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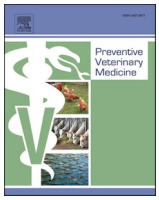

A scoping review of antimicrobial resistance in the Australian dairy cattle industry

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ABSTRACT

Introduction: Quantification of antimicrobial resistance (AMR) is beneficial to inform policies and direct prudent antimicrobial use.
Aim: This study aimed to assess the current published evidence of AMR from passive and active *ad hoc* surveillance activities within the Australian dairy cattle industry.
Methods: Following a scoping review framework 373 articles published before January 2023 were retrieved using the keyword search function from two online databases (PubMed® and Web of Science™ Core Collection). The duplicate articles were removed and the title, abstract, and full text of the remaining articles were reviewed following the study objectives and inclusion criteria (location, subject/theme, and data). Data from the remaining articles were extracted, summarised, interpreted and the study quality assessed using the Grades of Recommendations, Assessment, Development, and Evaluation guidelines.
Results: A total of 29 articles dating from the 1960 s until 2022 were identified to meet the study criteria (passive: $n = 15$; active: $n = 14$). Study characteristics such as sampling type, sampling method, and AMR assessment were all common characteristics from both passive and active surveillance articles, being milk samples, individual sampling, and phenotypic assessment respectively. Passive surveillance articles had a wider range in both the type of bacteria and the number of antimicrobials investigated, while active surveillance articles included a higher number of bacterial isolates and sampling from healthy populations. There was an overall low level of clinical AMR across all articles. Higher prevalence of non-wildtype *Escherichia coli, Salmonella* spp., and *Staphylococcus* spp., although limited in data, was suggested for commonly used Australian veterinary antimicrobials for these bacteria. The prevalence of phenotypic AMR varied due to the health and age status of the sampled animals. The articles reviewed in this study suggest the prevalence of AMR genes was higher for commonly used antimicrobials, although genes were not always related to the phenotypic AMR profile.
Conclusions: Published evidence of AMR in the Australian dairy cattle industry is limited as demonstrated by only 29 articles included in this review following selection criteria screening. However, collectively these articles provide insight on industry AMR prevalence. For example, the suggestion of non-wildtype bacteria within the Australian dairy cattle indicating a risk of emerging or increasing industry AMR. Therefore, further surveillance is required to monitor the development of future AMR risk within the industry. Additionally, evidence suggesting that animals varying in health and age differ in prevalence of AMR imply a requirement for further research into animal population demographics to reduce potential bias in data collated in both national and global surveillance activities.

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1. Introduction

Antimicrobials play an important role in maintaining optimal health, welfare, and productivity outcomes in livestock production. However, there is a risk of developing antimicrobial resistance (AMR) associated with antimicrobial use (AMU), that in turn may lead to future economic and disease management complications (Capozzi et al., 2019; Cooper and Okello, 2021). Additionally, any animal derived AMR may transfer into the human domain if resistant microorganisms, present within animal manure or irrigation water from livestock production sites, contaminate products for human consumption (Alonso et al., 2016; Reid et al., 2020). Australia has prioritised the integrated surveillance of human, animal, food and environmental AMR data, to formulate an approach towards AMU and any necessary response to developing resistance as part of the national AMR strategy (AGDH, 2019), a crucial part of the *One Health* concept. These combined efforts represent the *Global Action Plan* (GAP) for AMR with the coordination and implementation of risk management for non-human AMU and an increased capacity of surveillance and monitoring of AMR as objectives (OIE, 2016; -WHO, 2018; FAO, 2019). Consequentially it is essential to have a quantifiable appraisal of industry AMR to successfully fulfil this commitment, while also informing burden management and mitigation strategies (ACSQHC, 2019).

The quantification of AMR may include phenotypic and genotypic assessment. The most common method of phenotypic assessment includes the use of Clinical and laboratory Standards Institute (CLSI) breakpoints. This method classifies an organism according to the associated susceptibility of an antimicrobial; namely susceptible, susceptible-dose dependant, intermediate, or resistant. The categories are determined from clinical and pharmacological data representing the microbiological, pharmacokinetic, pharmacodynamic and clinical outcomes of the antimicrobial on a specific microbial organism (CLSI, 2020). Therefore, an isolate with an MIC value classified as susceptible suggests that the growth of the bacterial organism will be inhibited at or below the concentration of antimicrobial that can be provided by *in vivo* treatment at the site of infection (CLSI, 2020). Alternatively, interpretation of phenotypic AMR through epidemiological cut-off (ECOFF) values compiled by the European Union Committee on antimicrobial susceptibility (EUCAST) distinguishes between the intrinsic or 'wild type' populations and isolates having acquired mechanisms of resistance or 'non-wild type' populations. Based on statistical methods interpreting the inherent level of resistance to two-fold dilutions of antimicrobials, the MICs present uniformly as a gaussian histogram within wild single species bacterium populations (Turnidge et al., 2006). The actuation of acquired resistance, such as a gene coding for resistance, will provide an MIC value above the ECOFF, facilitating the early detection of acquired resistance (Barlow et al., 2022). Finally genotypic resistance is commonly assessed through both whole genome sequencing (WGS) or polymerase chain reaction (PCR) to identify known resistance genes within the genome of the bacteria.

The Australian *National Action Plan* (NAP), which is based on the GAP, lists the surveillance of Australian livestock industry AMR as an objective, although currently no formal ongoing surveillance has been implemented (DAFF, 2022). Information within the Australian dairy context has been provided to the industry through various published *ad hoc* studies. These studies comprise two categories of surveillance activities, passive and active, to provide a quantified appraisal. Passive surveillance is defined as the monitoring of the existing status from the routine collection of clinical data, whereas active surveillance is defined as the employment of a committed approach that includes clinically normal animals in the population (Thrusfield et al., 2018). To date there has not been a comprehensive industry review of the published peer-reviewed literature reporting on AMR surveillance activities in Australian dairy cattle. This study aimed to assess the published evidence of AMR provided by both passive and active *ad hoc* surveillance activities within the Australian dairy cattle industry. The question guiding this assessment was "What evidence is available in published peer-reviewed literature to assess the prevalence of AMR to commonly used antimicrobials for bacteria isolated from cattle in the Australian dairy industry?".

2. Methods

To answer this question, the review objectives were to (i) identify the published articles regarding passive AMR surveillance in Australian dairy cattle, (ii) identify the published articles regarding active AMR surveillance in the Australian dairy cattle, and (iii) to assess the study characteristics for both the passive and active surveillance articles. A scoping review methodology was chosen due to the broad nature of the research question and associated objectives requiring literature mapping across a range of research (Levac et al., 2010; Tricco et al., 2018). To achieve objectives (i) and (ii), a comprehensive search of the published literature about passive and active AMR surveillance in the Australian dairy cattle industry was performed without filtering the date of study or reporting language. To achieve objective (iii), the two types of AMR surveillance articles were then assessed to directly address the study question. The Joanna Briggs Institute (JBI) guidelines and the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Extension for Scoping Reviews (PRISMA-ScR) (Tricco et al., 2018; Peters et al., 2020) were employed for quality control during this scoping review, with the completed the PRISMA-ScR checklist provided in Supplementary Table 1 for transparency in our reporting. A protocol was not registered.

2.1. Search strategy

To investigate published passive and active AMR surveillance articles relevant to Australian dairy cattle surveillance, two web-based databases PubMed.gov and Web of Science™ Core Collection were searched using keyword-based search strings. The search string was refined until all articles known to these authors relating to the study question were included in the results. Initial and final searches were performed for all databases in July 2022 and January 2023 respectively, with no filtering for the date of publication or language of the articles. To investigate the available AMR relevant articles, the refined key-word string used to search both the PubMed.gov and Web of Science™ Core Collection databases was (Australia OR Australian OR Western Australia OR Victoria OR New South Wales OR Queensland OR Tasmania) AND (dairy OR cattle OR cow OR calf OR heifer OR calves OR bovine) AND (antimicrobial resistance OR antimicrobial resistant OR drug resistance OR multiple drug resistance OR resistance genes OR antibiotic resistance OR antibiotic resistant OR bacterial resistance) AND (bacteria OR microorganism).

2.2. Screening and study selection criteria

The identified articles were imported into EndNote™ X9 and combined into one list of AMR related articles. The duplicate articles were then removed, and the list was imported into the web-based platform Rayyan (Ouzzani et al., 2016) where the title, abstract, and full text were each reviewed for relevance to the study objectives. The criteria for study inclusion were (1) location: Australia, (2) subject: dairy cattle or commodities associated directly to dairy animals and AMR (milk, milk products, meat), and (3) data: original resistant bacteria or/and resistant genes data. Articles were required to be published with peer review being excluded if they were identified to be literature reviews (scoping or systematic); methodology studies; conference papers on published work; technical notes; not bacterial focussed such as viral, nematode or parasites focussed studies; and ambiguous reporting of results limiting the identification of the animal production origin of the isolate. Additionally, as recommended by JBI when performing scoping reviews the reference list from each article included in the final review were checked

for manuscripts that included all study objectives and criteria, but were not part of the database search results (Peters et al., 2020).

