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Systematic evaluation and meta-analysis of prevalence and trends for antibiotic resistance in Canine Pseudomonas infections

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ABSTRACT

A limited number of antibiotics are available to treat pathogenic *Pseudomonas* spp. infections in animals and among currently available antipseudomonal options, only fluoroquinolones can be administered topically, orally and parenterally. We hypothesised that canine *Pseudomonas* spp. isolates showed higher rates of resistance against fluoroquinolones compared to other antipseudomonal antibiotics. A systematic review and meta-analysis were conducted to determine prevalence and distribution patterns of antimicrobial resistance in *Pseudomonas* isolates from canine infections. Extracted data were stratified by type of infection, year of isolation, geographical location and tested antibiotics. Seventy-three studies met the inclusion criteria and antimicrobial susceptibility data were derived from 9911 isolates. Approximately 48% of isolates were from otitis externa, while other skin and systemic infections represented 52%. Data were analysed using a mixed effects transformed proportion meta-analysis model. Fluoroquinolones had the highest resistance proportions (0.27, 95% CI [0.22, 0.32]), and pradofloxacin and enrofloxacin had the highest intra-class proportions of resistance, 0.56 (95% CI [0.49, 0.63]) and 0.38 (95% CI [0.32, 0.44]) respectively. In contrast, relatively lower weighted proportions for resistance were observed for aminoglycosides and carbapenems, 0.15 (95% CI [0.11, 0.19]) and 0.08 (95% CI [0.05, 0.12]) respectively. Fluoroquinolones and aminoglycosides are routinely used to treat *Pseudomonas* spp. infections in dogs, but broad-spectrum beta-lactams are rarely used. These data imply a higher selection pressure for resistance against fluoroquinolones; this may may be exacerbated by use of antibiotics such as enrofloxacin empirically. Antimicrobial susceptibility testing should be used to guide the choice of fluoroquinolones for canine *Pseudomonas* spp. infections.

Introduction

Pathogenic *Pseudomonas* spp., including *Pseudomonas aeruginosa* (PA) are ubiquitous environmental bacteria that can cause opportunistic infections in both people and animals, especially those who are immune compromised (Elfadadny et al. 2024; Pereira et al. 2025). In humans, PA is mostly associated with infections in cases of trauma, burn injuries, cystic fibrosis and ventilator-associated pneumonia (Reynolds and Kollef, 2021). In companion animals, PA is commonly associated with infections of moist areas of the skin and ears in cases of otitis externa, the respiratory tract and urinary tract (Nuttall and Cole, 2007; Pereira et al. 2025). *Pseudomonas aeruginosa* is a member of the ESKAPEE group of priority bacterial pathogens (*Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, Escherichia coli*, and *Enterobacter* spp.) which are the most important causes of hospital-acquired infections and major drivers of antimicrobial resistance globally. The pathogenicity of PA is attributed to the expression of many different virulence factors that enable it to adhere to host tissues, promote inflammation and oxidative damage in host cells, and evade immune responses and antibiotics that are used clinically. Some of the critical virulence factors include the pili, flagella and lectins that enable bacterial adhesion to epithelial cells, expression of mucin and glycolipids that are involved in biofilm formation and colonization, and the expression of exotoxins, elastases and other lytic enzymes that inhibit protein synthesis and aid in degrading host tissues (Jurado-Martin et al. 2021; Qin et al. 2022).

