobial importance ratings, red for high importance, yellow for medium importance, green for low importance. Intrinsic resistance and drugs that were tested on fewer than 30 isolates of the species/genus are not included.

Table S1: Urine sample source by animal species, age and sex

	Dogs				Cats				
Age (whole years completed)	Fema le	Ma le	NR*	Total (% of dog samples)	Fem ale	Ma le	N R*	Total (% of cat samples)	Grand Total (% of all samples)
0	188	33	1	222 (5.9)	11	14	0	25 (1.3)	247 (4.4)
1-3	289	90	10	389 (10)	87	90	3	180 (10)	569 (10)
4-6	347	4	5	476 (13)	104	82	1	187 (10)	663 (12)
7-9	622	5	4	861 (23)	121	77	4	202 (11)	1063 (57)
10-12	736	1	5	1032 (27)	197	0	2	299 (16)	1331 (24)
13-15	521	4	1	686 (18)	344	99	3	446 (24)	1132 (20)
16+	71	26	1	98 (2.6)	434	77	0	511 (28)	609 (11)
Total		96				53			
(% from that species)	2774	3	27		1298	9	13		
	(74)	(26)	(<1)	3764	(70)	(29)	(<1)	1850	5614

*NR = not recorded. Female and male categories include both entire and desexed animals

Table S2: Multiple resistance patterns in *E. coli*

	Resistance combinations detected	n	Proportion	Comments
Two	AMX + SXT	75	2.3%	
	AMX + FQN	30	0.9%	
	AMX + LEX	16	0.5%	
	AMX + LEX + CVN	122	3.7%	Most frequent combination
Three	AMX + FQN + SXT	24	0.7%	
Four	AMX + AMC + LEX + CVN	63	1.9%	
	AMX + LEX + CVN + SXT	22	0.7%	
	AMX + LEX + CVN + FQN	11	0.3%	
Five	AMX + LEX + CVN + FQN + SXT	24	0.7%	
	AMX + AMC + LEX + CVN + SXT	8	0.2%	
Six	AMX + LEX + CVN + TET + FQN	5	0.2%	
Ten	AMX + AMC + LEX + CVN + CLI + TET + FQN + GEN + TIC + SXT	1	0.03%	Broadest resistance pattern detected

Only combinations detected in $\geq 0.2\%$ of all isolates, or representative of the broadest resistance pattern for this bacterial species are listed. AMX = amoxicillin (tested using ampicillin); AMC = amoxicillin-clavulanate; CLI = clindamycin; CVN = cefovecin ; TET = tetracyclines (doxycycline, tetracycline); FQN = any fluoroquinolone (enrofloxacin, marbofloxacin, ciprofloxacin); GEN = gentamicin; LEX = cephalixin; SXT = trimethoprim-sulfamethoxazole; TIC = ticarcillin.

Table S3: Multiple resistance patterns in *Enterococcus faecalis*

	Resistance combinations detected	n	Proportion	Comments
Two	FQN + TET	43	6.8%	Most frequent combination
	FQN + ERY	24	3.8%	
	FQN + CLI	9	1.4%	
	FQN + GEN	6	0.9%	
	FQN + AMX	2	0.3%	
	FQN + AMC	1	0.2%	
	TET + ERY	1	0.2%	
Three	FQN + AMX + AMC	11	1.7%	Broadest resistance patterns detected
	FQN + TET + GEN	8	1.3%	
	FQN + CLI + ERY	4	0.6%	
	FQN + TET + GEN	2	0.3%	
Four	FQN + AMX + AMC + TET	1	0.2%	
	FQN + AMX + TET + GEN	1	0.2%	
	FQN + AMX + AMC + ERY	1	0.2%	
Five	FQN + AMX + AMC + TET + ERY	3	0.5%	
	FQN + AMX + AMC + TET + GEN	2	0.3%	
	FQN + AMX + AMC + ERY + GEN	1	0.2%	

Only combinations detected in $\geq 0.2\%$ of all isolates, or representative of the broadest resistance pattern for this bacterial species are listed. AMX = amoxicillin (tested using ampicillin); AMC = amoxicillin-clavulanate; TET = tetracyclines (doxycycline, tetracycline); ERY = erythromycin; FQN = any fluoroquinolone (enrofloxacin, marbofloxacin, ciprofloxacin); GEN = gentamicin.

Table S4: Multiple resistance patterns in *Staphylococcus pseudintermedius*

	Resistance combinations detected	n	Proportion	Comments
Two	FQN + SXT	3	0.6%	Most frequent combination
	TET + ERY	3	0.6%	
	AMX + SXT	1	0.2%	
Three	AMX + LEX + CVN	13	2.5%	
	TET + ERY + SXT	3	0.6%	
	TET + FQN + SXT	1	0.2%	
	AMX + LEX + SXT	1	0.2%	
	AMC + LEX + CVN	1	0.2%	
Four	AMX + LEX + CVN + SXT	9	1.8%	
	AMX + AMC + LEX + CVN	3	0.6%	
	TET + FQN + GEN + SXT	1	0.2%	
Five	TET + FQN + ERY + GEN + SXT	2	0.4%	Broadest resistance pattern detected
	AMX + AMC + LEX + CVN + FQN	1	0.2%	
Six	TET + FQN + ERY + GEN + TIC + SXT	1	0.2%	
Eight	AMX + AMC + LEX + CVN + TET + ERY + GEN + SXT	1	0.2%	

Only combinations detected in $\geq 0.2\%$ of all isolates, or representative of the broadest resistance pattern for this bacterial species are listed. AMX = amoxicillin (tested using ampicillin); AMC = amoxicillin-clavulanate; CVN = ceftiofur ; TET = tetracyclines (doxycycline, tetracycline); ERY = erythromycin; FQN = any fluoroquinolone (enrofloxacin, marbofloxacin, ciprofloxacin); GEN = gentamicin; LEX = cephalexin; SXT = trimethoprim-sulfamethoxazole; TIC = ticarcillin.

Table S5: Multiple resistance patterns in *Proteus mirabilis*

	Resistance combinations detected	n	Proportion	Comments
Two	AMX + SXT	12	2.7%	Most frequent combination
	AMX + CVN	1	0.2%	
	AMX + FQN	1	0.2%	
	FQN + SXT	1	0.2%	
	LEX + CVN	1	0.2%	
Three	AMX + LEX + CVN	7	1.6%	Broadest resistance patterns detected
	AMX + FQN + SXT	3	0.7%	
Four	AMX + AMC + LEX + CVN	3	0.7%	
	AMX + LEX + CVN + SXT	2	0.5%	
	AMX + LEX + CVN + GEN	1	0.2%	

Only combinations detected in $\geq 0.2\%$ of all isolates, or representative of the broadest resistance pattern for this bacterial species are listed. AMX = amoxicillin (tested using ampicillin); AMC = amoxicillin-clavulanate; CVN = cefovecin ; FQN = any fluoroquinolone (enrofloxacin, marbofloxacin, ciprofloxacin); GEN = gentamicin; LEX = cephalexin; SXT = trimethoprim-sulfamethoxazole.

Document S6: Extract from CDS Manual, 10th Edition, pages 67-79

Source: <https://cdstest.net/manual/> Accessed 31/03/2026

11. Tables

A guide to the use of the tables

There are 4 sets of tables containing information essential for the performance of the CDS Test. These tables are intended for both Clinical and Veterinary laboratories. Antibiotics used in veterinary medicine only are flagged.

Calibration tables 1a, 1b, & 1c collectively summarise much of the basic information used in the CDS Test. They list all the organisms and antimicrobials tested, the media used, conditions of incubation, disc potencies, cut off sizes for unusual annular radii and the MICs for susceptible strains (breakpoints). The tables are updated regularly and operators should ensure that they are using the latest versions of these tables. It is most important to pay particular attention to the footnotes included with each table as these highlight exceptions, restrictions and some specific directions. For organisms not included in the Table of calibrations, extrapolate the testing from that established for similar organisms.

Surrogate disc testing tables 2a and 2b list those antimicrobials where the susceptibility can be inferred from the results obtained with a closely related agent, the “surrogate disc”. The table is arranged according to bacterial species and the relationship between the antimicrobials is valid only for the species indicated. This table is also updated regularly as data are accumulated which either invalidate the relationship or enable us to add agents to the list. Laboratories may find it useful to include a comment on the susceptibility report that the result reported with a particular antimicrobial indicates the susceptibility to another.

