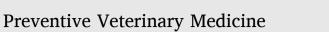
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Antimicrobial use on Australian dairy cattle farms – A survey of veterinarians

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ABSTRACT

Aims: The aims of this study were to determine antimicrobial prescription patterns and the factors affecting antimicrobial selection amongst Australian dairy veterinarians.

Methods: A structured questionnaire was administered to Australian dairy cattle veterinarians using the Qualtrics online survey platform. Questions focused on their (1) demographics; (2) opinions surrounding antimicrobial use, resistance, and stewardship; (3) decision-making drivers of both prescription and selection of commonly prescribed antimicrobials; (4) awareness on the guidelines for antimicrobial usage and sources of information concerning antimicrobials.

Key results: A total of 135 responses (14.1% response rate) from all eight dairying regions in Australia were received. The attitudes, perceptions, and concerns of dairy veterinarians towards antimicrobials indicated a high agreement regarding label indications (96%), consequences of off-label prescription (95%), and the presence of an antimicrobial resistance (AMR) risk (73%), when prescribing antibiotics. A four-dimensional categorical principal components analysis (CATPCA) model indicated most of the variation in opinion was due to AMR risk, trade-offs, prescription concerns and active substance concerns. The first active substance most dairy veterinarians chose for a scenario involving mastitis and dry cow therapy (DCT) treatment was cloxacillin. Decision-making drivers for antimicrobial choice when providing advice regarding the supply of antimicrobials for mastitis and DCT treatment were predominately clinical factors; however, diagnostics were rarely used in determining antimicrobial choice due to cost of implementation, diagnostic accuracy (sensitivity, specificity), and benefit issues. Non-clinical decision-making drivers included the perception of practicality for Australian Veterinary Association (AVA) prescription guidelines, opinions surrounding AMR risk and prescription concerns, consideration of Expert Advisory Group on Antimicrobial Resistance (EAGAR) scores, number of years worked with dairy farms, and the number of dairy farms they regularly consult for. When available at the practice, prescription policies were considered to impact on animal welfare outcomes and on the probability of AMR emergence. The major information sources influencing decision making on antimicrobial prescription for the Australian dairy veterinarians were clinical experience (93%) and product labels (81%).

Conclusions: Australian dairy veterinarians are generally aware of the risk of resistance to antimicrobials and the need for stewardship, with clinical factors having the most impact on antimicrobial prescription. However, non-clinical factors incorporating awareness of guidelines and their attitudes on antimicrobial resistance risk and prescription concerns impact on the choice and prescription of antimicrobials.

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1. Introduction

While antimicrobials benefit the health and productivity of animals in agriculture, their use selects for genotypic, and therefore potential phenotypic, resistant bacteria (Seveno et al., 2002; Oliver et al., 2011; Mukerji et al., 2017). The potential to transmit resistance directly, by transfer of bacteria or via the food-chain, may provide complications in the management and treatment of both animal and human disease (Oliver et al., 2011; Kidsley et al., 2018; Jayarao et al., 2019). Registered veterinarians have a functional role in reducing the risk of antimicrobial resistance (AMR) from developing in Australia, being the sole authorized prescribers of antimicrobials for animal health care. State governments guide this prescription, legislating antimicrobial use (AMU) with respect for AMR risk mitigation. This includes reference to Antimicrobial Importance Ratings (AIR), or Expert Advisory Group on Antimicrobial Resistance (EAGAR) scores, under the advice of the Australian Strategic and Technical Advisory Group (ASTAG). These scores incorporate the associated risk of resistance from the use of an antimicrobial substance and the availability of antibacterial alternatives within the context of human medicine (ASTAG, 2018). Antimicrobial substances are classified as low, medium, and high, with an increase in level of class implying less alternatives are available if resistance develops, while antimicrobials considered last line or critically important antimicrobials (CIA) are restricted or banned for use in animals (Western Australian Government, 2016; ASTAG, 2018). Furthermore the Australian Veterinary Association (AVA) provides guidance on the veterinary use of antimicrobial substances in reference to the ASTAG ratings through prescribing and dispensing guidelines (AVA, 2013). This also includes a 'traffic light' system for line of use when prescribing an active substance in animal applications within specific industries. Green active substances are first line treatment options, orange active substances are second line treatment options, and the restricted use active substances that are last line or CIA in human medicine graded red (AVA, 2013).

In addition to the management of AMU in diseases of animals, veterinarians provide professional advice and supervision regarding disease management, disease prevention, and AMU to producers in the production animal industries (LeBlanc et al., 2006; World Organistation for Animal Health (OIE), 2016). Considering the significance of veterinarians in animal related AMU, it is important to investigate the factors that impact on prescription patterns by veterinarians. In terms of the dairy industry, several international studies have analyzed these factors in recent years (Léger et al., 2015; McDougall et al., 2017; Scherpenzeel et al., 2018). However, none have evaluated veterinarians working within the Australian dairy industry. The overall aim of this study was to determine antimicrobial prescribing patterns and the factors affecting antimicrobial selection among veterinarians within the Australian dairy context. This aim was met through the following specific objectives; (1) determine the attitudes, perceptions, and concerns of Australian dairy veterinarians towards antimicrobial prescription, antimicrobial resistance and antimicrobial stewardship (AMS) in the dairy industry; (2) determine the decision-making drivers of antimicrobial choice and prescription on farm among dairy cattle veterinarians in Australia; and (3) determine Australian dairy cattle veterinarians awareness on the guidelines and information sources concerning antimicrobials.