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Pseudomonas aeruginosa exhibits intrinsic resistance to many antimicrobials commonly used in veterinary medicine, including tetracyclines, potentiated sulphonamides, and early generation beta-lactams. PA expresses complex, membrane-bound efflux-pumps such as MexAB-OprM and MexXY-OprM that actively expel antibiotics and other biocides from bacterial cells, contributing to intrinsic antimicrobial resistance (AMR) (Poole, 2001). Acquired resistance to the fluoroquinolones, aminoglycosides, polymyxins, and antipseudomonal beta-lactams is usually due to mutations of the antibiotic molecular targets, and acquisition of other antibiotic resistance genes (ARGs) horizontally (Botelho et al. 2019). The expression of tripartite efflux systems such as MexCD-OprJ and MexEF-OprN also contributes to acquired multidrug resistance via hyperexpression of these efflux genes (Poole, 2001). Among antipseudomonal agents, fluoroquinolones are unique in being widely available as systemic and oral formulations suitable for prolonged outpatient therapy. In companion animals and particularly dogs, fluoroquinolones have favourable pharmacokinetic features with respect to bioavailability, tissue distribution, metabolic clearance and toxicity profiles, and this offers an unmatched convenience for clinical application against many different types of infections (Ihrke et al. 1999; Bidgood and Papich, 2005; Madsen et al. 2019). The antipseudomonal beta-lactam antibiotics are effective time-dependent bactericidal drugs, with short elimination half-lives that are administered at shorter dosing intervals or by continuous intravenous infusion. Thus, the use of beta-lactams against systemic infections caused by PA in companion animals may necessitate prolonged hospitalisation or intensive outpatient management. Furthermore, many antimicrobial stewardship frameworks restrict the clinical use of many antipseudomonal beta-lactams including carbapenems in veterinary medicine (Hardefeldt et al. 2017; Schmerold et al. 2023; KuKanich et al. 2023). Aminoglycosides such as gentamicin and amikacin have antipseudomonal activity and are well absorbed following parenteral administration, but they are poorly absorbed from the gastrointestinal system with limited distribution in poorly vascularised and highly lipophilic tissues. Aminoglycosides are also commonly associated with ototoxicity, neuromuscular blockade and nephrotoxicity that may vary with the dose, dosing interval and duration, and specific drug within this class (Dowling, 2025). For therapeutic interventions against infections caused by pathogenic *Pseudomonas* spp, the use of polymyxins such as polymyxin B and colistin is limited to topical or local applications. This is primarily because polymyxins are nephrotoxic at systemic concentrations that would be bactericidal in most animals (Dowling, 2025; Ordooei Javan et al. 2015). Collectively, this overview on antipseudomonal drugs indicates that fluoroquinolones are the most practical option for animals requiring prolonged therapy for infections caused by *Pseudomonas* spp, and this is also reflected in some of the current antimicrobial prescription guidelines (Hardefeldt et al. 2017; Ibrahim et al. 2020). We hypothesised that *Pseudomonas* spp. isolates associated with canine infections exhibit higher prevalence of resistance against fluoroquinolones compared to other antipseudomonal antibiotics. The aim of this study was to conduct a systematic review and meta-analysis to determine the prevalence and distribution patterns of AMR in *Pseudomonas* spp. isolates from canine infections.

Materials and methods

Literature search strategy, study inclusion and exclusion criteria

The review protocol was developed and reported in accordance with the PRISMA-P 2015 guidelines (Moher et al. 2015). The specific aim was to determine whether there were differences in proportion of resistance to fluoroquinolones compared to other major antipseudomonal drugs in canine infections. A previous, unpublished study conducted so far indicated that most of the relevant literature was archived in Web of Science, Pubmed/Medline and Scopus, and these three databases were searched from dates of inception to the end of December 2024. The strategy was to capture peer reviewed, published data on the *in vitro* antimicrobial susceptibility testing (AST) of fluoroquinolones against canine *Pseudomonas* spp. isolates. This was because many legible studies only identified the pathogen as *Pseudomonas* spp. much as PA is the predominant species. The specific search terms used were "(Enrofloxacin OR Marbofloxacin OR Difloxacin OR Orbifloxacin OR Pradofloxacin OR Ciprofloxacin OR Fluoroquinolones) Resistance AND Pseudomonas AND (Dog OR Canine) Infections" in subject headings and keyword searches.