2.3. Data extraction

The data extracted from the full text of the retained articles included the type of surveillance (passive, active, or both), year of publication, the Australian state from which the study population was located, location of sample collection (abattoir or farm), the number of dairy animals included for sample collection in the study, age or age group of the sampled animals, the sample type collected (milk, milk filter, bile, soil, lungs, or if faecal; rectal swab/grab per rectum, faecal grab from intestine, or voided samples), the health status of animals collected from (healthy or identified disease), if individual or pooled sampling was used (if the sample was taken from an individual animal or pooled from multiple animals) the assessment method (phenotypic susceptibility of cultured bacterial isolates or the AMR genes quantification via sequencing) and the source of funding. For studies that assessed phenotypic AMR, the bacterial species isolated for AMR screening, number of isolates assessed, method of phenotypic assessment (disc diffusion, broth microdilution, or agar dilution) assessing AMR resistance the system used to interpret the resistance (ECOFF values, CLSI breakpoints or Clinical Decision Support (CDS) values), reporting of the identity of breakpoints used to interpret resistance included within the publication, the inclusion/exclusion of the range for MICs or disc diameters resulting from the antimicrobials investigated, the identity of the antimicrobials investigated, percentage of isolates of each bacteria species resistant to each individual antimicrobial, and the percentage of multiple drug resistant isolates (more than 3 antimicrobial cases) for each bacterial species were recorded. For the AMR gene quantification studies, the method of sequencing (WGS or PCR), number of isolates assessed, and the identity and quantity of genes present encoding AMR were recorded.

2.4. Quality appraisal

The articles found to conform to the study objectives and criteria were reviewed and evaluated by combing the methodologies of Gaire et al. (2021) and Audate et al. (2019) for the GRADE assessment and risk-of-bias approach (Guyatt et al., 2011). The quality of the included studies was appraised by the first author (MT) and validated by the last author (JWA).

2.5. Data summary and synthesis

Microsoft Excel (Microsoft Office, v16.41; 2021) was used to collate all of the data extracted from the relevant articles. Data was validated, coded, and imported into R v4.0.5 (R Core Team, 2021) for description

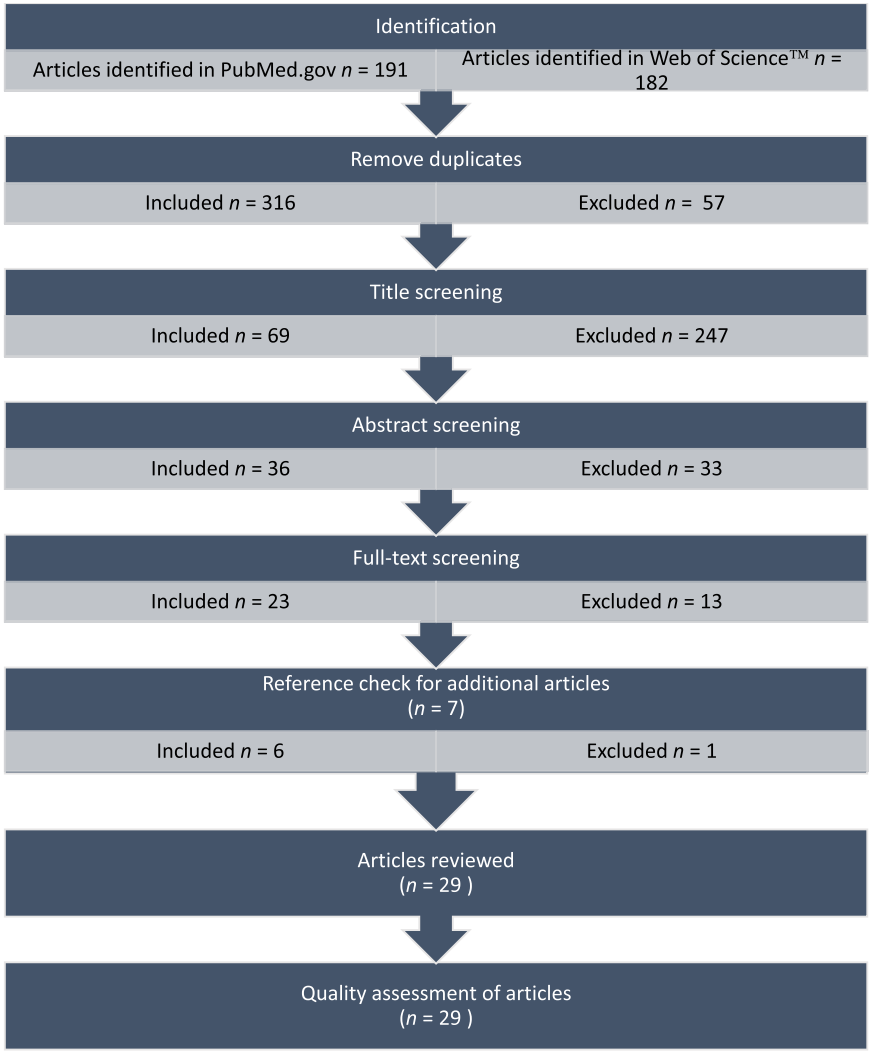

Fig. 1. The PRISMA-ScR flow diagram for the selection of sources of evidence for the literature scoping review on passive and active surveillance of antimicrobial resistance in the Australian dairy cattle industry.

and data visualization using ggplot2 package v3.3.5 (Wickham, 2016). Descriptive statistics were used to summarize article characteristics. To summarize the phenotypic AMR reported within the articles the data extracted was graphed for comparisons across bacteria and years. This comprised of either the reported clinical resistance based on CLSI breakpoints, or the reported ECOFF value interpreted phenotypic AMR within the articles. Additionally, articles that reported clinical resistance with CLSI breakpoints but also included the range for the Minimum Inhibitory Concentration (MIC) results for the isolates investigated were reinterpreted with the ECOFF values in Supplementary Table 2, and then graphed for comparison ($n = 8$). All assumptions and exclusions used in the extraction of the phenotypic data are presented in Supplementary Table 3, with complete references available in **Supplementary References.**

3. Results

The search strategy found 373 articles across the two databases. Fig. 1 depicts the screening process of these articles. In summary, after removing duplicates, title screening, and abstract review 36 articles were identified for full text review. From these identified articles 23 were found to conform to the study objectives and criteria. The examination of the reference list from these 23 articles provided an additional seven articles that conformed with the article screening process. One of these additional articles, Wanasinghe and Frost (1979), was not found, bringing the total number of articles selected for data extraction to 29.

3.1. General characteristics of articles

The general study characteristics for the 29 scoping review articles are provided in Supplementary Table 4, with a summary in Table 1. These articles comprised of 15 passive surveillance articles and 14 active surveillance articles. Regarding the year of publication 41.4% ($n = 12$) of the articles (passive: 40.0%, $n = 6$; active: 42.9%, $n = 6$) were published from 2020 to the 2022. Dairy cattle populations were more commonly sourced from individual Australian states, being highest for Victoria at 17.2% ($n = 5$) (passive: 13.3%, $n = 2$; active: 21.4%, $n = 3$) followed by New South Wales, Queensland, and WA each comprising 13.8% ($n = 4$) of the articles, with 13.3% ($n = 2$) being passive surveillance articles and 14.3% ($n = 2$) being active surveillance articles for all three states. Most articles related to samples collected from farms, totalling 72.4% ($n = 21$) of the articles (passive: 80.0%, $n = 12$; active 64.3%, $n = 9$). While the number of animals sampled was not reported in four of the articles and was provided as a range for another, the median number of animals collected from was calculated for the remaining 24 studies. This median was 335.5 animals (range: 3–3073 animals) for the passive surveillance articles, and 334.5 animals (range: 3–10279 animals) for the active surveillance articles. Most studies involved heifers, totalling 69% ($n = 20$) (passive: 66.7%, $n = 10$; active: 71.4%, $n = 10$), with only one passive surveillance article incorporating calves, and one active surveillance article incorporating both heifers and calves.

Milk samples were the most common sample type representing 58.6% of the articles ($n = 17$) (passive: 53.3%, $n = 8$; active: 64.3% $n = 9$). Passive surveillance articles incorporated mainly diseased dairy cattle, with 46.7% (n = 7) having mastitis, 13.3% ($n = 2$) with high incidence of mastitis, 13.3% ($n = 2$) with diarrhoea, 6.7% ($n = 1$) with endometritis, and 6.7% ($n = 1$) with salmonellosis. Active surveillance comprised of mostly healthy animals (92.8%; $n = 13$). Individual sampling was most common for both surveillance practices, being 73.3% ($n = 11$) and 85.7% ($n = 12$) of passive and active surveillance respectively. The AMR assessment method was commonly phenotypic (total; 62.1%, $n = 18$; passive: 60.0%, $n = 9$; active: 64.3%, $n = 9$), with genotypic assessment utilised in 6.9% ($n = 2$) of surveillance activities alone or in 31% ($n = 9$) of articles as a combination with phenotypic assessment. Funding sources were not provided for 41.8% ($n = 12$) of the articles. For those that listed a funding source, industry was the most

Table 1
Summary of the general characteristics for the passive and active surveillance articles on antimicrobial resistance, included in this scoping review.