2. Materials and methods

2.1. Study design

An anonymous, voluntary national online survey was made available

from March to June 2021 through the Qualtrics online survey software (Qualtrics, Provo, UT; qualtrics.com). An entry to win an iPad (valued at \$500) was provided to each respondent to incentivize questionnaire completion and hence increase the response rate. The target population, consisting of 955 registered Australian veterinarians working within the Australian dairy industry, was estimated using the percentage of respondents indicating dairy as a componential field of practice in the AVA Workforce Survey (AVA, 2019). Veterinarians practicing across Australia's dairying industry, encompassing the eight distinct geographical and regional development program areas generally recognized by industry (Dairy Australia, 2019), were invited to participate in the study through a non-probabilistic sampling method. An invitation to participate in the study with a link to the online survey was distributed electronically in the Veterinary Surgeons' Board Western Australia newsletter, via the AVA member Facebook page, and various dairy related social media groups (Australian Veterinarians in Public Health, Australian Veterinarian Network and Bovine Interest Group), Apiam Animal Health Clinics, and to practices listed as having an accredited cattle pregnancy check veterinarian on the 'My Cattle Vet' website (mycattlevet.com.au). The study was conducted with the approval of the Human Research Committee of Murdoch University, Approval No. 2021/004.

2.2. Sample size calculations

Sample size calculations were performed using the *Epitools* epidemiological calculator (Sergeant, 2018) to estimate the number of participants required for appropriate inferences to be made. This was achieved through an estimation of a single percentage with specified precision assuming that 50% of the target population (veterinarians) would be knowledgeable and aware of prudent AMU practices. We specified a 95% confidence interval and a 10% error rate, hence a minimum of 97 responses were required.

2.3. Questionnaire design

The questionnaire template was developed using a three-stage process employed by Aleri and Laurence (2020). The initial stage in this process involved collating and adapting questions from the New Zealand based study by McDougall et al. (2017) and similar published studies (Léger et al., 2015; Ekakoro and Okafor, 2019; Gibbons et al., 2013) to develop a draft questionnaire relevant to Australia. Academics and researchers were then involved in the second stage of development, reviewing the questions in accordance with the study objectives; namely (1) demographics, (2) attitudes, perceptions, and concerns towards antimicrobial use, resistance, and stewardship, (3) decision-making drivers for the prescription of antimicrobials, and (4) awareness of industry guidelines and sources of information for antimicrobial prescription in dairy cattle in Australia. The last stage in the questionnaire development involved pre-testing the questionnaire for clarity with five practicing veterinarians. The final template produced 22 closed and open-ended questions across four sections to investigate the study objectives and broad areas of interest (Supplementary material-Questionnaire).

2.4. Description of variables

2.4.1. Demographics

Section one of the questionnaire was related to the demographics of respondents' including general description questions to identify the region in which they practiced dairy, the number of years spent working with dairy farms, if they were a practice owner, the number of dairy farms they regularly serviced, and the percentage of professional time spent working with dairy cattle. In addition, respondents were asked to profile the average annual number of consultations, and annual average case numbers across six common on-farm dairy cattle diseases (acidosis, diarrhoea, lameness, mastitis, metritis, and respiratory disease).

2.4.2. Attitudes, perceptions, and concerns towards antimicrobials

The second section identified the level of agreement or disagreement of respondents to 14 statements using a five-point Likert-type scale (strongly disagree, disagree, neutral, agree, and strongly agree). These statements were in relation to their perceptions, knowledge, and beliefs regarding antimicrobial prescription, resistance, and stewardship.

2.4.3. Decision-making drivers of antimicrobial prescription

The third section explored the decision-making drivers for both the choice of active substance and the provision of antimicrobial prescription. Firstly, respondents were presented a consistent scenario for consultation that focused on clinical mastitis and dry cow therapy (DCT) treatment for the dairy cattle of a familiar client (Supplementary material- Questionnaire). They were asked to indicate the first choice of active substance, and second choice if the first active substance failed (initially or during previous treatment on farm the antimicrobial was not suitable or non-available), for which they would provide advice regarding the supply of antimicrobials. Secondly, to identify the factors affecting prescription, respondents were asked to identify the top two factors they consider in the provision of advice regarding the supply of antimicrobials in terms of (A) the active substance to be considered, (B) the prompting or request from farm/farmer, (C) the animal under consideration, (D) the likely pathogen, and (E) based on the practice decision or protocol.

2.4.4. Guideline awareness and information sources

The fourth section incorporated questions relating to knowledge and opinions on guidelines such as the AVA's prescribing guidelines, the existence and impact of employer based formal prescribing policy, the use of culture results in recent clinical cases, relation of EAGAR score in antimicrobial choice, if they would use a rapid testing (< 24 h) for identification of bacteria in mastitis cases and factors affecting the uptake of such a test, and the impact of the herd size on antimicrobial choice. Finally, a five-point Likert-type scale was provided for respondents to indicate how frequently they accessed different sources for information regarding antimicrobial use in dairy cattle.

2.5. Statistical analysis

The questionnaire data generated in the Qualtrics software were collated and entered into Microsoft Excel (Microsoft Office, version 16.41; 2020) for storage under the Production Animal Medicine Murdoch University online database. All data analysis and visualization were conducted in R v4.0.5 (R Core Team, 2021) using the likert package v1.3.5 (Bryer and Speerschneider, 2016), Gifi package v0.3-9 (Mair and Leeuw, 2019) and ggplot2 package v3.3.5 (Wickham, 2016). The percentage of responses were calculated to describe the questionnaire response rate; demographics; attitudes, perceptions and concerns of antimicrobial prescription, resistance, and stewardship; decision making drivers of antimicrobial prescription; and awareness of the guidelines and sources of information for antimicrobial prescription. The questionnaire response rate was estimated as a percentage of registered veterinarians working within the dairy industry using data from the Australian Veterinary Association Workforce Survey (The Australian Veterinary Association Ltd, 2019).

Analytical models were performed on the data about active substance choices for mastitis and DCT therapy. Missing data within this subset were accounted for using averaged measured values using the nearest neighbor imputation method (Beretta and Santaniello, 2016). To determine the underlying pattern of importance and priority of the 14 Likert scale statements concerning the respondents' attitudes, perceptions, and concerns towards antimicrobials, categorical (also known as nonlinear) principal components analysis (CATPCA) was performed. CATPCA can determine relationships between mixed measurement (nominal, ordinal, and numeric) data by overcoming multicollinearity and reducing the dimension of the data, while accounting for as much variance as possible (Linting and van der Kooij, 2012). To fit the CATPCA model the categories for the Likert-scale statement variables were transformed with assigned optimal scale values (strongly disagree = 1 to strongly agree = 5) (Manisera et al., 2010). Additionally, dairying region (nominal), years worked (numeric) and practice owner (nominal) were added to the CATPCA as supplementary variables. The data were treated as ordinal, with the optimum number and importance of components assessed through the variance accounted for (VAF) value for each component, the associated scree plots and the eigenvalue according to Kaiser's criterion (Linting et al., 2007). The Varimax orthogonal rotation was used to rotate the components to simplify interpretation of the CATPCA.