Quality assurance tables 3a, 3b, & 3c list the 12 reference strains, the media, and the incubation conditions of testing and the expected range of zone sizes observed with each disc of a stated potency. The footnotes explain how the acceptable ranges of zone sizes were derived and recommend the indications for and the frequency of testing the reference strains.

Table 4 is a guide through the maze of testing and reporting the susceptibility of Gram negative aerobic species to β -lactam antibiotics. The production of one or more β -lactamases is an important and common mechanism of resistance in these species but, for several reasons, resistance may be difficult or impossible to demonstrate by the usual methods of antibiotic susceptibility testing. The table sets out, in some detail, those species where resistance should be assumed on the basis of previous documentation of the presence of a stable mechanism of resistance and those where susceptibility can be reliably demonstrated by the disc test. This table also relies heavily on the footnotes to draw attention to exceptions and special circumstances.

11.1. Calibrations

Table 11.1.a. Calibrations: *Gram Positive Organisms*

Antibiotics, disc potencies, annular radii and MIC for susceptible strains, media and incubation conditions.

Antibiotic	Disc potency (µg)	Exception to the standard interpretation ^a	MIC (mg/L)
<i>Corynebacterium</i> species			
(Blood Sensitest, CO₂, 35-37°C)^b			
Ampicillin ^c	5	4 mm	≤ 2
Benzylpenicillin	0.5 u		≤ 0.125
Chloramphenicol	30		≤ 8
Ciprofloxacin	2.5		≤ 1
Clindamycin ^d	2		≤ 0.5
Erythromycin	5		≤ 0.5
Florfenicol ^e	30		≤ 8
Fusidic acid	2.5		≤ 0.5
Marbofloxacin ^e	5		≤ 2
Moxifloxacin	2.5		≤ 1
Pradofloxacin ^e	5		≤ 2
Quinupristin/Dalfopristin	15		≤ 2
Rifampicin	1		≤ 0.5
Teicoplanin	15	2 mm	≤ 8
Tetracycline	10		≤ 4
Tigecycline	15		≤ 1
Vancomycin	5	2 mm	≤ 4
Enterococci			
(Blood Sensitest, CO₂, 35-37°C)			
Ampicillin ^f	5	4 mm ^f	≤ 4
Chloramphenicol	30	4 mm	≤ 8
Doxycycline ^g	30	4 mm	≤ 16
Florfenicol ^e	30		≤ 8
Fosfomycin ^g	200		≤ 64
Gentamicin	200		≤ 256
Linezolid	10		≤ 4
Marbofloxacin ^e	5		≤ 2
Nitrofurantoin ^g	200	4 mm	≤ 64
Pradofloxacin ^e	5		≤ 2
Quinupristin/Dalfopristin ^h	15		≤ 2
Streptomycin	300	4 mm	≤ 512
Teicoplanin	15	2 mm	≤ 8
Tetracycline	10		≤ 4
Tigecycline	15		≤ 1
Vancomycin ^{i,j}	5	(See foot note) ⁱ	≤ 4

^a The standard 6 mm cut-off applies where no exception has been specified.

^b Slow growers are incubated for 48h.

^c *Corynebacterium* species: benzylpenicillin 0.5 u/ampicillin 5 µg: If the inhibitory zone is < 6 mm with a benzylpenicillin 0.5 u disc and ≥ 4 mm with an ampicillin 5 µg disc, report the susceptibility as follows: "There is decreased susceptibility to penicillin, ampicillin and amoxycillin with the MIC between 0.25 mg/L and 2.0 mg/L."

^d Isolates with inducible clindamycin resistance (iMLS_B phenotype) will have a large zone to clindamycin, but should be reported as resistant (see section 4.7).

^e Antibiotic calibrated for veterinary medicine.

^f Perform a nitrocefin based test to detect β-lactamase activity if the zone of inhibition has a sharp edge and an annular radius > 4 mm. β-lactamase positive isolates are reported as resistant.

^g For testing urine isolates only.

^h *Enterococcus faecalis* is intrinsically resistant to pristinamycin and quinupristin/dalfopristin.

ⁱ A zone of inhibition with a hazy edge and a light growth towards the disc indicates a low level resistance to vancomycin (VanB type), irrespective of the size of the inhibitory zone. The light growth will be more evident if the plate is reincubated for 48 h.

^j *Enterococcus gallinarum* and *Enterococcus casseliflavus* possess the natural vanC type resistance and should be reported as resistant (see section 4.2.7).

Table 11.1.a. Calibrations: *Gram Positive Organisms* cont.

Antibiotics, disc potencies, annular radii and MIC for susceptible strains, media and incubation conditions.

Antibiotic	Disc potency (µg)	Exception to the standard interpretation ^a	MIC (mg/L)
<i>Listeria</i> species			
(Blood Sensitest, CO₂, 35-37°C)			
Ampicillin	5		≤ 1
Gentamicin	10		≤ 1
Trimethoprim-sulfamethoxazole	1.25/23.75		≤ 0.5/9.5
<i>Staphylococci</i>			
(Sensitest, Air 35-37°C)			
Ampicillin ^k	5		≤ 0.5
Benzylpenicillin ^l	0.5 u		≤ 0.06
Cefoxitin ^m	10		≤ 4
Ceftaroline ⁿ	5		≤ 1
Cephalexin ^k	100		≤ 16
Chloramphenicol	30		≤ 8
Ciprofloxacin	2.5		≤ 1
Clindamycin ^o	2		≤ 0.5
Erythromycin	5		≤ 0.5
Florfenicol ^k	30		≤ 8
Fusidic acid	2.5		≤ 0.5
Gentamicin	10		≤ 1
Linezolid	10		≤ 4
Marbofloxacin ^e	5		≤ 2
Moxifloxacin	2.5		≤ 1
Mupirocin	5		≤ 2
Neomycin ^e	30	4 mm	≤ 8
Nitrofurantoin ^g	200		≤ 32
Novobiocin ^e	5		≤ 1
Oxacillin ^p	1		≤ 0.25
Pradofloxacin ^e	5		≤ 2
Quinupristin/Dalfopristin	15		≤ 2
Rifampicin	1		≤ 0.5
Teicoplanin	15	2 mm	≤ 8
Tetracycline	10		≤ 4
Tigecycline	15		≤ 1
Trimethoprim	5		≤ 4
Trimethoprim-sulfamethoxazole	1.25/23.75		≤ 1/19
Vancomycin	5	2 mm	≤ 4

^a The standard 6 mm cut-off applies where no exception has been specified.^c Antibiotic calibrated for veterinary medicine.^g For testing urine isolates only.^k For testing *Staphylococcus saprophyticus* only.^l Not for testing *Staphylococcus saprophyticus*.^m For testing *Staphylococcus aureus* and *Staphylococcus lugdunensis* only.ⁿ For testing MRSA only.^o Isolates with inducible clindamycin resistance (iMLS_B phenotype) will have a large zone to clindamycin, but should be reported as resistant. Inducible clindamycin resistance can be detected as described in section 4.7.^p For testing coagulase-negative staphylococci (except *Staphylococcus saprophyticus* and *Staphylococcus lugdunensis*).

Table 11.1.a. Calibrations: *Gram Positive Organisms* cont.

Antibiotics, disc potencies, annular radii and MIC for susceptible strains, media and incubation conditions.