Characteristic	Passive (%) ($n = 15$)	Active (%) ($n = 14$)	Total (%) ($n = 29$)
Publication Year			
Prior to 1969	-	4 (28.6)	4 (13.8)
1970 – 1979	1 (6.7)	1 (7.1)	2 (6.9)
1980 – 1989	2 (13.3)	-	2 (6.9)
1990 – 1999	1 (6.7)	-	1 (3.4)
2000 – 2009	1 (6.7)	2 (14.3)	3 (10.3)
2010 – 2019	3 (20.0)	2 (14.3)	5 (17.2)
2020 – January 2022	6 (40.0)	6 (42.9)	12 (41.4)
State[a]			
Multiple states (not specified)	-	3 (21.4)	3 (10.3)
NSW	2 (13.3)	2 (14.3)	4 (13.8)
QLD	2 (13.3)	2 (14.3)	4 (13.8)
QLD, VIC	1 (6.7)	1 (7.1)	2 (6.9)
SA	1 (6.7)	-	1 (3.4)
TAS	-	-	-
VIC	2 (13.3)	3 (21.4)	5 (17.2)
WA	2 (13.3)	2 (14.3)	4 (13.8)
NSW, QLD, SA, TAS, VIC, WA	3 (20.0)	-	3 (10.3)
NSW, QLD, SA, VIC	-	1 (7.1)	1 (3.4)
VIC, SA	-	1 (7.1)	1 (3.4)
VIC, TAS	1 (6.7)	-	1 (3.4)
Location			
Abattoir	-	4 (28.6)	4 (13.8)
Dairy processor	-	1 (7.1)	1 (3.4)
Farm	12 (80.0)	9 (64.3)	21 (72.4)
Farm bulk milk tank, commercial	-	1 (7.1)	1 (3.4)
Not stated	2 (13.3)	-	2 (6.9)
Number of animals sampled[2]	335.5 (46 – 3073)	354.5 (3 – 10279)	335.5 (3 – 10279)
Age of animals sampled			
Adult	-	4 (28.6)	4 (13.8)
Calves (dairy and dairy beef)	1(6.7)	-	1 (3.4)
Heifer	10 (66.7)	10 (71.4)	20 (69.0)
Heifer and calf	-	1 (7.1)	1 (3.4)
Not stated	3 (20.0)	-	3 (10.3)
Sample Type			
Faecal- rectal	1 (6.7)	1 (7.1)	2 (6.9)
Faecal- rectal and bile	1 (6.7)	-	1 (3.4)
Faecal- intestine	-	4 (28.6)	4 (13.8)
Faecal- voided sample	-	1 (7.1)	1 (3.4)
Faecal, milk filter, and soil	1(6.7)	-	1 (3.4)
Milk	8 (53.3)	9 (64.3)	17 (58.6)
Not stated	2 (13.3)	-	2 (6.9)
Vaginal discharge	1 (6.7)	-	1 (3.4)
Health status			
Diarrhoea	2 (13.3)	-	2 (6.9)
Endometritis	1 (6.7)	-	1 (3.4)
Healthy	-	13 (92.8)	13 (44.8)
Healthy/ high incidence mastitis[3]	2 (13.3)	-	2 (6.9)
Mastitis	7 (46.7)	-	7 (24.1)
Mastitis and healthy	-	1 (7.1)	1 (3.4)
Salmonellosis	1 (6.7)	-	1 (3.4)
Not stated	1 (6.7)	-	1 (3.4)
Sampling			
Individual	11 (73.3)	12 (85.7)	23 (79.3)
Individual and pooled	-	1 (6.7)	1 (3.4)
Pooled	3 (20.0)	-	3 (10.3)
Not stated	-	2 (14.3)	2 (6.9)
AMR assessment method			
Genotype	1 (6.7)	1 (7.1)	2 (6.9)
Phenotype	9 (60.0)	9 (64.3)	18 (62.1)
Both	4 (26.7)	5 (35.7)	9 (31.0)
Funding source[4]			
Provided			
Industry	7 (46.7)	5 (35.7)	12 (43.4)

(*continued on next page*)

Table 1 (*continued*)

Characteristic	Passive (%) ($n = 15$)	Active (%) ($n = 14$)	Total (%) ($n = 29$)
Government- Australian	5 (33.3)	4 (28.6)	9 (31.0)
Government- International	-	2 (14.3)	2 (6.9)
University	2 (13.3)	3 (21.4)	5 (17.2)
Not provided	5 (33.3)	7 (50.0)	12 (41.8)

[a] State locations are the Australian States: Australian Capital Territory (ACT), New South Wales (NSW), Queensland (QLD), South Australia (SA), Tasmania (TAS), Victoria (VIC), and Western Australia (WA); [2]The median (minimum – maximum) of animals sampled; [3]High incidence mastitis was either not defined (Khazandi et al., 2018), or stated as problematic (Hoare and Barton, 1972), no further indication was provided on how this status was determined; [4]Articles may list more than one funding source with provided funding sources classified into industry, government, and university. The actual funders reported in the articles are available in Supplementary Table 4.

common source (43.4%: $n = 12$), followed by the Australian government (31.0%: $n = 9$) and university (17.2%: $n = 5$) across all articles regardless of surveillance method.

3.2. Phenotypic AMR assessment characteristics

Table 2 summarizes the phenotypic AMR characteristics for the articles involved in this scoping review. Across the 27 articles describing phenotypic AMR, nine species of bacteria were assessed. Most of these articles related to *Enterobacteriaceae* (total 70.4%: 78.6% passive, 61.5% active) or *Staphylococcus* spp. (total 66.7%: 71.4% passive, 61.5% active). The median number of bacterial isolates assessed were 37 isolates (range: 1 – 257 isolates) and 70.5 isolates (range: 3 – 10279 isolates) for passive and active surveillance articles respectively. The method of assessment of the MIC was predominately CLSI breakpoints (total 48.1%: $n = 13$), with the year for interpretation varying across 11 editions, not necessarily related to the most current available for the year of article publication. ECOFFs were referenced in one passive and for three active surveillance articles as a MIC assessment method, while CDS tests were referenced in one passive surveillance article. In nine of the articles analyzed no interpretation method was described. The reporting of all cutoff or breakpoints utilized for the interpretation of the MICs through the associated MIC assessment method was presented in 14.8% ($n = 4$) of the articles. A range in the MIC results was provided and available for interpretation in 25.9% ($n = 7$) of the articles analyzed.

Overall, 64 different antimicrobials belonging to 27 antimicrobial classes were used to assess phenotypic resistance (Supplementary Table 5). A total of 49 different antimicrobials were assessed across the passive surveillance articles and 44 across the active surveillance articles. Tetracycline (total: 96.3% $n = 26$; passive: 92.9%, $n = 13$; active: 100%, $n = 13$) was the most common antimicrobial tested for phenotypic resistance, followed by chloramphenicol (total: 77.7%, $n = 21$; passive: 78.6%, $n = 11$; active: 76.9%, $n = 10$), streptomycin (total: 63.0%, $n = 17$; passive: 50.0%, $n = 7$; active: 76.9%, $n = 10$), ampicillin (total: 59.3%, $n = 16$; passive: 50.0%, $n = 7$; active: 69.2%, $n = 9$), and gentamicin (total: 55.5%, $n = 15$; passive: 50.0%, $n = 7$; active: 61.5%, $n = 8$). First to fourth generation cephalosporins were assessed to varying degrees across the articles being highest for third generation ceftiofur (total: 37%, $n = 10$; passive: 28.6%, $n = 4$; active: 46.2%, $n = 6$) and ceftriaxone (total: 22.2%, $n = 6$: passive: 0%, $n = 0$; active: 46.2%, $n = 6$) and second generation cefoxitin (total: 29.6% $n = 8$; passive: 28.6%, $n = 4$; active: 30.8%, $n = 4$).