Logistic regression models were developed to describe the relationship of possible drivers of active substance treatment choice for mastitis and DCT by respondents. This was achieved through a three-step process. Initially a Causal Model was built to describe possible drivers of the first active substance choice, and second active substance treatment choice for mastitis and DCT by respondents (Supplementary material-Casual model). The outcome variables (first active substance choice for mastitis, second active substance choice (if the first failed) for mastitis, first active substance choice for DCT, and the second active substance choice (if the first failed) for DCT) were binary coded using the associated importance in human medicine and EAGAR score as directed by AVA and ASTAG (AVA, 2013; ASTAG, 2018), and indicated in Table 4. Therefore, 1 = classified as low EAGAR score, first line active substances and all non-antimicrobial measure responses provided under 'other' on the questionnaire (namely culling or internal teat sealant); and 0 = medium to high EAGAR scores or second- and third-line active substances. The identified explanatory variables used included: the consolidated information defined by the unrotated four principal components of the CATPCA (PC1, PC2, PC3, PC4), dairying region (the eight dairying regions in Australia generally recognized by industry and 'multiple practice regions' if respondents indicated that they practiced across regions listed as separate categories), years worked (numeric variable), practice owner (yes or no), number of dairying farms (numeric variable), percentage of time spent servicing dairy clients (>25, 25-50 or >50%), AVA guidelines seen to be practical (no, not aware, or yes), AVA guidelines seen to be reasonable (yes or no), formal prescription policy in the veterinary business (true or false), number of times used culture results for diagnosis in the last 10 cases (<5 or >5 cases), and weighting of EAGAR score on choice of active substance (none, some, or a lot). The identified explanatory variables were screened for multicollinearity using the visual assessment and correlation of generalized pair plots and associated generalized variance-inflation factors (GVIF) greater than 10, being removed if either was the case. Finally, four logistic regression analyses were performed to define the outcome variables (first and second active substance treatment choice for both mastitis and DCT) with all remaining potential explanatory variables identified in the Causal Model. To refine the models a "criterion-based approach" was used, namely the quantification of information loss due to model simplification and outcome prediction accuracy, accordingly the Akaike Information Criterion (AIC) was minimized and the area under curve (concordance statistic) maximized. Hosmer-Lemeshow goodness of fit tests were performed on final models, with odds ratios and confidence intervals calculated for the associated explanatory variables. The significance level was set at P < 0.05.

3. Results

3.1. Response rate

A total of 135 responses were received from veterinarians practicing across the eight Australian dairying regions (Table 1), with the questionnaire response rate approximately 14.1% of the target population. The response rate for each question was variable, with a detailed summary available in supplementary material (Supplementary material-Overall question response rate).

3.2. Demographics

3.2.1. General descriptions

The median years worked with dairy farms was 10.0 years (IQR: 3.5 - 22.0). Practice owners made up 24.4% of the respondents. The median number of dairy farms on average respondents regularly consulted was 10.0 (IQR: 3.5 - 30.0), with a median of 30.0% (IQR: 15.0 - 70.0) of the respondent's professional time spent with dairy cattle.

3.2.2. Common diseases ailments

Lameness was the most common indication for veterinary consultation with a median of 10 animal cases per farm indicated on average per annum (IQR: 4.0 - 21.2) (Table 2). Diarrhea in calves was the indication resulting in the highest number of animals examined per visit, with a median of 15 animal cases per farm indicated on average per annum (IQR: 5.0 - 30.0) (Table 2).

3.3. Attitudes, perceptions, and concerns towards antimicrobials

3.3.1. Frequencies and percentages

In relation to statements regarding respondents' attitudes, perceptions, and concerns towards antimicrobials, "Consciously thinking about label indications and withholding periods for antimicrobial prescription" and the "Risk and consequence of off-label prescription" had the largest percentage of respondents' agreeing or strongly agreeing on a 5point Likert scale, being 96% and 95%, respectively (Fig. 1). Most respondents demonstrated an agreement with the statement that "antibiotics are a diminishing resource", with 65% agreeing or strongly agreeing (Fig. 1).

3.3.2. CATPCA analysis

A total of 163 responses, or 8% of the data set used for analytical modeling were missing, requiring the nearest neighbor imputation method. The four-dimensional CATPCA solution generated to

Table 1

Frequency and percentage for each of the Australian dairying regions that respondents identified as working within. $^{\rm a}$

-	-	
Dairying region	Location	Frequency ¹ (%)
Murray Dairy	Murray Region; Northern Victoria and Southern New South Wales	21 (20.0)
Westvic Dairy	Western Victoria	20 (19.0)
Western Dairy	Western Australia	16 (15.2)
Gipps Dairy	Gippsland Region, Victoria	15 (14.3)
Subtropical Dairy	Subtropical Region; Queensland and New South Wales	12 (11.4)
Dairy NSW	New South Wales	10 (9.5)
Dairy Tas	Tasmania	9 (8.6)
Consultant ²	N/A	5 (4.8)
Dairy SA	South Australia	5 (4.8)

^a The number of responses n = 105; ¹Some veterinarians practiced in multiple regions, therefore more than one regions were identified by some respondents providing a higher frequency total; ²consultant refers to dairy cattle veterinarians that were not providing clinical veterinary services at the time of questionnaire.