Antibiotic	Disc potency (µg)	Exception to the standard interpretation ^a	MIC (mg/L)
<i>Streptococci & Erysipelothrix</i> species (Blood Sensitest, CO₂, 35-37°C)			
Ampicillin ^q	5	4 mm	≤ 2
Benzylpenicillin	0.5 u		≤ 0.125
Cefotaxime	0.5	4 mm	≤ 0.5
Cefotaxime ^q	5		≤ 2
Ceftriaxone	0.5	4 mm	≤ 0.5
Ceftriaxone ^q	5		≤ 2
Chloramphenicol	30		≤ 8
Clindamycin ^o	2		≤ 0.5
Erythromycin	5		≤ 0.5
Florfenicol ^f	30		≤ 8
Marbofloxacin ^e	5		≤ 2
Moxifloxacin	2.5	4 mm	≤ 1
Nitrofurantoin ^g	200	4 mm	≤ 32
Pradofloxacin ^e	5		≤ 2
Quinupristin/Dalfopristin	15		≤ 2
Rifampicin	1		≤ 0.5
Teicoplanin	15	2 mm	≤ 8
Tetracycline	10		≤ 4
Tigecycline	15		≤ 1
Trimethoprim-sulfamethoxazole	1.25/23.75		≤ 0.5/9.5
Vancomycin	5	2 mm	≤ 4

^a The standard 6 mm cut-off applies where no exception has been specified.^e Antibiotic calibrated for veterinary medicine^g For testing urine isolates only^o Isolates with inducible clindamycin resistance (iMLS_B phenotype) will have a large zone to clindamycin, but should be reported as resistant. Inducible clindamycin resistance can be detected as described in section 4.7.^q NOT for testing *Streptococcus pneumoniae* from CSF. If *Streptococcus pneumoniae* or any other *Streptococcus* species from a site other than CSF is resistant to benzylpenicillin 0.5 u, cefotaxime 0.5 µg or ceftriaxone 0.5 µg then test ampicillin 5 µg, cefotaxime 5 µg and ceftriaxone 5 µg.

Table 11.1.b. Calibrations: *Gram Negative Organisms*

Antibiotics, disc potencies, annular radii and MIC for susceptible strains, media and incubation conditions.

Antibiotic	Disc potency (µg)	Exception to the standard interpretation ^a	MIC (mg/L)
<i>Acinetobacter</i> species, Enterobacteriaceae & Vibrionaceae (Sensitest, air, 35-37°C)^b			
Amikacin	30	4 mm	≤ 16
Amoxycillin-clavulanic acid ^c	40/20		≤ 8/4
Ampicillin ^d	25		≤ 8
Azithromycin ^e	15	4 mm	≤ 16
Aztreonam	30		≤ 8
Cefazolin	30		≤ 4
Cefepime	10		≤ 2
Cefotaxime	5		≤ 1
Cefotetan	30		≤ 8
Cefoxitin	30		≤ 8
Cefpodoxime	10		≤ 2
Ceftazidime	10		≤ 4
Ceftolozane-tazobactam	30/10		≤ 2
Ceftriaxone	5		≤ 1
Cefuroxime	30		≤ 8
Cephalexin ^c	100		≤ 16
Chloramphenicol	30		≤ 8
Ciprofloxacin	2.5		≤ 1
Doripenem	10		≤ 4
Ertapenem ^f	10		≤ 4
Florfenicol ^h	30		≤ 8
Fosfomycin ^g	200		≤ 32
Gentamicin	10	4 mm	≤ 2
Imipenem ⁱ	10		≤ 4
Marbofloxacin ^h	5		≤ 2
Meropenem	5		≤ 2
Moxifloxacin	2.5		≤ 1
Nalidixic acid ^c	30		≤ 4
Neomycin ^h	30	4 mm	≤ 8
Nitrofurantoin ^g	200		≤ 32
Norfloxacin ^g	10		≤ 4
Piperacillin-tazobactam ^c	50/5		≤ 16/2
Polymyxin B ^j	300 u	4 mm	≤ 1
Pradofloxacin ^h	5		≤ 2
Spectinomycin ^h	25		≤ 32
Streptomycin ^h	25		≤ 16
Tetracycline	10	4 mm	≤ 4
Ticarcillin-clavulanic acid ^c	75/10		≤ 16/2
Tigecycline ⁱ	15		≤ 1
Tobramycin	10	4 mm	≤ 2
Trimethoprim	5		≤ 4
Trimethoprim-sulfamethoxazole	1.25/23.75		≤ 1/19

^a The standard 6 mm cut-off applies where no exception has been specified.^b *Yersinia enterocolitica* is incubated in air at 30° C.^c If an ESBL is present, report amoxycillin-clavulanic acid, ticarcillin-clavulanic acid and piperacillin-tazobactam for isolates from uncomplicated UTI only.^d Test ampicillin 25 and cephalexin 100 in parallel. Strains resistant to cephalexin but appear susceptible to ampicillin (presence of chromosomal inducible AmpC β-lactamase) are reported as resistant to ampicillin/amoxicillin.^e For the testing of *Salmonella* Typhi and other *Salmonella* species isolated from blood culture.^f *Acinetobacter* species are considered resistant to ertapenem.^g For testing urinary isolates only. *Acinetobacter* species are considered inherently resistant to Fosfomycin.^h Antibiotic calibrated for veterinary medicine.ⁱ *Proteus* species, *Providencia* species and *Morganella morganii* are considered resistant to tigecycline, refer to section 5.5 regarding imipenem testing.^j Polymyxin B tested for screening purposes only.

Table 11.1.b. Calibrations: Gram Negative Organisms cont.

Antibiotics, disc potencies, annular radii and MIC for susceptible strains, media and incubation conditions.

Antibiotic	Disc potency (µg)	Exception to the standard interpretation ^a	MIC (mg/L)
<i>Moraxella catarrhalis</i> (Blood Sensitest, 5% CO ₂ , 35-37°C)			
Benzylpenicillin	0.5 u		≤ 0.25
Cefaclor	30		≤ 4
Cefpodoxime	10		≤ 2
Cefuroxime	30		≤ 4
Chloramphenicol	10		≤ 4
Ciprofloxacin	2.5		≤ 1
Erythromycin	5		≤ 0.5
Florfenicol ^b	30		≤ 8
Marbofloxacin ^b	5		≤ 2
Moxifloxacin	2.5		≤ 1
Tetracycline	10		≤ 4
Trimethoprim-sulfamethoxazole	1.25/23.75		≤ 1/19
<i>Campylobacter</i> species (Blood Sensitest, microaerophilic, 42°C)			
Ciprofloxacin	2.5		≤ 1
Erythromycin	5	4 mm	≤ 0.5
Gentamicin	10		≤ 1
Tetracycline	10		≤ 4
<i>Haemophilus</i> species (HTM agar ^j , 5% CO ₂ , 35-37°C)			
Amoxycillin-clavulanic acid	10/5		≤ 2/1
Ampicillin	5		≤ 1
Cefaclor	30		≤ 4
Cefotaxime	0.5		≤ 0.25
Cefotaxime	5		≤ 1
Cefpodoxime	10		≤ 2
Ceftriaxone	0.5		≤ 0.25
Ceftriaxone	5		≤ 1
Cefuroxime	30		≤ 4
Chloramphenicol	10		≤ 2
Ciprofloxacin	2.5		≤ 1
Florfenicol ^b	30		≤ 8
Marbofloxacin ^b	5		≤ 2
Moxifloxacin	2.5		≤ 1
Tetracycline	10		≤ 4
Trimethoprim-sulfamethoxazole	1.25/23.75		≤ 1/19

^a The standard 6 mm cut-off applies where no exception has been specified.^b Antibiotic calibrated for veterinary medicine.^j Haemophilus Test Medium Base containing 15 mg/L of freshly prepared haematin and NAD.

Table 11.1.b. Calibrations: *Gram Negative Organisms* cont.

Antibiotics, disc potencies, annular radii and MIC for susceptible strains, media and incubation conditions.

Antibiotic	Disc potency (μg)	Exception to the standard interpretation ^a	MIC (mg/L)
<i>Helicobacter pylori</i>			
(Chocolate Columbia Blood Agar, microaerophilic, 35-37°C)			
Amoxycillin	2		≤ 1
Ciprofloxacin	2.5		≤ 1
Erythromycin ^k	5		≤ 0.5
Metronidazole	5		≤ 4
Rifampicin ^l	5		≤ 2
Tetracycline	10		≤ 4
<i>Neisseria meningitidis</i>			
(Blood Sensitest, 5% CO₂, 35-37°C)			
Benzympenicillin	0.5 u	4 mm	≤ 0.25
Cefotaxime	0.5		≤ 0.25
Ceftriaxone	0.5		≤ 0.25
Chloramphenicol	10		≤ 2
Ciprofloxacin	2.5		≤ 1
Rifampicin	1		≤ 0.5

^a The standard 6 mm cut-off applies where no exception has been specified.^k Erythromycin 5 μg is the surrogate disc for reporting the susceptibility to clarithromycin. The MIC of clarithromycin for susceptible strains is ≤ 0.5 mg/L.^l Rifampicin 5 μg is the surrogate disc for reporting the susceptibility to rifabutin.

Table 11.1.b. Calibrations: Gram Negative Organisms cont.