3.2.1. Phenotypic AMR based on CLSI breakpoints

Fig. 2 displays the percentage of phenotypic AMR of Gram-negative bacteria isolated from dairy cattle from different states of Australia at the abattoir or farm, and year of study, based on CLSI breakpoints. Fig. 2A depicts the results of five articles that investigated *E. coli* phenotypic AMR, being interpreted through five editions of CLSI breakpoints (2000, 2002, 2008, 2015, and 2018). The three passive surveillance studies included intestinal faeces from animals displaying scours (Stephens, 2003), milk samples from mastitic heifers (Dyson et al., 2022), and vaginal discharge of heifers with suspected endometritis (Ludbey et al., 2022), while the two active surveillance articles cultured bacteria from the faecal matter of healthy animals at the abattoir (Barlow et al., 2015) and on farm (Jordan et al., 2005). Although the passive surveillance articles demonstrate *E. coli* isolates have up to 62.1% tetracycline resistance and 51.7% ampicillin resistance (Stephens, 2003), both active surveillance articles found less than 10% AMR for all antimicrobials assessed.

Four different CLSI editions (1990, 2002, 2006, and 2015) were used across the four articles detailing clinical AMR for *Salmonella* spp. These articles included *Salmonella* spp. isolated from dairy cattle through passive surveillance including intestinal faeces from cattle with salmonellosis

Table 2
Summary of the phenotypic AMR assessment characteristics for the passive and active surveillance articles included in the scoping review ($n = 27$).

Characteristic	Passive (%) ($n = 14$)	Active (%) ($n = 13$)	Total (%) ($n = 27$)
Bacteria assessed[a]			
Bacillus spp.	2 (14.3)	2 (15.4)	4 (14.8)
Clostridiaceae	1 (7.1)	-	1 (3.7)
Enterobacteriaceae	11 (78.6)	8 (61.5)	19 (70.4)
Enterococcus spp.	1 (7.1)	-	1 (3.7)
Staphylococcus spp.	10 (71.4)	8 (61.5)	18 (66.7)
Streptococcus spp.	6 (42.9)	2 (15.4)	8 (29.6)
Pasteurella spp.	1 (7.1)	-	1 (3.7)
Pseudomonas spp.	2 (14.3)	-	2 (7.4)
Other/various/combination	-	1 (7.7)	1 (3.7)
Sample number[2]	37 (1 – 257)	70.5 (3 – 10279)	NA
MIC assessment			
Agar dilution	2 (14.3)	2 (15.4)	4 (14.8)
Broth microdilution	2 (14.3)	5 (38.5)	7 (25.9)
Disc diffusion	8 (57.1)	6 (46.2)	14 (51.9)
MIC evaluator strip	-	1 (7.1)	1 (3.7)
MIC evaluator strip and Etest strips	1 (7.1)	-	1 (3.7)
AMR interpretation method			
CDS test[3]	1 (7.1)	-	1 (3.7)
CLSI breakpoints[4]			13 (48.1)
1990[5]	1 (7.1)	-	
2000[5]	-	1 (7.7)	
2002[5]	1 (7.1)	-	
2006	1 (7.1)	-	
2008	1 (7.1)	-	
2013	-	1 (7.7)	
2014	-	1 (7.7)	
2015	1 (7.1)	1 (7.7)	
2017	-	1 (7.7)	
2018	2 (14.3)	-	
2020	1 (7.1)	-	
ECOFF[6]	1 (7.1)	3 (23.1)	4 (14.8)
Not reported	3 (21.4)	6 (46.2)	9 (33.3)
Reporting of all Cutoff / breakpoints used			
Yes	1 (7.1)	3 (23.1)	4 (14.8)
No	12 (85.7)	11 (84.6)	23 (85.2)
Range for MIC results provided			
Yes	3 (21.4)	4 (30.8)	7 (25.9)
Yes (results not split by production origin)	-	1 (7.7)	1 (3.7)
No	10 (71.4)	9 (69.2)	19 (70.4)

[a] Note multiple bacteria may be assessed within a single article as detailed in Supplementary Table 4; [2]The median (minimum – maximum) of isolates assessed; [3]CDS test: Calibrated. Dichotomous Sensitivity test; [4]CLSI: Clinical and Laboratory Standards Institute; [5]Reported as NCCLS breakpoints: National Committee for Clinical Laboratory Standards the former name of CLSI; [6]ECOFF: Epidemiologic Cutoff values.

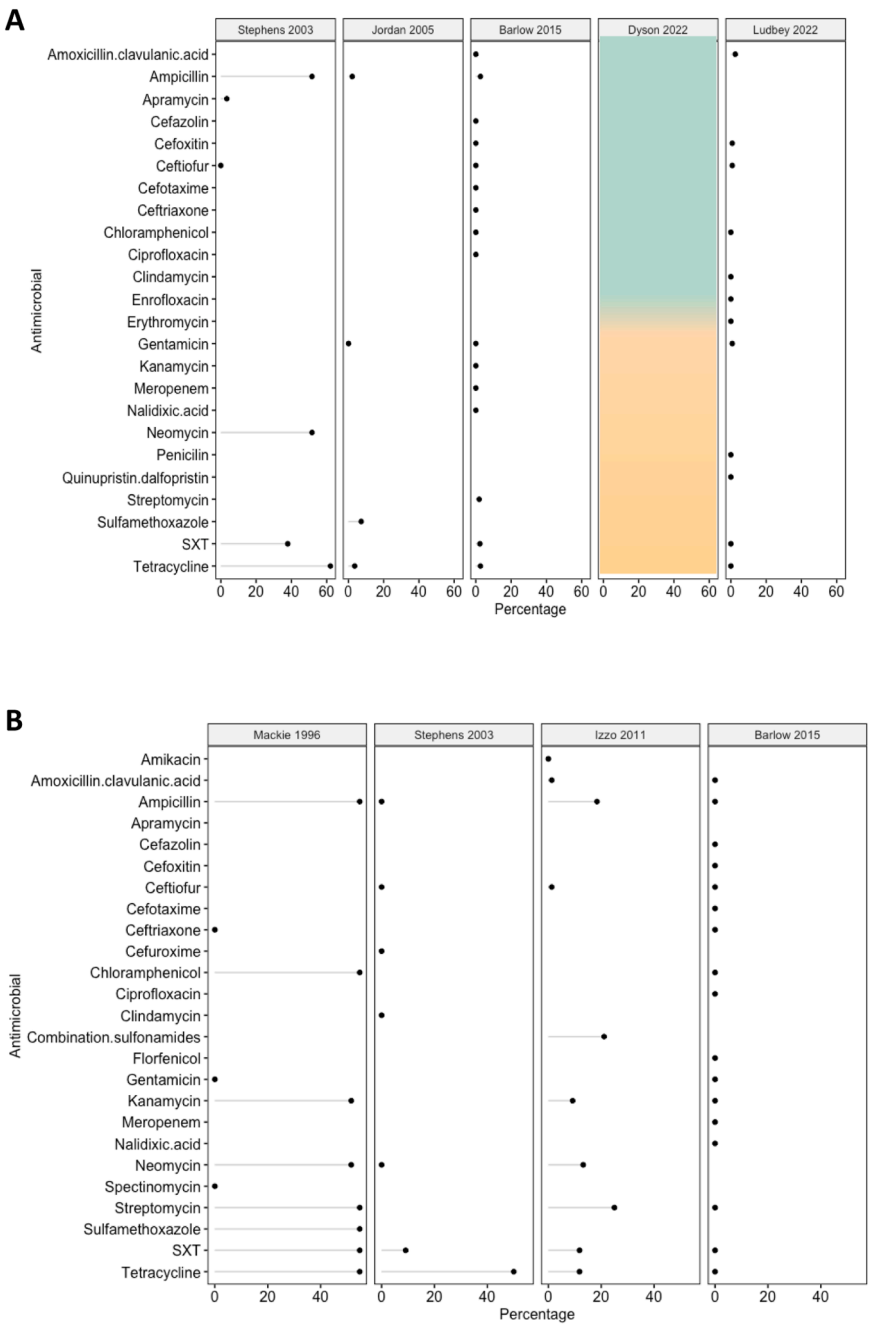

Fig. 2. Percentage (%) of phenotypic resistance in Gram negative bacteria *E. coli*, and *Salmonella* spp., isolated from Australian dairy cattle across articles, based on CLSI breakpoints[1]. [1]Publications identified as first author (year). Graph background indicates sample origin with all antimicrobials listed tested in all states indicated: New South Wales (blue), Victoria (orange), Queensland (purple), South Australia (dark green), Tasmania (light green), Western Australia (yellow), and all states except NT & ACT (white); A: *E. coli* isolated from intestinal faeces on farm (P: Stephens, 2003), voided faeces on farm (A: Jordan 2005), faeces at abattoir (A: Barlow 2015), milk samples (P: Dyson 2022) and vaginal discharge (P; Ludbey 2022); B: *Salmonella* spp. isolated from rectal faeces plus bile (P: Mackie 1996), intestinal faeces on farm (P: Stephens, 2003), rectal faeces on farm (P: Izzo 2011) intestinal faeces at abattoir (A: Barlow 2015); Passive (P) and active (A) surveillance.