The study only included data from primary research published in English with evaluations of antimicrobial susceptibility based on at least ten canine *Pseudomonas* spp. isolates. Only studies on isolates associated with canine infections were considered. For each of the studies considered for this review, the designation of bacterial isolates as resistant or susceptible to any of the represented antibiotics was based on breakpoints and guidelines established by either the European Committee on Antimicrobial Susceptibility Testing (EUCAST) or the Clinical and Laboratory Standards Institute (CLSI) at the time of each publication. For all included studies, data based on a re-characterisation of the same isolates to determine proportions that were multidrug resistant, and animal species other than dogs were excluded. Reviews, book series or chapters, editorial notes, short surveys and case reports based on individual animals were not considered. In Scopus which is a more comprehensive database, irrelevant subject headings including biochemistry, genetics and molecular biology, agricultural and biological studies, multidisciplinary and experimentally controlled studies were also excluded. Non-clinical studies were excluded after reviewing abstracts and the main text.

Data extraction and quality assessment

Duplicate records across the searched databases were removed using Endnote Version 20. All article titles, abstracts and accompanying reference lists were screened to remove irrelevant records, enabling the generation of a comprehensive reference list. Retrieved primary data items were independently assessed in duplicate and deemed eligible for data extraction (RTK and IF). Data were extracted from text, tables and figures and this included authors and year of publication, country or region of origin for isolates, when the isolates were identified and tested, type of infection, and the specific body sites where the isolates were obtained. Additional data on methods used for AST, the total number of isolates tested and the proportion that was resistant to respective antibiotics, and the total number of animals from which the isolates were recovered was also extracted. Individual studies had to meet all these qualitative measures to qualify for data extraction. However, reporting on number of animals involved in each study was variable and this was not used as a disqualifying factor.

Analysis and presentation of extracted data

For qualitative and quantitative evaluations, the prevalence of antibiotic resistance in canine *Pseudomonas* isolates was stratified into rational groups based on tested antibiotic classes, types of infection, start and end year of data collection, and geographical regions. Data were analysed using a multi-level mixed effects logit transformed proportion meta-analysis model in R (version 4.5.2) with meta (version 8.2–1) and metafor (version 4.8–0) packages. Studies and drugs nested within studies were the random effects because many of the studies tested more than one drug. Estimates of the proportion of drug-resistant isolates and the associated 95% CI were used to evaluate drugs. Null hypothesis statistical tests with associated p values and arbitrary thresholds were not considered (Wasserstein et al. 2019).