Antibiotics, disc potencies, annular radii and MIC for susceptible strains, media and incubation conditions.

Antibiotic	Disc potency (µg)	Exception to the standard interpretation ^a	MIC (mg/L)
<i>Pasteurella</i> species (Blood Sensitest, 5% CO ₂ , 35-37°C)			
Ampicillin ^m	5		≤ 2
Benzylpenicillin	0.5 u	4 mm	≤ 0.25
Cefotaxime	0.5		≤ 0.06
Ceftriaxone	0.5		≤ 0.06
Ciprofloxacin	2.5		≤ 1
Erythromycin ^h	5	4 mm	≤ 2
Florfenicol ^h	30		≤ 8
Marbofloxacin ^h	5		≤ 2
Moxifloxacin	2.5		≤ 1
Pradofloxacin ^h	5		≤ 2
Tetracycline	10		≤ 4
<i>Pseudomonas</i> species, <i>Burkholderia</i> species & <i>Chryseobacterium</i> species (Sensitest, air, 35-37°C)			
Amoxycillin-clavulanic acid ^a	40/20		≤ 8/4
Amikacin	30	4 mm	≤ 16
Aztreonam	30		≤ 8
Cefepime	10		≤ 2
Cefpirome	10		≤ 2
Ceftazidime	10		≤ 4
Ceftolozane-tazobactam	30/10		≤ 2
Ciprofloxacin	2.5		≤ 1
Doripenem	10		≤ 4
Ertapenem	10		≤ 4
Florfenicol ^h	30		≤ 8
Fosfomycin ^g	200		≤ 32
Gentamicin	10	4 mm	≤ 4
Imipenem	10		≤ 4
Marbofloxacin ^h	5		≤ 2
Meropenem	5		≤ 2
Moxifloxacin	2.5		≤ 1
Norfloxacin ^g	10		≤ 4
Piperacillin-tazobactam	50/5		≤ 16/2
Polymyxin B	300 u	4 mm	≤ 2
Pradofloxacin ^h	5		≤ 2
Ticarcillin ^h	75		≤ 32
Ticarcillin-clavulanic acid	75/10		≤ 16/2
Tobramycin	10	4 mm	≤ 4
Trimethoprim	5		≤ 4
Trimethoprim-sulfamethoxazole	1.25/23.75		≤ 2/38
<i>Stenotrophomonas maltophilia</i>^a (Sensitest, air, 35-37°C)			
Trimethoprim-sulfamethoxazole ^o	1.25/23.75		≤ 2/38

^a The standard 6 mm cut-off applies where no exception has been specified.^g For testing urine isolates only.^h Antibiotic calibrated for veterinary medicine.^m *Pasteurella multocida* is tested against ampicillin 5 µg and NOT benzylpenicillin 0.5 u.ⁿ *Burkholderia pseudomallei* is usually susceptible to amoxycillin-clavulanic acid and can be tested against this antibiotic.^o See Section 5.10 for notes on testing antibiotic susceptibilities of Sulphonamide resistant *Stenotrophomonas maltophilia*.

Table 11.1.c. Calibrations: *Anaerobic Organisms*.

Antibiotics, disc potencies, annular radii and MIC for susceptible strains, media and incubation conditions.

Antibiotic	Disc potency (μg)	Exception to the standard interpretation ^a	MIC (mg/L)
Anaerobic organisms^b			
(Supplemented Brucella Medium Base, anaerobic, 35-37°C)^c			
Amoxycillin-clavulanic acid	2/1	4 mm	$\leq 2/1$
Benzylpenicillin	0.5 u		≤ 0.25
Cefoxitin	10		≤ 4
Clindamycin ^d	2	4 mm	≤ 0.5
Meropenem	5		≤ 2
Metronidazole	5	4 mm	≤ 2
Moxifloxacin	2.5	4 mm	≤ 2
Piperacillin-tazobactam	50/5		$\leq 8/2$

^a The standard 6 mm cut off applies where no exception has been specified^b Slow growers should be incubated for 48 h.^c Brucella Medium Base containing 5% defibrinated horse blood, haemin 5 mg/L and vitamin K 1 mg/L.^d An erythromycin 5 μg disc must be placed 13mm edge to edge to detect inducible clindamycin resistance as described in section 4.7.

11.2. Surrogate discs

Table 11.2.a. Surrogate disc testing: *Gram Positive Organisms*

Antibiotics that can be reported based on susceptibility results obtained with a surrogate disc.

Antibiotic reported	Surrogate disc used	Disc potency (ug)
<i>Corynebacterium</i> species		
Amoxycillin/Ampicillin/Penicillin V	Benzympenicillin	0.5 u
Azithromycin/Clarithromycin/Roxithromycin	Erythromycin	5
Carbapenems	Benzympenicillin	0.5 u
Cefovecin ^a /Ceftiofur ^a /other Cephalosporins ^b	Benzympenicillin	0.5 u
Enrofloxacin ^a /Orbifloxacin ^a	Moxifloxacin	2.5
Lincomycin	Clindamycin	2
Norfloxacin ^c	Ciprofloxacin	2.5
Pristinamycin	Quinupristin/Dalfopristin	15
Tetracyclines	Tetracycline	10
Tylosin ^a	Erythromycin	5
Enterococci		
Amoxycillin/Benzympenicillin	Ampicillin	5
Enrofloxacin ^a /Orbifloxacin ^a	Moxifloxacin	2.5
Pristinamycin ^d	Quinupristin/Dalfopristin	15
<i>Listeria</i> species		
Amoxycillin/Benzympenicillin	Ampicillin	5
Staphylococci (except <i>S. saprophyticus</i> from urine)		
Amoxycillin/Ampicillin/Penicillin V	Benzympenicillin	0.5 u
Amoxycillin-clavulanic acid	Oxacillin ^e /Cefoxitin ^f	1/10
Azithromycin/Clarithromycin/Roxithromycin	Erythromycin	5
Carbapenems	Oxacillin ^e /Cefoxitin ^f	1/10
Cefovecin ^a /Ceftiofur ^a /other Cephalosporins ^b	Oxacillin ^e /Cefoxitin ^f	1/10
Cloxacillin/Dicloxacillin/Flucloxacillin	Oxacillin ^e /Cefoxitin ^f	1/10
Enrofloxacin ^a /Orbifloxacin ^a	Moxifloxacin	2.5
Framycetin ^a	Neomycin	30
Lincomycin	Clindamycin	2
Norfloxacin ^c /Ofloxacin	Ciprofloxacin	2.5
Pristinamycin	Quinupristin/Dalfopristin	15
Tetracyclines	Tetracycline	10
Tylosin ^a	Erythromycin	5
<i>Staphylococcus saprophyticus</i> from urine		
Amoxycillin/Benzympenicillin/Penicillin V	Ampicillin	5
Amoxycillin-clavulanic acid	Cephalexin	100
Cefovecin ^a /Ceftiofur ^a /other Cephalosporins ^b	Cephalexin	100
Cloxacillin/Dicloxacillin/Flucloxacillin	Cephalexin	100
Enrofloxacin ^a /Orbifloxacin ^a	Moxifloxacin	2.5
Norfloxacin ^c /Ofloxacin	Ciprofloxacin	2.5
Tetracyclines	Tetracycline	10

^a Antibiotic used in veterinary medicine only.

^b Ceftazidime is inactive against Gram positive organisms.

^c Reporting of norfloxacin is for urine isolates only.

^d *Enterococcus faecalis* is intrinsically resistant to pristinamycin and quinupristin/dalfopristin.

^e Oxacillin is used for testing coagulase-negative staphylococci (except *Staphylococcus saprophyticus* and *Staphylococcus lugdunensis*).

^f Cefoxitin is used for testing *Staphylococcus aureus* and *Staphylococcus lugdunensis*.

Table 11.2.a. Surrogate disc testing: *Gram Positive Organisms* cont.

Antibiotics that can be reported based on susceptibility results obtained with a surrogate disc.