(Stephens, 2003), rectal faeces (Izzo et al., 2011) or rectal faeces plus bile from dairy cattle with diarrhoea (Mackie et al., 1996). Antimicrobial resistance of *Salmonella* spp. isolates described in these articles was up to 54.8% resistance for ampicillin, chloramphenicol, streptomycin, sulfamethoxazole, tetracycline, and sulfamethoxazole-trimethoprim. The one active surveillance article that isolated *Salmonella* spp. from healthy dairy cattle at the abattoir (Barlow et al., 2015) reported no resistance to any antimicrobial assessed (Fig. 2B).

Fig. 3 displays the percentage of phenotypic AMR of Gram-positive bacteria based on CLSI breakpoints, based on samples from dairy cattle from different states of Australia at abattoir or farm. Four articles reported the isolation of *Bacillus* spp.; two farm passive surveillance articles (one on milk samples from mastitic dairy cattle (Chung et al., 2021) and one on vaginal discharge of heifers with suspected endometritis (Ludbey et al., 2022)), and two active surveillance articles regarding milk samples (one from mastitic and healthy animals on farm (Al-Harbi et al., 2021) and one from the milk processor (Radmehr et al., 2020)) (Fig. 3A). Across these articles four different editions of the CLSI breakpoints (2013, 2017, 2018, and 2020) were referenced for MIC interpretation, with the three on farm studies suggesting a similarly low prevalence of phenotypic AMR resistance, being highest for penicillin (52%) clindamycin (50% and 50.8%) and erythromycin (48.6% and

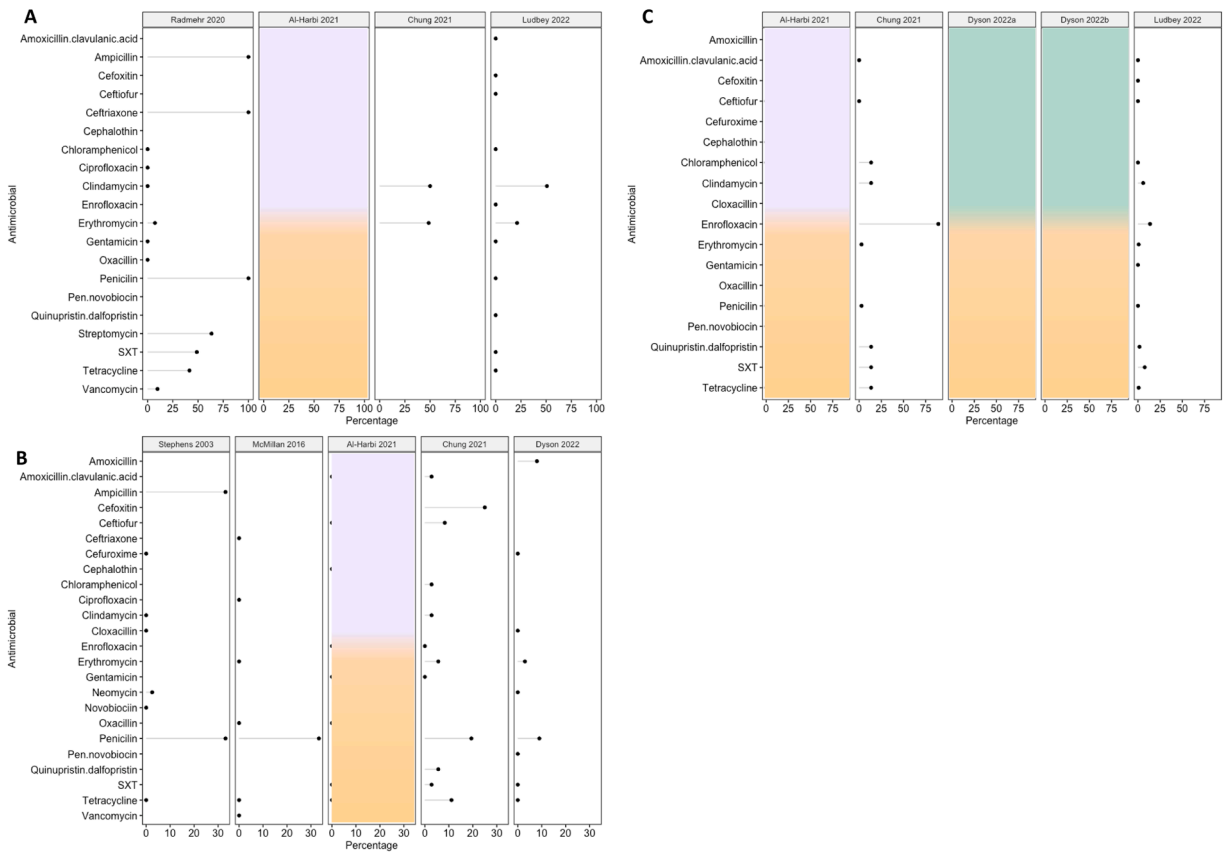

Fig. 3. Percentage (%) of phenotypic AMR for gram positive bacteria, *Bacillus* spp., *S. aureus,* and *Streptococcus* spp. isolated from Australian dairy cattle across publications based on CLSI breakpoints[1]. [1]Publications identified as first author (year). Graph background indicates sample origin with all antimicrobials listed tested in all states indicated: New South Wales (blue), Victoria (orange), Queensland (purple), South Australia (dark green), Tasmania (light green), Western Australia (yellow), and all states except NT & ACT (white); A: *Bacillus* spp. isolated from milk samples at the processor (A: Radmehr 2020), farm (A: Al-Harbi 2021; P: Chung 2021) and vaginal discharge on farm (P: Ludbey 2022); B: *S. aureus* isolated from milk samples on farm (P: Stephens, 2003, Chung 2021, Dyson2022), (A: McMillan 2016, Al-Harbi, 2021); C: *Streptococcus* spp. isolated from milk samples on farm (A: Al-Harbi 2021, P: Chung 2021) *Streptococcus dysgalactiae* (P: Dyson 2022a), and *Streptococcus uberis* (P: Dyson 2022b) and vaginal discharge (Ludbey, 2022). Passive (P) and active (A) surveillance.

21.2%). However, the resistance reported for *Bacillus* spp. from the processor (Radmehr et al., 2020) was 100% resistance for ampicillin, penicillin, and ceftriaxone.

The phenotypic AMR (CLSI editions 2002, 2008, 2013, 2014, and 2020) for *Staphylococcus aureus* isolated through passive surveillance from milk samples of mastitic dairy heifers (Stephens, 2003; Al-Harbi et al., 2021; Chung et al., 2021; Dyson et al., 2022), and on farm active surveillance of milk samples from healthy heifers (McMillan et al.,

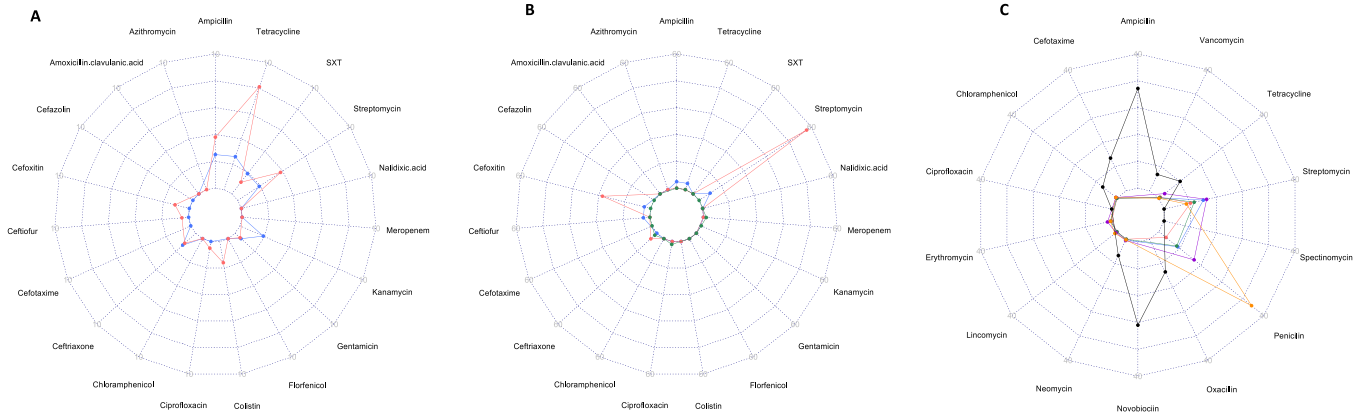

Fig. 4. Percentage of resistant *E. coli*, *Salmonella* spp., and *Staphylococcus* spp. isolated from Australian dairy cattle across first author and year of publication of publications based on phenotypic AMR characteristics and ECOFFs[1]. [1]Publications identified as first author (year) for brevity in this figure. A: *E. coli* isolated from intestinal faeces at the abattoir (Barlow, 2015) (blue) and (Barlow, 2022) (red) across multiple states; B: *Salmonella* spp. isolated from faecal samples at the abattoir (Barlow, 2015) (green) and (Abraham, 2022) (blue) across multiple states and from calves and heifers on Western Australian farms (Aleri, 2022) (red); C: *Staphylococcus* spp. with *S. aureus* isolated from milk samples on farm across multiple states and years (Frost, 1981: 1974–75:orange, 1976: purple, 1977: green,1978: red, 1979: blue), coagulase-negative *Staphylococci* from milk samples collected on farm in South Australia (Khazandi, 2018) (black).