Table 2

The median number of farms and animals per farm indicated by respondents as
requiring on-farm veterinary consultation on average per annum for six common
ailments. ^a

Ailment		Number of farms/ annum (IQR)	Number of animals/farm/ annum (IQR)
Acidosis		1.0 (0 – 3.0)	3.0 (0.5 – 5.0)
Diarrhea	Adult	3.0 (2.0 – 6.0)	3.0 (1.0 – 9.0)
	Calves	6.0 (4.0–15.8)	15.0 (5.0 - 30.0)
Lameness		10.0 (4.0 – 21.2)	10.0 (3.0 – 25.0)
Mastitis		5.0 (2.0 – 10.0)	10.0 (3.5 – 30.0)
Metritis		6.0 (2.0 – 16.2)	5.0 (2.0 - 20.0)
Respiratory	Adult	5.0 (2.0 - 10.0)	3.4 (2.0 - 10.0)
disease	Calves	5.0 (2.0 – 10.0)	10.0 (3.0 – 20.0)

^a The number of responses n = 84. IQR: interquartile range.

consolidate the 14 Likert statements relating to dairy veterinarians' attitudes, perceptions, and concerns towards antimicrobials explained 66.7% of the variance in the data (Table 3). The variables that contributed large loading values to the four principal components were used to describe the dimensions (Table 3). The first principal component explaining 21.5% of the variance was named "Risk of AMR", being dominated by the statements "AMR is a genuine risk on my clients' farms", "The AMR risk impacting on farm staff is very small", and "AMR risk due to prescription by vets is overstated by the authorities". The second principal component explaining 19.2% of the variance can be described as "Trade-offs". While the third and fourth component described as "Prescription concerns" and "Active substance concerns" explained 13.7% and 12.3% of the variance, respectively. There was no significant difference between object scores for any of the four dimensions for the complementary variables; dairying region, years worked or practice owner.

3.4. Choice in active substance prescribed

3.4.1. Frequencies and percentages

The number of respondents that would choose each of the commonly prescribed antimicrobials as advice regarding the supply of antimicrobials for mastitis or DCT when considering the scenario of a familiar dairy farm client with a bulk milk cell count (BMCC) average above 250,000 cells/mL for the six months prior; a mastitis incidence rate of less than five clinical cases per 100 cows in the first two weeks of lactation; less than two clinical cases per 100 cows in six months after lactation; and 15% of cases being retreated within the first month of initial therapy is indicated in Table 4.

3.4.1.1. Mastitis treatment. Cloxacillin was the active substance most respondents (50.8%) indicated they would choose to prescribe as their first treatment for mastitis. If the first active substance failed, most respondents indicated their second choice in active substance would be oxytetracycline/oleandomycin/neomycin (20.0%) or trimethoprim/ sulphamethoxazole (18.3%).

3.4.1.2. DCT treatment. Cloxacillin was the active substance most respondents (67.2%) indicated they would choose to prescribe as their first treatment for DCT. The secondary choice of active substance respondents indicated they would choose for DCT treatment, if the first active substance failed, included cephalonium (31.0%), cefuroxime (15.5%), or cloxacillin/ampicillin (12.1%). Internal teat sealant and culling were both indicated as non-antimicrobial treatment options for DCT within the 'other' option on the questionnaire.

3.4.2. Multivariable logistic regression analysis

The significant associations from the multivariable logistic regression models developed to describe the relationship of possible drivers of first active substance treatment choice, and second active substance

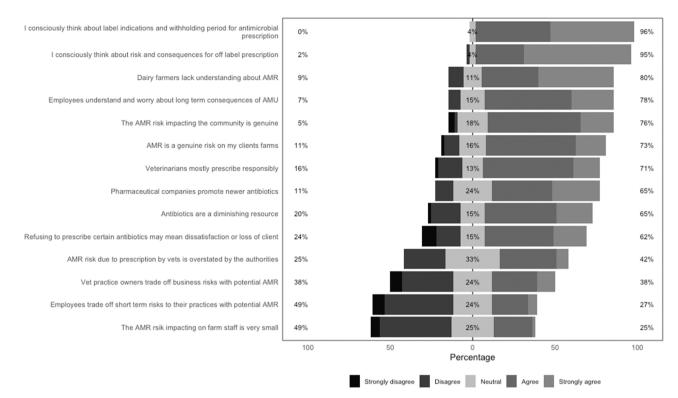


Fig. 1. The percentage of responses from Australian dairy veterinarians regarding their level of agreement on a Likert 5-point scale for statements concerning attitude, perception, and concerns for antimicrobial use. The percentages on the left of each row represent the responses that were 'strongly disagree' and 'disagree', the percentage in the middle of each row represents the 'neutral' responses, while the percentage on the right-hand side of each row represents the responses that 'agree' or 'strongly agree'. AMR: antimicrobial resistance; AMU: antimicrobial use.

treatment choice (if the first failed), for both mastitis and DCT as the outcome variable, are summarized in Table 5. Belief that the AVA's "*Guidelines for prescribing, authorizing and dispensing veterinary medicines*" (AVA, 2013) were "practical" significantly contributed to the choice of first active substance for mastitis treatment (P = 0.048). The likelihood for selecting a first line active substance decreased when the respondents believed the guidelines were "practical" vs "not practical" (OR = 0.09; 95% CI = 0.00 – 0.80).

When the second choice in active substance treatment (if the first failed) for mastitis was fitted as the outcome variable dimension PC1 (P = 0.012) from the CATPCA significantly contributing to the estimation, having the largest relative importance of the explanatory variables on the second choice of active substance for mastitis' odds (OR = 9.85; 95% CI = 2.02 – 73.72). Consideration for EAGAR scores were also significant in the model (P = 0.046), with an increased likelihood that a first line antimicrobial would be chosen if consulting "a lot" compared to "no consultation" (OR = 4.31; 95% CI = 1.15 – 22.52).

In terms of the DCT, multivariable logistic regression models developed to describe the relationship of possible drivers for the choice in antimicrobial are summarized in Table 6. When the first active substance treatment choice for DCT was fitted as the outcome variable, dimension PC3 (P = 0.046) from the CATPCA, the number of years worked with dairy farms (P = 0.050), and the number of dairy farms they regularly consult for (P = 0.034) significantly contributed to the estimation. The results suggest that odds of a first line active substance being chosen reduces by 14% for every year increase or by 16% for every extra farm consulted. When the second choice of active substance treatment (if the first failed) for DCT was fitted as the outcome variable, no significant associations with the Causal Model predictor variables were established.