Antibiotic reported	Surrogate disc used	Disc potency (ug)
Streptococci^a		
Amoxycillin/ amoxycillin-clavulanic acid/ Ampicillin/Penicillin V	Benzylpenicillin	0.5 u
Amoxycillin/ amoxycillin-clavulanic acid / Benzylpenicillin	Ampicillin ^b	5
Amoxycillin-clavulanic acid ⁱ	Benzylpenicillin	0.5 u
Amoxycillin-clavulanic acid ⁱ	Ampicillin	5
Azithromycin/Clarithromycin/Roxithromycin	Erythromycin	5
Carbapenems	Benzylpenicillin	0.5 u
Cefovecin ^a /Ceftiofur ^a	Benzylpenicillin	0.5 u
Cefovecin ^a /Ceftiofur ^a	Cefotaxime ^j	5
Cephalosporins (except Ceftiofur) ^a	Cefotaxime/Ceftriaxone ^k	0.5/5
Enrofloxacin ^a /Orbifloxacin ^a	Moxifloxacin	2.5
Flucloxacillin	Benzylpenicillin	0.5 u
Lincomycin	Clindamycin	2
Pristinamycin	Quinupristin/Dalfopristin	15
Tetracyclines	Tetracycline	10
Tylosin ^a	Erythromycin	5

^a Antibiotic used in veterinary medicine only.^b For streptococci groups A, B, C, G and *Streptococcus anginosus* group, the susceptibility to benzylpenicillin, ampicillin, amoxycillin and cephalosporin antibiotics (except ceftazidime) is extrapolated from the testing of benzylpenicillin 0.5 u.^c NOT for testing *Streptococcus pneumoniae* from CSF. Test if isolate is resistant to benzylpenicillin 0.5 u, cefotaxime 0.5 mg or ceftriaxone 0.5 mg and reported as having a decreased susceptibility.^d For the reporting of all *Streptococcus* species including *S. pneumoniae* from sites other than CSF. If the organism is resistant to benzylpenicillin 0.5 u and susceptible to Ampicillin 5 µg, report as having a decreased susceptibility.^e If the organism is resistant to benzylpenicillin 0.5 u and susceptible to cefotaxime 5 µg, report as having a decreased susceptibility to Cefovecin^a/Ceftiofur^a.^f If the organism is resistant to cefotaxime/ceftriaxone 0.5 and susceptible to cefotaxime/ceftriaxone 5µg, report as having a decreased susceptibility.

Table 11.2.b. Surrogate disc testing: Gram Negative Organisms

Antibiotics that can be reported based on susceptibility results obtained with a surrogate disc.

Antibiotic reported	Surrogate disc used	Disc potency (ug)
Acinetobacter, Enterobacteriaceae & Vibrionaceae species		
Amoxycillin	Ampicillin	25
Cefovecin/Ceftiofur ^a	Cefotaxime	5
Cephalothin ^b	Ampicillin	25
Ceftriaxone	Cefotaxime	5
Cefotaxime	Ceftriaxone	5
Colistin	Polymyxin B	300 u
Enrofloxacin ^a /Orbifloxacin ^a	Moxifloxacin	2.5
Framycetin ^a	Neomycin	30
Ofloxacin	Ciprofloxacin	2.5
Piperacillin	Ampicillin	25
Tetracyclines	Tetracycline	10
Ticarcillin ^a	Ampicillin	25
Moraxella catarrhalis		
Azithromycin/Clarithromycin/Roxithromycin	Erythromycin	5
Amoxycillin/Ampicillin/Penicillin V	Benzympenicillin	0.5 u
Amoxycillin-clavulanic acid	Cefuroxime/Cefaclor	30
Cefovecin ^a /Ceftiofur ^a	Cefuroxime/Cefaclor	30
Cephalosporins	Cefuroxime/Cefaclor	30
Enrofloxacin ^a /Orbifloxacin ^a	Moxifloxacin	2.5
Ofloxacin	Ciprofloxacin	2.5
Tetracyclines	Tetracycline	10
Campylobacter species		
Azithromycin /Clarithromycin ^a /Roxithromycin ^a	Erythromycin	5
Enrofloxacin ^a /Orbifloxacin ^a /Ofloxacin	Ciprofloxacin	2.5
Tetracyclines	Tetracycline	10
Haemophilus influenzae/Haemophilus species		
Amoxycillin	Ampicillin	5
Cefepime	Cefotaxime/Ceftriaxone	0.5
Cefotaxime	Ceftriaxone	0.5
Cefpirome	Cefotaxime/Ceftriaxone	0.5
Ceftazidime	Cefotaxime/Ceftriaxone	0.5
Cefovecin ^a /Ceftiofur ^a	Cefuroxime/Cefaclor	30
Ceftriaxone	Cefotaxime	0.5
Cephalexin	Cefuroxime/Cefaclor	30
Enrofloxacin ^a /Orbifloxacin ^a	Moxifloxacin	2.5
Ofloxacin	Ciprofloxacin	2.5
Tetracyclines	Tetracycline	10
Helicobacter pylori		
Clarithromycin	Erythromycin	5
Rifabutin	Rifampicin	5

^a Antibiotic used in veterinary medicine only^b Not for *Acinetobacter* species.

Table 11.2.b. Surrogate disc testing: *Gram Negative Organisms* cont.

Antibiotics that can be reported based on susceptibility results obtained with a surrogate disc.

Antibiotic reported	Surrogate disc used	Disc potency (ug)
<i>Neisseria meningitidis</i>		
Ampicillin/Amoxycillin	Benzylopicillin	0.5 u
Cefotaxime	Ceftriaxone	0.5
Cefovecin ^a /Ceftiofur ^a	Benzylopicillin	0.5 u
Ceftriaxone	Cefotaxime	0.5
Enrofloxacin ^a /Orbifloxacin ^a	Moxifloxacin	2.5
<i>Pasteurella</i> species		
Amoxycillin/Benzylopicillin	Ampicillin	5
Amoxycillin-clavulanic acid	Ampicillin	5
Ampicillin/Amoxycillin ^c	Benzylopicillin	0.5 u
Cephalexin	Ampicillin	5
Cefovecin ^a /Ceftiofur ^a	Ampicillin	5
Enrofloxacin ^a /Orbifloxacin ^a	Moxifloxacin	2.5
Norfloxacin /Ofloxacin	Ciprofloxacin	2.5
Tetracyclines	Tetracycline	10
<i>Pseudomonas</i> species, <i>Burkholderia</i> species & <i>Chryseobacterium</i> species		
Colistin	Polymyxin B	300 u
Enrofloxacin ^a /Orbifloxacin ^a	Moxifloxacin	2.5
Norfloxacin/Ofloxacin	Ciprofloxacin	2.5

^a Antibiotic used in veterinary medicine only.^c *Pasteurella multocida* is tested against ampicillin 5 µg and NOT benzylopicillin 0.5 u.

Appendix 2: Supplementary materials for Chapter 4

Pet Owners and Antibiotics: Knowledge, Opinions, Expectations, and Communication Preferences

Document S1: Pet owner questionnaire

Document S1: Pet owner questionnaire

Pet Owner Survey

Start of Block: Welcome and thank you

Q1 Hi there, Aussie Dog or Cat Owner!

Thank you very much for taking 15 minutes out of your day to help me with my PhD research. I really look forward to reading your responses. Every answer gives me a better understanding of what pet owners think and feel about antibiotics. I will use this information to design resources for vets, that help them communicate more effectively with owners about this topic.

Please click on this link and read the participant information document before proceeding. [20200818 pet owner pls v2](#)

To move through the survey, **click the arrow buttons** at the bottom of each section. At the end you will be asked whether you'd also like to be interviewed. Don't forget to click the very last arrow button in order to submit your responses.

When you're done, if you would **pass the survey link on** to just one or two (or twenty-five) friends who own a dog or cat, anywhere in Australia, it would help me tremendously!

Warmest thanks,
Ri Scarborough, BVSc (Hons), PhD Candidate, University of Melbourne
(UniMelb human research ethics approval 2057499.1)

End of Block: Welcome and thank you

Start of Block: First, I'd like to know a little bit about you, please.



Q2 This survey is for Australian residents who own (or have previously owned) a cat or dog. What is your residential postcode, please?

.....

Q3 And which of these best describes where you live?

- ☐ Capital city, inner urban
- ☐ Capital city, outer urban
- ☐ Regional city or large town
- ☐ Small town
- ☐ Rural or remote property not in a town

.....

Q4

What is your gender?

We ask this to check we are getting responses from a broad sample of pet owners. If you prefer not to answer, you can skip this question.

- ☐ Male
- ☐ Female
- ☐ Non-binary

Q5 What is your age?

We ask this to check we are getting responses from a broad sample of pet owners. If you prefer not to answer, you can skip this question.