2016), was below 34% for all antimicrobials assessed. Antimicrobial resistance was highest to penicillin (33.3%) in an active surveillance study (McMillan et al., 2016) (Fig. 3B).

Streptococcus spp. were isolated from milk samples (Al-Harbi et al., 2021; Chung et al., 2021; Dyson et al., 2022) and vaginal discharge (Ludbey et al., 2022) (Fig. 3C), and AMR interpreted through CLSI (2008, 2013, 2018, and 2020 editions). Only one article regarded active surveillance activities for a combination of mastitic and healthy dairy cattle (Al-Harbi et al., 2021), while the other four passive surveillance articles were evaluating diseased animals, having either mastitis, or in the case of Ludbey et al. (2022) were suspected of endometritis. The active surveillance article demonstrated 50% resistance for gentamicin and 30% resistance for oxacillin in *Streptococcus* spp. while the passive surveillance articles provided up to 90% tetracycline resistance (*S. dysgalactiae*) and 89.2% enrofloxacin resistance (*Streptococcus* spp.) (Fig. 3C).

There was one passive surveillance article that investigated the sensitivity of *Clostridium perfringens* (Santos et al., 2022), isolated from the faeces of dairy cattle, milk filters, and soil on farm in Victoria (Santos et al., 2022), suggesting clinical resistance in 50% of isolates to tetracycline and 37.5% of isolates to clindamycin and erythromycin.

3.2.2. ECOFF phenotypic AMR

The phenotypic AMR of bacteria isolated from cattle in the Australian dairy industry based on ECOFFs are presented in Fig. 4. An active surveillance article describing *E. coli* isolated from intestinal faeces at the abattoir in 2015 across multiple states demonstrated either no 'non-wildtype' bacteria or low resistance to ampicillin, ceftriaxone, gentamicin, kanamycin, streptomycin, and sulfamethoxazole-trimethoprim (Barlow et al., 2015) (Fig. 4A). The active surveillance article on intestinal faeces at the abattoir in 2022 (Barlow et al., 2022), a follow up for the Barlow et al. (2015) study, reported an increase in the percentage of "non-wildtype" bacteria for the assessed *E. coli* isolates to ampicillin (2.5–3.8%), cefoxitin (0–1.1%), ceftiofur (0–0.5%), ciprofloxacin (0–0.5%), streptomycin (19–3.8%), and tetracycline (2.6–8.1%) (Fig. 4A). Fig. 4B displays the ECOFFs for *Salmonella* spp. isolated from the active surveillance of faecal samples at the abattoir (Barlow et al., 2015; Abraham et al., 2022) across multiple states, and from calves and heifers on WA farms (Aleri et al., 2022). The only "non-wildtype" *Salmonella* spp. isolated from faeces collected at the abattoir in 2015 were resistant to ceftriaxone (1.3%), ciprofloxacin (1.3%), and meropenem (1.3%) (Barlow et al., 2015), which was reduced to 0% in 2022 in a follow up study at the abattoir for these three antimicrobials (Abraham et al., 2022). However, the percentage of 'non-wildtype' *Salmonella* spp. identified as resistant to ampicillin (0–2.9%), cefoxitin (0–2.9%), ceftiofur (0–2.9%), streptomycin (0–5.9%), and tetracycline (0–2.9%) increased (Abraham et al., 2022). In contrast, the on-farm assessment in WA in 2022 (Aleri et al., 2022) recorded resistance of 'non-wildtype' *Salmonella* spp. as 22.2% to cefoxitin, 3.7% for ceftriaxone, and 57.4% for streptomycin. (Fig. 4B). ECOFFs for *Staphylococcus* spp., including *S. aureus* isolated from milk samples on farm across multiple states (Frost and O'Boyle, 1981) and coagulase-negative Staphylococci (CoNS) from milk samples collected on farm in South Australia (Khazandi et al., 2018) are presented in Fig. 4C. The proportion of 'non-wildtype' *S. aureus* isolated from the 1657 milk samples in Frost and O'Boyle (1981) was split across five years. There was a significant reduction of 'non-wildtype' *S. aureus* reported over this period for penicillin (35.3% in 1974–75–7.2% in 1979), while streptomycin increased from 6.8% to 8.1%. In comparison, coagulase-negative Staphylococci isolated from milk samples of mastic dairy cattle was reported to be proportionally high for 'non-wildtype' regarding ampicillin (29.7%), cefotaxime (10.8%), novobiocin (24.8%), oxacillin (10.8%) and tetracycline (8.1%) (Khazandi et al., 2018) (Fig. 4C).

3.3. Genotypic AMR assessment characteristics

There were eleven articles that assessed genotypic AMR, with the characteristics utilised by the passive ($n = 5$) and active ($n = 6$) surveillance articles presented in Supplementary Table 6. The isolated organisms assessed in these articles included *Bacillus* spp. (total: 9%, $n = 1$; passive: 0%, $n = 0$; active: 16.7%, $n = 1$), *Clostridiaceae.* (total: 9%, $n = 1$; passive: 20%, $n = 1$; active: 0%, $n = 0$), *Enterobacteriaceae* (total: 36.4%, $n = 4$; passive: 20%, $n = 1$; active: 50%, $n = 3$), *Staphylococcus* spp. (total: 27.3%, $n = 3$, passive: 40%, $n = 2$; active: 16.7%, $n = 1$), *Streptococcus* spp. (total: 9%, $n = 1$; passive: 20%, $n = 1$; active: 0%, $n = 0$), and one active surveillance study that assessed the resistant genome of various bacteria. The method of genomic assessment across these eleven articles included PCR (total: 27.3%, $n = 3$; passive 20%, $n = 1$; active: 33.3%, $n = 2$) and WGS (total:63.6% $n = 7$; passive: 60%, $n = 3$; active: 66.7%, $n = 4$), with one study (passive) using a combination of both methods. The median number of isolates assessed genotypically across both passive and active surveillance articles was 63 isolates (range: 14 – 252 isolates) for PCR and 20 isolates (range: 3 – 166 isolates) for WGS. Six of the articles assessed the prevalence or presence of virulence genes and ten articles assessed the prevalence/presence of AMR genes.

The drug class and prevalence of AMR genes identified from bacteria isolated through passive and active surveillance articles about Australian dairy cattle are displayed in Table 3. Three articles described *Salmonella* spp. isolated from faeces of dairy cattle with salmonellosis (Abraham et al., 2014), from healthy dairy animals at the abattoir (Abraham et al., 2022), and from healthy heifers and calves on farm (Aleri et al., 2022). Apart from the 41% prevalence of aac(6') gene coding for an aminoglycoside modifying enzyme identified in one study (Aleri et al., 2022), there was a low prevalence of AMR gene prevalence across the three studies regarding aminoglycosides, penicillins, sulphonamides, tetracyclines, third/fourth generation cephalosporins, and trimethoprim. The single article detailing *E. coli* isolated from faecal samples of healthy dairy cattle at the abattoir in 2022 (Barlow et al., 2022) reported between 10% and 40% prevalence of genes providing resistance to aminoglycosides, fluoroquinolones, penicillins, sulphonamides, tetracyclines, and trimethoprim. *Staphylococcus* spp. isolated from milk samples of high incidence mastitis dairy heifers on farm (Khazandi et al., 2018) demonstrated up to 50% prevalence of AMR genes relating to macrolides, penicillins and tetracyclines. This was high compared to the genomic description of *Staphylococcus* spp. isolated from dairy cattle (O'Dea et al., 2020), having less than 7.8% prevalence for these same drug classes. However, this second study demonstrated a 24.7% prevalence of *norA*, a fluoroquinolone resistance gene. *Streptococcus* spp. isolated from milk samples of mastitic dairy heifers on farm (Vezina et al., 2021) reported a low prevalence of resistance genes to lincosamides (*InuC* 3.7% and *InuD* 11.1%), macrolides (mel/mef (A) 7.4%), penicillins (*mrsE* 7.4%) and streptogramin (*vatD* 7.4%). AMR gene prevalence for the one study reporting various bacteria isolated from bulk milk tanks, filters, and commercial origin in 2020 included sulphonamides (*sul2* 72%), tetracyclines (*tetA* 62%), macrolides (*ermA* 44%), and penicillins (39% $bla_{TEM\text{-}1B}$; 29% blaZ; 5% mecC).