3.5. Factors affecting antimicrobial prescription

When providing advice regarding the supply of antimicrobials the "spectrum of activity" (54.2%), "own experience with on farm efficacy" (32.2%) and "withholding period" (30.5%) were all important factors respondents indicated to be within the top two they accounted for regarding the active substance to be considered (Table S1). There were six alternative responses ("other") given by respondents which were not provided as options in the questionnaire under active substance factors. Three were concerning factors not directly related to the active substance to be considered, while the remaining three responses implied AMR related considerations: "avoiding more selective drugs than a first line approach", "evidence of AMR" and "importance of active in human health" (Table S1).

Respondents indicated that the most important factor concerning the prompting or request of the farm or farmer which influence decisions, when providing advice regarding the supply of antimicrobials, was the "history of response to therapy on-farm" (70.2%) (Table S2). The "on-farm disease patterns" and "farmer's likely/proven compliance" were also important factors, indicated by 59.6% and 50.9% of respondents, respectively.

"Diagnosis" was indicated by 100% of respondents in their top two factors under deliberation when providing advice regarding the supply of antimicrobials regarding the animal/s under consideration (Table S3). When regarding the likely pathogen, the factors respondents indicated for consideration included "confirmation of bacterial culture" (77.2%), "likely sensitivity (farm history or suspected pathogen sensitivity from experience)" (77.2%) and "sensitivity by the diagnostic laboratory" (40.4%) (Table S4). "Personal training as a veterinarian" was a dominant factor based on practice decision or protocol that veterinarians considered in their top two factors when deciding on the when providing advice regarding the supply of antimicrobials by 91.2% of respondents (Table S5). Additional considerations concerning the

Table 3

The sum of square (SS) loadings, variance explained by each component (VAF), cumulative VAF and component loadings for the four-dimensional CATPCA analysis of the 14-Likert statements on Australian dairy cattle veterinarians' attitudes, perceptions, and concerns towards antimicrobials following Varimax rotation.

Variable	PC1	PC2	PC3	PC4 Active
	AMR risk	Trade- offs	Prescription concerns	substance concerns
SS loadings	3.008	2.692	1.923	1.721
VAF	0.215	0.192	0.137	0.123
Cumulative VAF	0.215	0.407	0.544	0.667
Loadings of statements				
Antibiotics are a diminishing resource	0.544	-0.515		
AMR risk due to prescription by vets is overstated by the authorities	-0.692	-0.160	0.152	
AMR is a genuine risk on my clients' farms	0.880	-0.339		
The AMR risk impacting on farm staff is very small	-0.885	0.251		0.145
The AMR risk impacting the community is genuine	0.145	-0.785		
Consciously think about label indications and withholding period for antimicrobial prescription		0.138	0.148	0.686
I consciously think about risk and consequences for off-label prescription	-0.124	-0.244		0.786
Pharmaceutical companies promote newer antibiotics more than old ones			-0.119	0.723
Refusing to prescribe certain antibiotics may mean dissatisfaction or loss of client			0.828	
Vet practice owner's trade-off business risks with potential AMR	0.176	-0.860	-0.143	
Employee's trade-off short term risks to their practices with potential AMR	0.194	-0.842		
Employees understand and worry about long- term consequences of AMU	0.497	-0.161	0.626	0.249
Veterinarians mostly prescribe responsibly	-0.191		0.813	
Dairy farmers lack understanding about AMR	0.526	0.203	-0.29	

PC: principal component; Bolded loadings: large loading values used to describe the dimensions.

practice decision or protocol influencing the decision-making process included the "cost/ benefit to the farmer" (56.1%) and "prescribing policy of the practice" (50.9%).

3.6. Prescription guidelines

3.6.1. AVA and industry guidelines

The AVA "Guidelines for prescribing and dispensing veterinary medicines" were thought "practical" by 55.4% of the respondents, while the remainder indicated that they were "not aware of the guidelines" or that it was "not practical" (25.0% and 19.6%, respectively). Of those respondents aware of the guidelines the majority thought they were reasonable (92.9%). When the respondents were asked to indicate if they believed the AVA guidelines to be "descriptive" or "prescriptive", the majority (78.0%) indicated a "descriptive" nature. EAGAR scores were indicated to have no weighting when considering antimicrobial choice for 50% of respondents, "somewhat" for 40.7% and "a lot" for 9.3% of respondents.

3.6.2. Formal prescription policy

A formal prescribing policy for antimicrobial selection was present at the practice of 36.4% of the respondents. The extent to which respondents felt the formal prescribing policy positively impacted on animal welfare outcomes was "always" (15%), "often" (25%), "occasionally" (15%), "somewhat" (15%), and "very little" (30%) degree. The prescribing policy was thought to impact on the emergence of AMR "often" (15%), "occasionally" (35%), "somewhat" (35%), and "very little" (15%), however no respondents believed this to occur "always".

3.7. Sources of information on antimicrobials

3.7.1. Case specific information sources

Of the last ten clinical mastitis cases requiring antimicrobial prescription, most of the respondents (61.3%) indicated that less than a third had been based on specific culture results, with 16.6% of respondents indicating no culture results were used (Table S6). The difference in the approach to prescribing antimicrobials due to herd size was indicated to be "very little" (37.0%), "occasionally" (13.0%), "somewhat" (29.6%), "often" (16.7%) and "always" (4.0%) by respondents.

3.7.2. Rapid identification of causation

Most (94.3%) of the respondents would use rapid culture (< 24 h) for infection confirmation, such as mastitis, if it was available. The prominent factors provided by respondents as being important in the uptake and continued use of rapid testing included "cost (price, efficiency, or the cost benefit)" (70.0%); "ease of use/interpret" (56.0%); and "diagnostic accuracy" (34.0%) (Table S7). Four respondents indicated that they or their clients use "rapid mastitis culture kits" or "test plates" with one respondent indicating that farmers "have been pleasantly surprised that in some cases antibiotics are not indicated".