- ☐ 20 or under
- ☐ 21-30
- ☐ 31-40
- ☐ 41-50
- ☐ 51-60
- ☐ 61-70
- ☐ over 70

Q6 What is the highest level of education you have completed?

We ask this to check we are getting responses from a broad sample of pet owners. If you prefer not to answer, please skip this question.

- ☐ I did not complete primary school
- ☐ Primary school
- ☐ Secondary school certificate
- ☐ Diploma or Certificate
- ☐ Bachelor degree
- ☐ Postgraduate qualification

Q7

Please select the fields in which you have ever:
- undertaken any university study; and/or
- worked

Select all that apply

- ☐ Human health
- ☐ Animal health
- ☐ Agriculture or animal production
- ☐ Scientific research
- ☐ Science education
- ☐ NONE of the above

Q8 What kind of pet/s do you currently own?

Select all that apply

- ☐ Dog
- ☐ Cat
- ☐ I don't own a dog or cat at the moment, but I have in the past

End of Block: First, I'd like to know a little bit about you, please.

Start of Block: Block 2

Q9 When was the last time you took a cat or dog to a vet for ANY of the following: an illness, e.g. diarrhoea, vomiting, fever, coughing, not eating, change in urination a wound or abscess; or another skin or ear problem?

- ☐ In the last 6 months
- ☐ 6-12 months ago
- ☐ 1-2 years ago
- ☐ More than 2 years ago

Skip To: End of Block If When was the last time you took a cat or dog to a vet for ANY of the following: an illness, e.g.... = More than 2 years ago

Q10 Now think back to *before* you took your animal to the vet.
Did you *hope* or *expect* that your pet would get medication for this problem?

- ☐ Yes
- ☐ No
- ☐ Not sure

Display This Question:

If Now think back to before you took your animal to the vet. Did you hope or expect that your pet wo... =
Yes

Q11 In a few words, please explain *why* you hoped or expected your animal would get medication.

Q12 Did your animal get antibiotics for this problem?

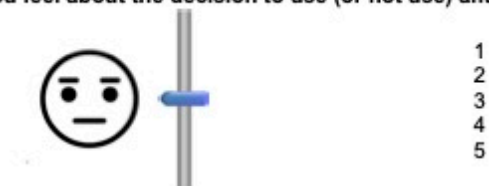
There are many types of antibiotics, and they come in many forms. They are commonly: injected by the vet given by mouth as tablets, capsules, pastes or liquid, or applied to the skin or ear directly as a cream, ointment or lotion

- ☐ Yes
- ☐ No
- ☐ Not sure

Display This Question:

If Did your animal get antibiotics for this problem? There are many types of antibiotics, and they... != Not sure

Q13 How did you feel about the decision to use (or not use) antibiotics at that time?



End of Block: Block 2

Start of Block: Vets can say the same thing in different ways. What's most helpful to you?

Q14 Imagine your vet has examined your unwell pet and determined the he/she probably (or certainly) does NOT need antibiotics. Which of these statements from your vet would make you feel most comfortable with a decision NOT to give antibiotics?

Note: These are similar, but not the same. Pick the one that immediately feels best.

- ☐ Your pet doesn't need antibiotics today, but here are some things we can do to make him/her more comfortable.
- ☐ Here are some things we can do to make your pet more comfortable, but he/she doesn't need any antibiotics today.

Q15 Which of these statements from your vet would make you feel most comfortable with a decision NOT to give antibiotics?

- ☐ In my experience, giving antibiotics does not help this to get better any faster.
- ☐ Clinical trials have shown that using antibiotics does not help this to get better any faster.
- ☐ Your pet's immune system can fight this off without antibiotics, if we just give it some time.

Q16 Which of these statements from your vet would make you feel most comfortable with a decision NOT to give antibiotics?

- ☐ It's best for your animal not to have antibiotics unless they are really needed, and in this case he/she doesn't need them.
- ☐ Antibiotics can have negative effects on your pet, so it's good that he/she doesn't need them today.
- ☐ It's important that we use antibiotics only when they're needed, and your animal doesn't need them today.

Q17 Which of these statements from your vet would make you feel most comfortable with a decision NOT to give antibiotics?

- ☐ I'm not too worried about your pet's condition at the moment, so I don't think he/she needs antibiotics.
- ☐ Your pet is still eating and drinking, temperature is normal, gum colour is good and the chest is clear, so I am comfortable that he/she doesn't need antibiotics.

End of Block: Vets can say the same thing in different ways. What's most helpful to you?

Start of Block: Block 6

Q18 Imagine your vet has told you that your pet's condition *usually* resolves by itself in about 3 days, but occasionally that doesn't happen and then it might need antibiotics. Which of these statements from your vet would make you feel most comfortable with a decision NOT to give antibiotics today?

- ☐ If it's not getting better in 3 days, please give me a call and I'll arrange some antibiotics for you to pick up.
- ☐ If it's not getting better in 3 days, please come back in to the clinic and we'll re-check your animal, no charge, and decide on treatment then.
- ☐ If it's not getting better in 3 days, please come back in and pick up some antibiotics. I'll leave a note on your electronic file that any of our staff can give those to you, without another consultation.
- ☐ If it's not getting better in 3 days, please come back in and pick up some antibiotics. Here is a prescription that you can bring back to this clinic and give to any member of our team. Then they can give you the antibiotics, without another consultation.

End of Block: Block 6

Start of Block: Block 3

Q19 Have you ever wanted a vet to give your cat or dog antibiotics, specifically?

- ☐ Yes, and I have asked for them specifically
- ☐ Yes, and I have hinted that I wanted them, but I have never asked
- ☐ Yes, but I have never hinted or asked
- ☐ Never

Q20 Have you ever been surprised, disappointed or frustrated when a vet did *not* give your cat or dog antibiotics?

- ☐ Yes, very
- ☐ Yes, a little
- ☐ Never

Display This Question:

If Have you ever been surprised, disappointed or frustrated when a vet did not give your cat or dog... !=
Never

Q21 Why were you surprised, disappointed or frustrated?

Give as much detail as you can.

Page 6 of 10



Q22 Imagine your vet has said your pet needs antibiotics. There are two choices:

- 1) the best antibiotic for the job, which is a tablet that needs to be given twice a day for 5 days
- 2) A single injection lasting 14 days, given by the vet, but it's not the best antibiotic for the job.

Choose UP TO THREE things from this list that are most likely to convince you to choose the tablets over the injection.

- ☐ The tablets are much less likely to create antibiotic-resistant bacteria (superbugs) in your pet
- ☐ The tablets are less than half the price of the injection
- ☐ The tablets are 10% more likely to cure your pet
- ☐ The tablets are much less likely to cause side effects in your pet
- ☐ If the tablets don't work or cause nasty side effects, we can easily stop them and change to a different treatment. But if that happens with the injection, we can't take it out.
- ☐ The tablets are the most responsible choice for public health
- ☐ The tablets are the best choice according to the Australian Veterinary Prescribing Guidelines

End of Block: Block 3

Start of Block: Block 5

Q23 How much do you agree with the following statements about vets and treatment choices?

	Strongly DISAGREE	Somewhat disagree	NEUTRAL	Somewhat agree	Strongly AGREE
Vets should make treatment as cheap as possible for owners	☐	☐	☐	☐	☐
I would be annoyed if my animal was not cured the first time, and I had to go back to the vet	☐	☐	☐	☐	☐
Vets should make treatment as convenient as possible for owners	☐	☐	☐	☐	☐
When an animal is sick, sometimes all it needs is some nursing care and time	☐	☐	☐	☐	☐
If I take a sick pet to the vet, I would be upset if it didn't get any medication	☐	☐	☐	☐	☐
If my sick pet doesn't get any medication, I feel that I haven't got good value from the vet consultation	☐	☐	☐	☐	☐
I trust my vet to do the right thing by my animal	☐	☐	☐	☐	☐
I would probably choose a cheaper treatment option, over a more effective option that was more expensive	☐	☐	☐	☐	☐
I would probably choose an easier treatment option, over a more effective option that was more work for me	☐	☐	☐	☐	☐
When my pet is sick, I want my vet to give me a few different treatment options and let me decide	☐	☐	☐	☐	☐
When my pet is sick, I want my vet to give me one clear recommendation that is the best thing for my pet	☐	☐	☐	☐	☐
If my pet is sick and the vets says antibiotics "probably" won't help, I would still want my pet to get antibiotics, just in case.	☐	☐	☐	☐	☐

End of Block: Block 5

Page 8 of 10

Q24 How much do you agree with the following statements?