3.4. GRADE assessment and risk of bias summary

The individual study rating for quality of evidence using the GRADE guidelines for all the articles in this review is provided in Supplementary Table 7 and summarised in Table 4. All but one article clearly stated the research objective and 69% clearly specified and defined the study population. Most articles (86.9%) did not justify the sample size, power descriptions, variance, and effect estimate. The inclusion or partial exclusion/ inclusion criteria for observational studies was 20.7% and 37.9% of the articles respectively, with 13.8% of articles assessing the exposure(s) over time. Many studies included specification of all procedures used (75.9%), reported valid and reliable data collection tools

Table 3
Drug class and prevalence of AMR genes identified from bacteria isolated through passive and active surveillance articles concerning Australian dairy cattle[1].

Drug class	Gene	Article							
		Abraham 2014	Abraham 2022	Aleri 2022	Barlow 2022	Khazandi 2018	O'Dea 2020	Vezina 2021	Various
Aminoglycosides	*aac(6')*			41					
	aphA1	3.5							
	spc						0.6		
	str						0.6		
	strA				30				
	strB				30				
Fluroquinolenes	*norA*						24.7		
	QnrS1				10				
Lincosamides	*lnuC*							3.7	
	lnuD							11.1	
Liptopeptide	*mprf*								
Macrolides	*ermA*						0.6		
	ermB								44
	ermC					50	0.6		5
	ermQ								
	mel/mef(A)							7.4	
Pencilins	bla_{TEM}	5.9							
	bla_{TEM-1B}				40				39
	blaZ					50	7.8		29
	mecA					13.5			0
	mecA homologs					10.8			
	mecC								5
	mrsE							7.4	
Streptogramin	*vatD*							7.4	
Sulphamides	*int1*	3.5							
	sul2	7.1			20				72
Tetracyclines	*tetA*	3.5	2.9		30				62
	tetB	3.5			10				
	tetK					50			46
	tetM								38
Third/fourth generation cephalosporins	bla_{CMY-2}		2.9						
	bla_{CTEM}		2.9						
	bla_{DHA-16}			1.8					
Trimethoprim	*dfrA14*				20				
	dfrA5		2.9						
	dhfrV	4.7							

Note the colour of the bar indicates the bacteria isolated, length of bar is the prevalence indicated by the number to the immediate right Article is identified by the first authors surname and year of publication. [1]*Salmonella* spp. (blue) isolated from salmonellosis dairy cattle, healthy dairy animals at the abattoir and heifer/calves on farm; *E. coli* (red) isolated from faecal samples of healthy dairy cattle at abattoir; *Staphylococcus* spp. (green) isolated from the milk samples of high incidence mastitis dairy heifers on farm and dairy cattle *Streptococcus* spp. (purple) isolated from milk samples of mastitic dairy heifers on farm and various bacteria (yellow) isolated from healthy dairy heifers on farm.

(75.9%), used statistical methods to examine and measure outcomes (41.4% yes and 48.4% partially) and considered the limitations of the methodology used on the results (34.5% yes, 34.5% partially). Ethical issues were addressed in 34.5% of the articles, with difficulty in knowing this due to a lack of reporting in 65.5% of articles.

4. Discussion

The aims of this scoping review were achieved with a total of 29 published articles identified detailing both the passive and active surveillance of bacterial AMR in Australian dairy cattle. It is possible that the number and scope of the identified publications may restrict complete representation of the Australian dairy industry. For example, most passive surveillance data sort by veterinarians would predominately be for disease diagnosis, and may not have been published in peer review articles, excluding this information from this review. However, this scoping review was focussed on only the published surveillance data similiar to that of a recently published scoping review detailing AMU and AMR in North American and Canadian beef cow/calf production (Wilhelm et al., 2023), due to the accessibility and repeatability of the data provided in published peer reviewed articles. Though not complete, valuable information concerning the prevalence of AMR to commonly used antimicrobials for bacteria isolated from Australian dairy cattle, was provided by the articles included in this scoping review.

We summarized the quality of the evidence for all articles in this scoping review with the recommended evaluation of the quality of evidence and the risk of bias (O'Connor and Sargeant, 2015). While the articles analysed mostly had clear objectives and defined study populations, there was a low inclusion of repeated measures, sample size justification, and consideration of limitations or bias in data collection. The authors believe that a continuity in reporting of *ad hoc* research would provide longitudinal epidemiological compliant data comparable across years, management practices, industries, and countries. Reporting recommendations to aid this process include the identification of the work as an AMR study alongside the identity of the animal population and antimicrobials studied within the title. An outline within the methodology of the population to be sampled in terms of location, sample types, sampling techniques, equipment required, and processing

Table 4
Summary of the GRADE assessment and risk of bias summary for the retained articles on the quantifiable resistance of bacteria to antimicrobials isolated from cattle in the Australian dairy industry ($n = 29$).

Quality criteria[1]	Number of studies (%)
1. Was the research question or objective in this paper clearly stated?	
Yes	28 (96.5)
No	1 (3.4)
2. Was the study population clearly specified and defined?	
Yes	20 (69.0)
No	5 (17.2)
Partially	4 (13.8)
3. Was a sample size justification, power description, or variance and effect estimates provided?	
Yes	2 (6.9)
No	25 (86.2)
Partially	2 (6.9)
4. Inclusion/exclusion criteria stated if observational study?	
Yes	6 (20.7)
No	11 (37.9)
Partially	11 (37.9)
Not applicable	1 (3.4)
5. Are group treatment and controls stated if experimental study?	
Partially	1 (3.4)
Not applicable	28 (96.5)
6. Random assigned treatment groups for sampling units if experimental study?	
No	1 (3.4)
Not applicable	28 (96.5)
7. Was the exposure(s) assessed more than once over time?	
Yes	4 (13.8)
No	25 (86.2_
8. Are all procedures used in the study specified?	
Yes	22 (75.9)
No	2 (6.9)
Partially	4 (13.8)
9. Were data collection tools shown to be valid?	
Yes	22 (75.9)
No	1 (3.4)
Partially	6 (20.7)
10. Were data collection tools shown to be reliable?	
Yes	22 (75.9)
No	1 (3.4)
Partially	6 (20.7)
11. Did the statistical methods examine changes in outcome measures? Were statistical tests done that provided p values for changes?	
Yes	
No	12 (41.4)
Partially	3 (10.3)
	14 (48.3)
12. Has consideration been given to any limitations of the methods or data that may have affected the results?	
Yes	
No	10 (34.5)
Partially	10 (34.5)
	9 (31.0)
13. Have ethical issues been addressed and was confidentiality respected?	
Yes	10 (34.5)
Can't tell	19 (65.5)

is valuable information for extracting and comparing results between studies. The reporting of the CLSI breakpoints or ECOFF values used in the interpretation of the MICs would also improve comparisons between studies. This is based on the revisions between editions, such as the multiple CLSI breakpoint revisions since 2010, complicating and potentially changing the interpretation of resistance (Humphries et al., 2019). Additionally, based on the challenges of analysis requiring many assumptions to extrapolate the data from the scoping review articles, the authors suggest the inclusion of the range in MIC antimicrobial concentrations when reporting AMR surveillance data. These ranges provide the opportunity for reinterpretation of resistance values using up to date criteria, providing direct comparisons of individual studies. Furthermore, the significance of the clinical MIC breakpoints used for interpreting AMR, being human for this review, must be highlighted. This is because the breakpoints used for interpreting the resistance of a bacterium to an antimicrobial may diverge between species due to differing pharmacodynamics and pharmacokinetics between species. Therefore, the interpretations made from this scoping review may be primarily relevant to human medicine implications, and less complete and reliable for bovine medicine implications.

There were many similarities in the study characteristics for the two types of surveillance articles. For example, both passive and active articles commonly involved milk samples, individual sampling, and phenotypic assessment for the sampling type, sampling method, and AMR assessment method respectively. One major difference between the two types of surveillance articles was the broader variety in bacteria investigated for passive surveillance articles. However, even with the increased range in bacterial organisms, passive surveillance articles were not comprehensive. For example, no Australian dairy industry AMR data is currently available for zoonotic pathogens such as *Mannheimia haemolytica* and *Pasteurella multocida* that are causative of respiratory disorders, the mastitic causing *Trueperella pyogenes, Mycoplasma bovis*, causative of both respiratory and mastitic disease, or the common North American pathogen *Histophilus somni* causative of endothelium thrombi. These and other pathogens of significance may be investigated in future passive surveillance studies, furthering the range of information observed. The advantage of this information includes the provision of valuable feedback on animal health, strengthening the veterinarian to farmer relationships while incurring a lower associated expense (Thrusfield et al., 2018), and providing insight in the situation in a certain disease or a certain area. Conversely, active surveillance provides accurate representations of disease estimates. This is due to the general methodology of active surveillance being well-designed surveys with higher median number of bacteria isolates, instead of voluntary submissions to laboratory for sensitivity testing for phenotypic AMR (Thrusfield et al., 2018), reducing associated bias. Therefore, both forms of surveillance are beneficial and required for future AMR investigations to provide quantified AMR information valuable to the Australian dairy industry.