3.7.3. Ongoing educational sources

The frequency with which respondents consulted different sources of information regarding the use of antimicrobials in dairy cattle is presented in Fig. 2. While clinical experience, product labels and laboratory tests were all considered by most respondents "often" or "always" (93%, 81%, and 78%, respectively), the percentage of responses for "never" and "rarely" consulted were highest for AVA directorate and nutritionists for feed antimicrobials. One respondent also indicated "herd screening tests" as another source of information they consulted regarding antimicrobial use in dairy cattle.

4. Discussion

This is the first study to examine antimicrobial prescription patterns and the factors affecting antimicrobial selection among veterinarians within the Australian dairy context. While there may be bias among respondents and accuracy in estimating the 14.1% response rate, comparisons with the AVA's (2019) Workforce Survey of 1236 veterinarians suggest the population demographics of this study are comparable to the Australian veterinarian workforce. For example, assuming the veterinarian graduate age of 25 years, 35 years of age represents approximately 10 years industry experience. The results of the AVA survey suggests that 50% of the Australian veterinary workforce is under 44 years of age, with 30% being under 34 years of age, which are

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Table 4

The frequency for the prescription of each active substance as a first choice, and second if the first one was to fail, for the treatment of mastitis and DCT on farm.^a.

Active or Other ¹	Importance ²	Line of use ³	Mastitis		DCT	
			1st choice	2nd choice	1st choice	2nd choice
Penethamate	Low/ N/A	First	0	6	0	1
Penicillin			3	0	1	0
Ampicillin			1	0	2	1
Oxytetracycline			0	2	0	1
Oxytetracycline/oleandomycin/neomycin			3	12	0	1
Tylosin			0	1	0	0
Other: Culling			0	0	0	1
Other: Internal teat sealant			1	0	4	4
Total			8	21	7	9
Amoxicillin/clavulanic acid	Medium	Second	5	2	1	3
Cloxacillin			31	7	41	5
Cloxacillin/ampicillin			10	4	7	7
Cloxacillin/penicillin			1	1	1	0
Cephalonium			0	0	1	18
Cephapirin			0	4	1	4
Cefuroxime			5	7	1	9
Trimethoprim/sulphamethoxazole			1	11	1	0
Total			53	36	54	46
Ceftiofur	High	Third	0	2	0	3
Cefquinome			0	1	0	0
Total			0	3	0	3

^a Respondents considered a familiar dairy farm client with BMCC averaged above 250,000 for six months prior, > 5 clinical cases/100 cows in the first 2 weeks of lactation, > 2 clinical cases/100 cows in 6 months after lactation and 15% of cases retreated within the first month of initial therapy. The number of responses were variable with Mastitis 1st choice n = 61, Mastitis 2nd choice n = 60, DCT 1st choice n = 61, and DCT 2nd choice n = 58. Other¹: treatment options indicated by the respondents' within the 'other' section of the questionnaire; Importance²: presented in terms of human health (EAGAR Scores) (ASTAG, 2018); Line of use³: associated with the AVA guidelines (The Australian Veterinary Association Ltd, 2013).

Table 5

Summary of multivariable logistic regression analysis for the association of choice in active substance for mastitis treatment verses potential predictor variables (P < 0.05 significance level).

Outcome variable	Predictor variable	Category	β	S.E. (β)	z value	p-value	OR (95% CI)
1st active substance mastitis	(Intercept)		-0.981	0.677	-1.45	0.147	
	AVA guidelines practical	No					
		Not aware	-0.341	0.880	-0.39	0.699	0.71 (0.12-4.36)
		Yes	-2.420	1.221	-1.98	0.048	0.09 (0.00-0.80)
Number in data frame $= 61$, Num	ber in model = 61, $Missing = 0$, Al	C = 47.3, C-statistic	= 0.736, H&L =	- Chi-sq (8) 0.00	(p = 1.000)		
2nd active substance mastitis	(Intercept)		-0.021	0.579	-0.04	0.971	
	PC1		2.288	0.906	2.53	0.012	9.85 (2.02–73.72)
	PC3		1.192	0.668	1.79	0.074	3.30 (1.11–14.53)
	Formal prescribing policy	True					
		False	-1.157	0.750	-1.54	0.123	0.31 (0.07-1.31)
	EAGAR weighting	None					
		Some	1.217	1.0.8	1.18	0.236	3.38 (0.55-40.46)
		A lot	1.460	0.733	0.99	0.046	4.31 (1.15-22.52)
Number in data frame $= 61$, Num	ber in model = 61, $Missing = 0$, AI	C = 73.8, C-statistic	= 0.774, H&L =	- Chi-sq (8) 8.01	(p = 0.433)		

β: coefficient for the logistic regression independent variable. S.E. (β): standard error of the coefficient; OR: estimated odds ratio (Expβ); CI: confidence intervals; Cstatistic: concordance statistic, is equal to the AUC (area under curve); H & L: Hosmer-Lemeshow goodness of fit test.

Table 6

Summary of multivariable logistic regression analysis for the association of choice in active substance for DCT treatment verses potential predictor variables (P < 0.05 significance level).