	Strongly DISAGREE	Somewhat disagree	NEUTRAL	Somewhat agree	Strongly AGREE
The risks of antibiotics are so small that they're not worth worrying about	☐	☐	☐	☐	☐
Antibiotics almost always help a sick animal get better quicker	☐	☐	☐	☐	☐
All infections, whether viral or bacterial, should be treated with antibiotics	☐	☐	☐	☐	☐
Giving my pet antibiotics can have a negative effect on its health	☐	☐	☐	☐	☐
Giving my pet antibiotics could have a negative effect on my health	☐	☐	☐	☐	☐
Giving my pet antibiotics could have a negative effect on people and animals outside my household	☐	☐	☐	☐	☐
Bacteria are known to transfer from pets to their owners	☐	☐	☐	☐	☐
Bacteria are known to transfer from owners to their pets	☐	☐	☐	☐	☐
Bacteria that are resistant to antibiotics ("superbugs") are a serious problem in Australia	☐	☐	☐	☐	☐
Vets should only give antibiotics to my pet only when they are really needed	☐	☐	☐	☐	☐
Vets have a responsibility to protect animal and human public health	☐	☐	☐	☐	☐
I'd prefer my pet not to receive antibiotics, if they can be avoided	☐	☐	☐	☐	☐

Q25 Is there anything else you would like to tell the researchers about your thoughts or experiences with vets, pets and antibiotics?

End of Block: Almost at the end now. Thanks so much for sticking with it!

Start of Block: Block 4

Q26 After completing this survey, some owners will be invited to take part in a 45-minute interview to explore their thoughts and experiences around antibiotic use. The interview will be led by one or two University researchers and will be done online using a secure Zoom meeting, at a time that suits you. The interview will be audio-recorded and the content analysed.

Participants who complete an interview will receive a \$20 Coles Myer gift voucher as partial compensation for their time.

Would you like to be considered for an interview?

- ☐ Yes, I am happy to be invited to an interview
- ☐ No, I don't want to be invited to an interview.

Display This Question:

If After completing this survey, some owners will be invited to take part in a 45-minute interview t... = Yes, I am happy to be invited to an interview

Category (% missing data)		n	Proportion	
Gender (41%)	Female	56	92%	
	Male	5	8%	
	Non-binary	0	0%	
Age group (41%)	30-	20	33%	
	31-40	9	15%	
	41-50	15	25%	
	51-60	12	20%	
	61+	5	8%	
Pets owned (39%)	Dog(s) only	28	44%	
	Cat(s) only	14	22%	
	Dog(s) and cat(s)	17	27%	
	Past pets only	4	6%	
Australian state of residence (51%)	VIC	34	67%	
	NSW	12	24%	
	QLD	1	2%	
	All other states/territories (total)	33	6%	
Residential area description (41%)	Capital city, inner urban	29	48%	
	Capital city, outer urban	14	19%	
	Regional city or large town	12	20%	
	Small town	6	12%	
SEIFA quintile of residential area (49%)	1 - least advantaged	1	2%	
	2	5	9%	
	3	12	23%	
	4	6	11%	
	5 - most advantaged	29	55%	
Highest education (41%)	School	6	10%	
	Diploma or Certificate	19	31%	
	Bachelor degree	23	38%	
	Postgraduate qualification	13	21%	
Fields of university study or work (0%)	Animal production or agriculture	3	3%	
	Animal health	9	9%	
	Human health	20	19%	
	Scientific research	1	1%	
	Science education	1	1%	
	None of the above	70	67%	

Table S1: Demographics of respondents excluded from analysis

Appendix 3: Supplementary materials for Chapter 5

‘Brave Enough’: A qualitative study of veterinary decisions to withhold or delay antimicrobial treatment in pets

Table S1. Participant’s estimates of the contribution made by different sectors to the overall problem of AMR in Australia.

	Estimated Contribution AMR	Stratified by Participant Interest Level in AMR/AMS		
	All (n = 22)	Low	Moderate	High
Human hospitals	33%	30%	27%	39%
Human community care	25%	23%	24%	27%
Companion animals (inc. horses)	15%	20%	14%	14%
Production animals	22%	22%	27%	17%
Other farming	6%	4%	8%	4%



Interview Guide

What factors influence the antimicrobial prescribing behaviours of companion animal veterinarians?

Note that the following text is indicative only. These are semi-structured interviews and the questions asked will adapt according to the responses given.

Establish rapport: Thank you very much for agreeing to this interview, I really appreciate your help. (Confirm willingness to proceed) You previously indicated that this would be a good time for you to speak to me uninterrupted for about an hour, is that still the case?

Introduce project: As you would have read in the information I emailed to you, I'm completing a PhD in veterinary science with a focus on veterinary prescribing decisions. Today I'm going to ask you some questions to understand how you use antibiotics in dogs and cats. I'm going to record the interview, but I haven't started recording yet. I'll let you know before I start recording, OK? After the interview, I'll have the audio recording transcribed. Then my colleagues and I will analyse the transcript, along with others, and we'll aim to publish our findings in a veterinary journal. You will not be identifiable from the publication. **Do you understand and agree to this?**

Establish purpose: I want to highlight from the outset that this research is about understanding *how* you decide on an antibiotic treatment, and it's really important to me that you are completely honest about how you make your decisions.

Highlight anonymity and confidentiality: I also want to reassure you that your responses are anonymous. When this interview is transcribed, you'll only be identified by a code. If we happen to mention any names or places in the interview, I'll remove them from the transcript. And I'm going to be extremely careful to ensure that there is no way anyone could re-identify you from the information that is published. **Do you have any questions** about this or any other aspect of the study before we get started?

(Notify that recording will begin) OK, I'm going to start the audio recording now.

Warm up questions: Where did you study veterinary science? How long have you worked at your current clinic? Where had you worked prior to that? Have you always worked with small animals?

Warming up to questions about antibiotics: And when it comes to using antibiotics in dogs and cats, how do you think your use compares with other vets?

About using antibiotics when they are not needed: Many vets say they have had cases that they knew wouldn't benefit from antibiotics, but for a range of reasons, they prescribed antibiotics anyway. Has this happened to you? Can you tell me more about that? Try to get them to think of a specific case. What factors contributed to your decision in that case? How did you choose which antibiotic to give and for how long? How did it make you feel to prescribe something when you didn't believe it would help?

Choosing an antibiotic when it is needed: Of course, in many cases, it is obvious that antibiotics would help. **What factors do you usually consider when choosing an antibiotic?** What factors are most

important? Would you ever look up information about antibiotic type and dose? If so, where? If they don't mention AMR risk, ask if they consider AMR risk when choosing an antibiotic.

Think-aloud scenarios:

Now I'm going to present a couple of hypothetical clinical scenarios and get you to "think aloud" through each one and make a plan to manage the case. I'll provide some information and you can ask for any additional information you feel you need to make a decision.

Case Study 1:

You are presented with Dash, a 2 year-old female neuter German Shepherd cross with a 4-day history of abnormally frequent, small volume urinations, but no change in drinking, appetite or activity. The owner says Dash is otherwise very healthy and has never had a problem like this before. On examination, the dog is bright and has a normal temperature. You decide to collect urine via cystocentesis. You get a good sample. The urine is grossly cloudy. USG is normal. Dipstick is negative for glucose and ketones. You stain the urinary sediment with Sedi-Stain, and under the microscope you see abundant white cells, abundant rod-shaped extracellular bacteria, a few red cells, no crystals or casts.

What management options are you considering at this point? Would you like any other information before deciding what to do? (If yes) Why do you want to know that?

What would you typically do next? Offer owner culture and sensitivity? – why, why not?

How would you treat this? Which antibiotic? How long will you treat for? Why did you choose this antibiotic? Which other antibiotics might you consider using for this case? Can you think of a situation where you would choose a different antibiotic for the same illness in a similar animal? Why?

Managing owner challenge: When you propose the course of oral antibiotics, the owner says, "I've got a lot on and I just don't think I'm going to remember to give all those tablets. My friend's dog had this problem and she got an antibiotic injection instead. That's what I would like." What thoughts go through your head at this time? What do you say to the owner?