There were three methods of assessing phenotypic AMR summarised in this review, namely CDS, CLSI breakpoints, and ECOFF values. CDS was not a common method of assessment, being referenced in only one passive surveillance article, consequently the data from the associated study was not used in any comparisons or evaluations in this scoping review. Mostly, the authors for articles that interpreted clinical resistance using CLSI breakpoints included reported low levels of AMR, irrespective of the surveillance. Radmehr et al. (2020) were exceptions to this generalisation reporting a high level of resistance to ampicillin, penicillins, and ceftriaxone for *Bacillus cereus*, an important foodborne pathogen and food spoiler. There was also a trend for passive surveillance articles about *E. coli*, *Salmonella* spp., and *Streptococcus* spp. to report higher clinical phenotypic AMR compared to the active surveillance articles. These anomalies may in fact be due the strong selective pressure exerted upon drug-sensitive pathogens even with appropriate AMU (Laxminarayan et al., 2013). Therefore, bacteria from antimicrobial treated or diseased animals isolated in the passive surveillance articles would potentially have higher resistance levels compared to the bacteria from animals with a predominately healthy status involved active surveillance articles.

The value of the additional information provided by the third method of phenotypic AMR assessment listed above, ECOFF values, has meant that the majority of states in Australia have used EUCAST for testing sensitivity of human clinical isolates to antimicrobials since 2017 (ACSQHC, 2019). Additionally, use of ECOFF values as interpreting criteria for broth microdilution is the preferred methodology by the

European Food Safety Authority (EFSA, 2019). However, only 14.8% of the articles in this scoping review used ECOFF values, and only 25.9% of the articles reported the MIC ranges allowing for the reinterpretation of data with ECOFF values. Nevertheless, from the comparison between the findings across the small number of articles detailing ECOFF interpreted phenotypic AMR provided by this scoping review, a higher prevalence of "non-wild type" CoNS isolated from milk samples of mastic dairy cattle regarding ampicillin cefotaxime, novobiocin, oxacillin, and tetracycline (8.1%) (Khazandi et al., 2018). These findings again suggest that the health status of the animals sampled, and thus bacterial source for antimicrobial sensitivity assessment, impacts on the resultant AMR prevalence reported.

Antimicrobials commonly used in the Australian dairy industry to treat infectious conditions, such as ampicillin, penicillin, tetracyclines, sulphonamides and macrolides (DHAC and DAFF, 2000; AVA, 2022), were assessed across most of the articles included in this scoping review. However, there was a wider range of antimicrobials included in susceptibility testing in the active surveillance articles. This increased the depth in antimicrobial assessment provided by these active surveillance articles is valuable in industry AMR assessment. This is because the antimicrobials prescribed for treatment and the method of antimicrobial application, are circumstantial. Mastitis for example, the main driver of AMU in dairy cattle (Krömker and Leimbach, 2017), requires a clinical exam and diagnosis of the contributory bacteria prior to treatment. Gram-negative bacterial infections are treated by veterinarians intravenously with oxytetracycline, which is in contrast to treatment recommended for Gram-positive bacteria being cloxacillin, amoxycillin, Penethamate hydrochloride and trimethoprim/sulphonamide (AgVic and UoM, 2023). Therefore, increasing the breadth of antimicrobials investigated provides opportunity to incorporate more of the antimicrobials used within the Australian dairy industry to provide a more objective appraisal of the AMR situation. Additionally, the assessment of a wider range in antimicrobials allows for the inclusion of antimicrobials with high importance in the treatment of human disease. For example, ceftiofur and virginiamycin are restricted for exceptional bovine medical circumstances only, alongside ciprofloxacin and gentamicin that are both prohibited from use in dairy cattle (AVA, 2022). However, even with these stringent rules reducing or excluding the use of these antimicrobials within the dairy industry, there is an implied *One Health* aspect to AMU due to the potential risk of transfer for any resultant AMR in animal production into the human domain. It is therefore important that AMR surveillance should include testing for resistance to antimicrobials that are restricted for human use, a more likely scenario with active surveillance.

Whole genome sequencing (WGS) in antimicrobial susceptibility testing enables the recognition of genetic relationships, identifying epidemiological associations between isolates (Köser et al., 2012). Not surprisingly, resistant gene prevalence was identified for bacteria assessed across the articles in this scoping review for aminoglycoside, macrolide, penicillin, sulphonamides, and tetracycline. While these are all antimicrobial classes commonly used in the treatment of dairy cattle ailments, as referenced above, the predicted genomic and phenotypic susceptibility patterns are not always equivalent. This was demonstrated for example by the AMR gene *norA* identified for *Staphylococcus* spp. in 24.7% of isolates, while all isolates were susceptible to enrofloxacin and marbofloxacin (O'Dea et al., 2020). Therefore, while it is important to identify the resistance genes present, examining the phenotypic susceptibility of bacterial isolates is also essential.

The proactive AMR monitoring conducted by MARAN in the Netherlands has informed a decade of antibiotic reduction policies. The benefit of these policies is apparent with the over 70% reduction in veterinary active sales coinciding with a reduction in livestock AMR (SWAB, 2022). However, it is argued that the required cost and logistics of an ongoing surveillance program impede its development in Australia. These limitations are also acknowledged as restricting the implementation of appropriate policy internationally from surveillance activities lacking comprehensive, dynamic and reliable data required to estimate the level of AMR (Schnall et al., 2019). One such example is the Danish AMR surveillance program, which is one of the most advanced globally, conceding that small sample sizes currently limit the detectability of emerging or changing resistance patterns in Denmark (DANMAP, 2018). This may be in part due to the significant employment of resources for specimen collection and laboratory isolation, limiting the implementation and scope of AMR surveillance (Shaban et al., 2014). Additionally, many international examples of surveillance sampling resistance from faecal samples at the abattoir, reducing the associated cost and representative of the potential consumer risk (Aarestrup, 2004), may not be relevant to operational antimicrobial stewardship practices on-farm. This increases the importance of *ad hoc* active and passive surveillance on farm activities to provide data to inform on future industry AMR risks and mitigate resistance. However, reliance within the Australian dairy industry on *ad hoc* surveillance to determine AMR risk impedes any comparison across studies, years, and industry due to the lack of epidemiological selection power (Aarestrup, 2004). Therefore, the quality of these *ad hoc* studies and the reporting of the results needs to be as uniform and inclusive as possible to provide usability for analysis.

While scoping reviews are not defined as comprehensive, searching additional databases and grey literature may have provided additional relevant studies. To reduce the probable impact of this limitation, the reference list of all scoping review articles was included in the search strategy of this review. However, one article proved difficult to locate and was knowingly excluded from this review. The authors do not believe this article would have affected the main objective of the review in assessing the AMR in the dairy industry, as publications before the first edition of the CLSI guidelines in 1986 were not standardised in the assessment of resistance. For example, for articles reviewed in this study that were published before 1980, either used no reviewed guidelines for resistance decisions to be based ($n = 3$) or interpreted the results through the presence of an inhibition zone around the antimicrobial disc as the isolate sensitive to the antimicrobial regardless of diameter ($n = 3$), thus reducing the reliability of the results. For this reason, they were excluded from the analysis of this review.

5. Conclusion

The aims of this review were achieved with 29 articles identified detailing both the passive and active surveillance of bacterial AMR in Australian dairy cattle. The articles as a collective have low inclusion of repeated measures, sample size justification, and consideration of limitations or bias in data collection. Additionally, varying methodologies and reporting between articles requiried several assumptions to extrapolate the data. However, while limited in number and industry representation, an insight into the prevalence of AMR in the Australian dairy industry was provided the scoping methodology of this review. This included a suggested low prevalence of clinical resistance incursion and low AMR gene prevalence in the Australian dairy cattle industry. Variations in the level of AMR, due to the health and age status of the sampled animals, suggest the need for improved population demographics definition to limit potential reporting bias for both national and global surveillance. The ECOFF interpreted phenotypic AMR suggests an associated risk of emerging or increased resistance with the presence of 'non-wild type' *E. coli*, *Salmonella* spp. and *Staphylococcus* spp., and therefore the priority for AMR dairy cattle surveillance in Australia. In place of an ongoing national dairy industry active surveillance program, and for future national and global passive surveillance activities, we recommend continuity for the reporting of both passive and active *ad hoc* AMR research activities to increase data usability and facilitate analysis.

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CRediT authorship contribution statement

MT and JWA conceived the study; MT and JWA designed the components; MT drafted original manuscript and developed the figures; MT, TJGML, KT, SM, DSB, ALB, IDR, and JWA reviewed and edited the writing; MT and JWA acquired the funding. All authors have read and agreed to the published version of the manuscript.

Declaration of Competing Interest

All authors have participated in (a) conception and design, or analysis and interpretation of the data; (b) drafting the article or revising it critically for important intellectual content; and (c) approval of the final version.
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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.2024.106161.

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