Outcome variable	Predictor variable	Category	β	S.E. (β)	z value	p-value	OR (95% CI)
1st active DCT	(Intercept)		1.2596	1.2962	0.97	0.332	
	PC3		2.2148	1.1122	1.99	0.046	9.16 (1.54–121.34)
	Years worked		-0.1555	0.0790	-1.96	0.050	0.86 (0.70-0.97)
	Number of dairying farms		-0.1733	0.0817	-2.12	0.034	0.84 (0.69–0.96)
	Culture results	< 5					
		> 5	2.7216	1.4270	1.91	0.056	15.20 (1.25-428.70)

β: coefficient for the logistic regression independent variable. S.E. (β): standard error of the coefficient; OR: estimated odds ratio (Exp^β); CI: confidence intervals; C-statistic: concordance statistic, is equal to the AUC (area under curve); H & L: Hosmer-Lemeshow goodness of fit test.

comparable to the median of 10.0 years (IQR = 3.5 - 22.0) working in the dairy industry. Additionally, a median of 30.0% (IQR: 15.0 - 70.0) of time spent with dairy cattle for respondents illustrates the familiarity

and experience for both dairy cattle and the dairy industry of respondents within the current study. Caution, however, must be expressed when analyzing the information regarding the number of

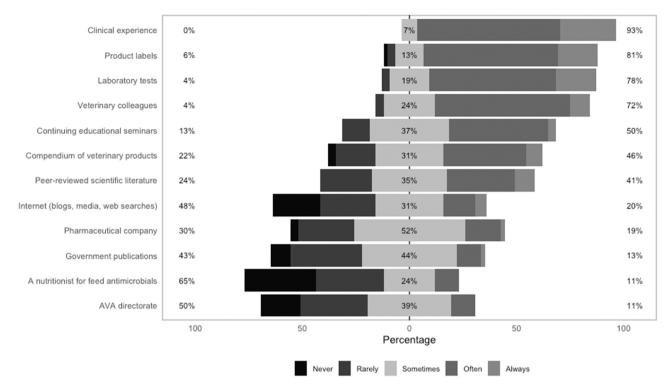


Fig. 2. The percentage of responses from Australian dairy veterinarians regarding the frequency with which they consult the different information sources regarding the use of antimicrobials in dairy cattle using a Likert 5-point scale. The percentages on the left of each row represent the responses that were 'strongly disagree' and 'disagree', the percentage in the middle of each row represents 'neutral responses', while the percentage on the right-hand side of each row represents responses that 'agree' or 'strongly agree'.

farms, and average cases per farm, requiring consultation by respondents for the various ailments. This is because these numbers are considered estimates, with information on previous consultations maintained by the practice, and indicated as not available to many veterinarians. Nevertheless, significant insights into the antimicrobial prescription practices, concerns, attitudes, and decision-making of veterinarians in the Australian dairy industry are provided by this study.

An awareness by Australian dairy veterinarians for the potential of AMR and the need for stewardship is evident from this study. Most respondents believed that "AMR was a genuine risk on my client's farm" (76%) and that "antimicrobials are a diminishing resource" (65%). This is despite the low prevalence of AMR suggested by ad hoc surveillance in the Australian dairy cattle industry (Jordan et al., 2005; Barlow et al., 2015; Aleri et al., 2022), and the perceived low risk for AMR in Australia due to strict regulations surrounding antimicrobial administration in animals and effective national quarantine (Shaban et al., 2014). There was also an overall higher level of concern and AMR awareness by the respondents compared with research concerning 206 dairy veterinarians in New Zealand (McDougall et al., 2017). For example, the percentage of veterinarians that responded to the online survey conducted by McDougall et al. (2017) indicating that they "agreed" or "strongly agreed" with the statements that "AMR was a genuine risk" and antimicrobials are a diminishing resource" in only 46% and 40.9%. While this may be geographically influenced, there is also half a decade between the studies with progress in extension and education potentially influencing AMR awareness and AMS. To provide focus for future engagement and extension with Australian dairy veterinarians it is necessary to understand response patterns for the attitudes, perceptions, and concerns towards antimicrobials. This was achieved using a CATPCA, with the resultant model comprising four underlying components that explained 66.7% of the original data variation. The predominant statements within the first principal component of the CATPCA suggest that providing evidence of the impacts of AMR or the limited nature of antimicrobials as a resource will have the most

influence in altering the overall attitudes, perceptions, and concerns towards antimicrobials. The second and third dimensions of the CATPCA indicate that it is also necessary to support veterinarians in encouraging and proactively promoting AMS on farm to minimize the trade-offs between potential loss of clients were a veterinarian to refuse prescription and antimicrobial choice. The final dimension suggests the active substance concerns of dairy veterinarians when prescribing antimicrobials.

The role of a veterinarian in reducing the emergence of AMR is most effective when emphasis is placed on AMS, ensuring antimicrobial selection results in the optimal active substance, dose, and duration in treating the ailment and reducing the risk of resistance (Cruickshank et al., 2014). There was a high importance was attributed to factors such as "spectrum of activity", "history of response to therapy", "diagnosis", "confirmation of bacterial culture" and "training" as decision-making drivers for providing an advice regarding the supply of antimicrobials by dairy cattle veterinarians. However, respondents also prioritized clinical concerns when considering antimicrobial prescription, the majority consciously considering "label indications", "withholding period" and "risk or consequence of off label prescriptions" when determining antimicrobial prescriptions. This was a similar finding to that of a study concerning New Zealand dairy veterinarians by McDougall et al. (2017), and reasonable to expect due to these factors being legal obligations of the veterinarian and hence a very high priority. However, respondents indicated that specific culture results, required to confirm the appropriate antimicrobial, were rarely collected when prescribing antimicrobials. An overwhelming majority of respondents indicated they would use rapid testing to confirm bacterial identification, however factors required to increase the uptake and ongoing use included "cost", "ease of use" and "diagnostic accuracy". This need for refined and available evidence-based therapeutic have been indicated in previous international research concerning veterinarians within and independent of the dairy industry (De Briyne et al., 2013; Krömker and Leimbach, 2017).