Case Study 2:

Your patient is Mr Claws, an 8 year-old male neuter domestic short hair cat. Four nights ago, Mr Claws got into a fight with another cat and now has an obvious abscess on the lateral side of his right hind limb, proximal to the stifle joint. The owner, says he has been grumpy and off his food for the last 24 hours and has a limp. When you initially try to take his temperature, he hisses and tries to scratch you. His owner grabs a towel from her cat carrier, and quickly wraps him up so you can insert the thermometer. You compliment her on her skills and she comments, "My parents used to breed cats so I know how to handle them!" The temperature is 39.5. As the cat hasn't had access to any food for several hours, you decide to anaesthetise, lance and flush the abscess and place a Penrose drain and Elizabethan collar.

What other management options are you considering at this point? Would you like any other information before deciding what to do? (If yes) Why do you want to know that?

What would you typically do next? Send pus for culture and sensitivity? – why, why not?

Do you want to give any other treatment? Why/not? Which antibiotic? How long will you treat for? Why did you choose this antibiotic? Which other antibiotics might you use for this case? Can you think of a situation where you would choose a different antibiotic for the same illness in a similar animal? Why?

Owner challenge re oral antibiotics: When you propose the course of oral antibiotics, the owner says, “I’ve got a lot on and I just don’t think I’m going to remember to give all those tablets. Isn’t there an injection you can give instead?” What thoughts go through your head at this time? What do you say to the owner?

Owner challenge re Convenia: When you propose the Convenia injection, the owner says, “I’m actually a hospital pharmacist and that seems like a really high level antibiotic to be giving. Is that the best option?” What thoughts go through your head at this time? What do you say to the owner?

Now let’s move on from hypotheticals to discussing how you actually use antibiotics in the course of your usual clinic practice.

Can you think of one or two specific cases when you have prescribed antibiotics but you didn’t think they were required? What factors contributed to your decisions to prescribe? Which of these do you think was the most important factor?

Can you think of a specific case when a colleague prescribed an antibiotic that was much broader spectrum and/or longer duration than suggested in the Australian Veterinary Prescribing Guidelines? What factors do you think contributed to that person’s decision to prescribe that way? Which of these do you think was the most important factor?

[Take notes and reflect back to interviewee the factors they have mentioned]

Vets in other studies have mentioned the following factors as contributors to using antibiotics when they were probably not needed. Do you think that these played a role for you and why/not?

- Client expectations of antibiotics (explicit, implicit, perceived)
- Lack of time/skill to explain why antibiotics are not needed
- Fear of client taking business elsewhere
- Fear of infection post-surgery
- Fear of having “missed something” that later deteriorates
- Fear of client complaint or professional discipline
- Accessibility of diagnostics to rule in/out bacterial infection (cost, speed, owner acceptance)
- Habit
- Influence of colleagues/clinic norms or protocols
- Perception that their own prescribing doesn’t contribute meaningfully to AMR

Are there other factors that you think play a role for you?

When antibiotics are needed, how do you select an antibiotic type, route and duration? (Can prompt with examples, e.g. cat with pneumonia; dog with gastroenteritis and signs of sepsis) **What if the owner isn't confident giving tablets?**

Can you think of one or two specific cases when you have prescribed an antibiotic that was much broader spectrum and/or longer duration than suggested in the Australian Veterinary Prescribing Guidelines? What factors contributed to your decision to prescribe that way? Which of these do you think was the most important factor?

[Take notes and reflect back to interviewee the factors they have mentioned]

Can you think of a specific case when a colleague prescribed an antibiotic that was much broader spectrum and/or longer duration than suggested in the Australian Veterinary Prescribing Guidelines? What factors do you think contributed to that person's decision to prescribe that way? Which of these do you think was the most important factor?

Vets in other studies have also mentioned the following factors as contributors to using antibiotics that were too broad spectrum or too long duration compared with guideline recommendations. One example is using a long-acting 3rd generation cephalosporin injection for a cat fight abscess with systemic illness. Do you think that these played a role for you and why/not?

- Responding to perceived or overt client pressure
- Feeling that broader spectrum is "safer bet"
- Not aware of guidelines
- No access to prescribing guidelines
- Not aware of the spectrum of action
- Lack of time/skill to teach client how to give tablets
- Accessibility of C&S to select appropriate antibiotic (cost, speed, owner acceptance)
- Habit
- Influence of colleagues/clinic norms or protocols
- Perception that their own prescribing doesn't contribute meaningfully to AMR

Are there other factors that you think play a role for you?

Assuming no barriers to change existed, if you could choose two things that would really help improve the appropriateness of antibiotic use in your practice or in Australian small animal practice in general, what would they be? Can be at any level from policy, to regulation, to education, skills training, informational resources.

Wrap up:

Thank you for helping me understand factors that influence antibiotic decisions in the clinic. We've now come to the end of my questions. Is there anything you would like to add before we stop the recording?

[Stop recording] I appreciate the time you took for this interview. Thanks again.

Document S3:Codebook

Background Factors	
Client factors	Including whether they have pet insurance, health literacy, attitudes, behaviour in consultation
Veterinarian's clinical experience and confidence	Include communication skills
Veterinarian's attitudes to antimicrobial use and AMR	How concerned do they feel?
Habits	
Veterinarians' workload, energy, time	
Workplace factors	Including culture, policies and procedures, location
Other	
Behavioural beliefs	
Fear of clinical deterioration	Include downstream consequences
Fear of failing to meet client expectations	Include downstream consequences
Perceived impact of withholding antimicrobials	Will it make a difference?
Time and workflow issues	What are the alternatives to giving antimicrobials in this situation? What is the work impact of that?
Normative beliefs	
Employer and colleagues	Expectations regarding antimicrobial use, contribution to practice profit, etc.
Pet owner	E.g., pre-existing expectations of receiving antimicrobials, awareness of AMR
Veterinary Board	Potential for complaints and professional reprimand
Other	Undergraduate lecturers, etc.
Control beliefs	
Availability of non-antibiotic treatment options	e.g., probiotics
Client factors	Including capacity to undertake non-antimicrobial therapy, or to competently 'watch and wait'
Diagnostic uncertainty and action bias	Feeling that you need to 'do something' even if you don't know what you're treating
Time pressure	Include availability of para-veterinary staff
Veterinarians' suggestions for improving antimicrobial use	
Veterinarian education and training	Webinars on antimicrobial use, communication skills
Para-veterinary staff education and training	Avoid setting client expectations of antimicrobials, enable non-antimicrobial treatment options
Client education	Improved understanding of AMR
Workplace culture	
Informational resources	Prescribing guidelines, webinars, other
Audit and sanctions	

Appendix 4: Supplementary materials for Chapter 6

Seeking simplicity, navigating complexity: how veterinarians select an antimicrobial drug, dose and duration for companion animals

Document S1: Example of traffic-light AST report



Veterinary Microbiology Laboratory

The University of Melbourne
Faculty of Science
250 Princes Highway Werribee VIC 3030
Phone: 03 9731 2044
Email: vet-micro@unimelb.edu.au

Owner: XXXX

Name: XXXX

Lab ref: XXXX

Species: Feline

Submitter: XXXX

Specimen information:

Cystocentesis urine

Date of Report: 29/10/2025

Date Submitted: 07/02/2024

Number of Specimens: 1

Test requested: Urine-C&S

Results

Intermediate Report:



Final Report:



Microscopy results: Gram negative bacilli +++

Culture results: 7/2/24 Cultures underway.
8/2/24 A heavy pure growth of *Escherichia coli*.
Antibiotic susceptibility testing in progress.
9/2/24 Report finalised.

Antimicrobial	<i>Escherichia coli</i>
Low importance	
Ampicillin (Amoxycillin)	S
Tetracycline	S
Trimethoprim/Sulfamethoxazole	S
Medium importance	
Amoxycillin+Clavulanate	S
Cephalexin	S
High importance	
Enrofloxacin/Marbofloxacin	S

Many of the antimicrobial susceptibility testing results reported will require off-label use. Compliance with the legal requirements of your jurisdiction is your responsibility.

Australian Veterinary Antibiotic Prescribing Guidelines

<https://vetantibiotics.science.unimelb.edu.au/>

ASTAG Antimicrobial Importance Ratings

<https://www.amr.gov.au/resources/importance-ratings-and-summary-antibacterial-uses-human-and-animal-australia>

Report prepared by: XXXX