Most of the antimicrobials used in the dairy industry relate to udder

disease, including therapy of clinical mastitis in lactating cows and DCT for subclinical mastitis treatment (Krömker and Leimbach, 2017). Although the aetiology of mastitis varies Australia wide due to different production system characteristics and seasonality across the geographical regions, bacterial infections involving streptococci, Escherichia coli, and staphylococci are common mastitic pathogens (Shum et al., 2009; Plozza et al., 2011; Chung et al., 2021). While cloxacillin, a semisynthetic beta-lactamase resistant penicillin is a treatment option, it is considered to have a "medium" EAGAR score and to be a "second line of use" by AVA (AVA, 2013; ASTAG, 2018). Therefore, the preferential prescription of cloxacillin as the first choice of active substance by most respondents for mastitis (50.8%) and DCT (67.2%) treatment is of high significance. In contrast, the broad spectrum antibiotic activity of oxytetracycline reinforced by oleandomycin and neomycin has a "low" classification EAGAR score and is considered a preferred first line active substance by the AVA (AVA, 2013; ASTAG, 2018). However, only 5% of respondents indicated oxytetracycline/oleandomycin/neomycin as the first choice active for mastitis treatment, and none for DCT treatment. A potential explanation for these choices is the influence of non-clinical factors. For example, respondents in our study indicated factors such as "withholding period", "farmer compliance", and "cost/benefit to farmer" to influence their choices on advice regarding the supply of antimicrobial considerations. These results are aligned with previous international research demonstrating veterinarians' awareness of AMS but the potential for altered prescription patterns due to client pressures and farm infrastructure (McDougall et al., 2017; Golding et al., 2019; Gibbons et al., 2013).

Furthermore, non-clinical factors, such as demographics, influence the antimicrobial prescription decision-making process of dairy veterinarians. This study suggested that, as the number of years veterinarians have worked for dairy farms and the number of dairy farms they consult for increases, the likelihood of choosing a first line active substance as the first choice in DCT treatment reduced. This contradicts with research investigating antimicrobial prescription attitudes and perceptions of Dutch veterinarians, suggesting higher pressures to prescribe antimicrobials by clients potentially contributing to action uncertainty for younger veterinarians (Speksnijder et al., 2015). However, a more recent study demonstrated that younger veterinarians had increased awareness of AMR risk, suggesting undergraduate training surrounding the AMS message has increased impact for less experienced veterinarians (McDougall et al., 2017). Additionally, more recent graduates have had more training in AMS than their older counterparts and therefore are more likely to be aware of this information. These results demonstrate a need to focus on continuing education for veterinarians, especially industry experienced veterinarians, in conveying the AMS message.

There is also a need to improve the availability of prescription policies to veterinarians with only 36.4% of respondents indicating they were available at their clinic. However, most of these respondents indicated the available policies had an impact on animal welfare outcomes and AMR emergence. Potentially, the implementation of prescription policies incorporating EAGAR scores across veterinary practices may improve AMS. Especially as half of the respondents indicated EAGAR scores had no weighting when considering antimicrobial choice yet considering these scores "a lot" significantly increased the odds of a first line active substance chosen as the antimicrobial treatment of mastitis if the first choice of treatment failed (OR = 4.31; CI = 1.15–22.52).

To help guide veterinarians in AMS, the AVA provides veterinarians with basic principles on the prudent use of antimicrobials. These guidelines are globally recognized, for prescribing, authorizing and dispensing veterinary medicines (AVA 2013). However, nearly half of the respondents in our study indicated the guidelines were impractical, or that they had no knowledge of them. Of the respondents with knowledge of the guidelines, they felt they were reasonable but primarily descriptive. Potentially a reason for this high percentage of

veterinarians perceiving a lack of relevance for the current AVA guidelines is their generic nature, being absent of dairy specific prescribing guidelines. While information on the use of veterinary medicines in the cattle industry are available to veterinarians through the relevant state departments of primary industries and Veterinary Surgeons' Boards, there is no dairy cattle counterpart (AVA, 2013). Potentially the lack of industry specific guidelines may have reduced their adoption or provided confusion in their interpretation, explaining the significant contribution of belief in the AVA guideline's practicality in estimating the first active substance chosen for mastitis treatment in our study. For example, following the intention of the AVA guidelines a first line active substance should be chosen for the treatment of mastitis, however our results demonstrated the opposite. There was an increased likelihood for a third- or fourth-line active substance to be chosen when the respondents believed the guidelines were practical versus not practical. This highlights the need for the guidelines to be well-defined and prescriptive in nature, reducing the opportunity for alternative interpretation and improve the effectiveness in achieving reduced AMR risk conferred through veterinary AMU.

It is also necessary to increase the awareness and application of prescribing guidelines considering the low reliance of veterinarians on peer-reviewed data, AVA guidelines, and government guidelines. While this may say something about access to literature, time to read literature, or trust in formal sources of information, it would be beneficial for future extension programs to define the reluctance to consult these information sources. In addition, it may be worth defining "clinical experience", and any potential influencing factors on this experience, as a source of information to base antimicrobial prescription. For example, regardless of reliability in the case and farm ailment numbers provided by respondents in this study, a low number of clinical mastitis cases of 5 farms/annum (IQR; 2-10) were indicated as requiring consultation. However, disease incidence data by previous Australian studies suggest a high clinical mastitis incidence rate of 44.4% of cows for Western Australian dairy farms (Department of Agriculture, 1968), while a survey involving 189 dairy farmers in New South Wales indicated an average herd prevalence of subclinical mastitis at 29% (Plozza et al., 2011). This suggests that severe mastitis cases would represent a high percentage of veterinarian consultations and potentially provide bias in prescription behavior.

5. Conclusion

The awareness of AMR by respondents was generally high, suggesting that Australian dairy veterinarians are knowledgeable about the need for AMS. Clinical factors dominated the decision-making process for antimicrobial use when determining antimicrobial prescriptions and providing advice regarding the supply of antimicrobials. Although it is not certain if there is a need for more information, or if accessibility and usability is the real issue, there is a need to increase the capacity to diagnose and confirm pathogens and resistances to increase appropriate antimicrobial choice. Non-clinical factors, such as demographics, and awareness of prescription guidelines, impacted on antimicrobial prescription, and attitudes on antimicrobial resistance risk and prescription concerns also impacted on the choice of antimicrobials prescribed. Therefore, it is essential that support through policy and AMS education is provided with effective communication to all industry stakeholders. While prescription concerns may be reduced through increased availability of detailed prescriptive policies and prescriptive guidelines.

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CRediT authorship contribution statement

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Conflict of interest

There are no conflicts of interest for the authors to declare.

Data Availability

The data that support this study will be shared upon reasonable request to the corresponding author.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.prevetmed.2022.105610.

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