Results

Characteristics of studies involved in the meta-analysis

A total of 566 studies were identified from data base searches and 90 of these were duplicate records that were removed from further analyses (Fig. 1). Titles and abstracts of the remaining 476 studies were screened against the established inclusion criteria, and an additional 403 articles were not considered for data extraction and further analyses. Out of 403 excluded articles, 249 were cases studies based on individual animals, reviews or irrelevant to the topic, 88 articles did not specifically examine AMR in *Pseudomonas* spp., 65 articles examined AMR in *Pseudomonas* isolates but not from dogs, and 1 article was based on less than 10 canine *Pseudomonas* spp. isolates. Data were extracted from 73 research articles. (Fig. 1; Supplemental Table 1) (Barrasa et al. 2000; Seol et al. 2002; Cohn et al. 2003; Tejedor et al. 2003; Authier et al. 2006; Hariharan et al. 2006; Tolar et al. 2006; Ledbetter et al. 2007; Lin and Petersen-Jones, 2007; McKay et al. 2007; Pedersen et al. 2007; Schick et al. 2007; Werckenthin et al. 2007; Wildermuth et al. 2007; Rubin et al. 2008; Zamankhan et al. 2010; Mekic et al. 2011; Harada et al. 2012; Lin et al. 2012; Bennett et al. 2013; Bugden, 2013; Petrov et al. 2013; Haenni et al. 2015; Jerzsele and Pasztine-Gere, 2015; Rheinwald et al. 2015; Arais et al. 2016; Hindley et al. 2016; Ludwig et al. 2016; Daodu et al. 2017; Pintaric et al. 2017; Serrano et al. 2017; Awosile et al. 2018; Hyun et al. 2018; Vingopoulou et al. 2018; Bourély et al., 2019; Dos Santos et al. 2019; Petrov et al. 2019; Scott et al. 2019; von Silva-Tarouca et al. 2019; de Jong et al. 2020; Eliasi et al. 2020; Gomez-Beltran et al. 2020; Hewitt et al. 2020; Park et al. 2020; Souza et al. 2020; Amphaiphan et al. 2021; Darwich et al. 2021; Degi et al. 2021; de Menezes et al. 2021; Hattab et al. 2021; Hayashi et al. 2021; Li et al. 2021; Nocera et al. 2021; Tsvetanova et al. 2021; Costa et al. 2022; Fessler et al. 2022; Kelly et al. 2022; KuKanich et al. 2022; Mavrides et al. 2022; Yudhanto et al. 2022; de Sousa et al. 2023; Elfadadny et al. 2023; Luciani et al. 2023; Pinthanon et al. 2023; Plokarz et al. 2023; Casemiro et al. 2024; Dinkova and Rusenova, 2024; Goss et al. 2024; Jangsangthong et al. 2024; Nainika et al. 2024; Rosales et al. 2024; Verdenius et al. 2024). Cumulatively, 9911 *Pseudomonas* spp. isolates from canine infections were screened for antimicrobial sensitivity. Of the screened isolates, 52% were classified as mixed and this included skin, urinary tract, ocular and respiratory infections, and 48% were classified specifically as otitis externa. (Fig. 2; Supplemental Table 2). The geographical representation of canine *Pseudomonas* spp. isolates in these published studies skewed towards Western Europe, North America and Australia. Other regions including Eastern Europe, South America, Africa and other parts of Australasia were represented by a combined total of less than 10% of the isolates (Fig. 2).

Prevalence of drug resistance in canine Pseudomonas isolates categorised by drug class

The highest prevalence of resistance was in fluoroquinolones (0.27, 95% CI [0.22, 0.32]) and aminoglycosides (0.15, 95% CI [0.11, 0.19]) (Table 1). Low and relatively similar proportions of resistant isolates were detected against polymyxins (0.12, 95% CI [0.05, 0.24]), carboxypenicillins (0.12, 95% CI [0.08, 0.18]), third generation cephalosporins (0.10, 95% CI [0.06, 0.16]) and carbapenems (0.08, 95% CI [0.05, 0.12]). In the comparison of the proportions of drug-resistant isolates across all drug classes with consideration for type of infection and geographical location, no differences were detected. For all specific drugs in the respective classes, significant levels of heterogeneity existed (Table 1). Among all fluoroquinolones represented by 10 or more studies, the highest prevalence of resistance was against pradofloxacin (0.56, 95% CI [0.49, 0.63]) and enrofloxacin (0.38, 95% CI [0.32, 0.44]) (Table 1). Similarly, for aminoglycosides that were represented by more than 10 studies, the highest proportion of resistance was against neomycin (0.45, 95% CI [0.22, 0.69]) and gentamicin (0.15, 95% CI [0.11, 0.19]).

Prevalence of drug resistance categorised by type of infection and geographical location

In all analysed studies, only fluoroquinolones and aminoglycosides were consistently tested against *Pseudomonas* spp. isolates for all represented types of infection. Among fluoroquinolones that are commonly used in veterinary medicine, enrofloxacin, marbofloxacin and pradofloxacin had the highest number of antimicrobial susceptibility tests (ASTs). For all these three fluoroquinolones, there were no marked differences in the proportion of drug-resistant isolates categorised by type of infection (Figs. 3, 4, 5 and Supplemental figure 1). Nonetheless, all isolates from ocular infections tended to have low pooled proportion

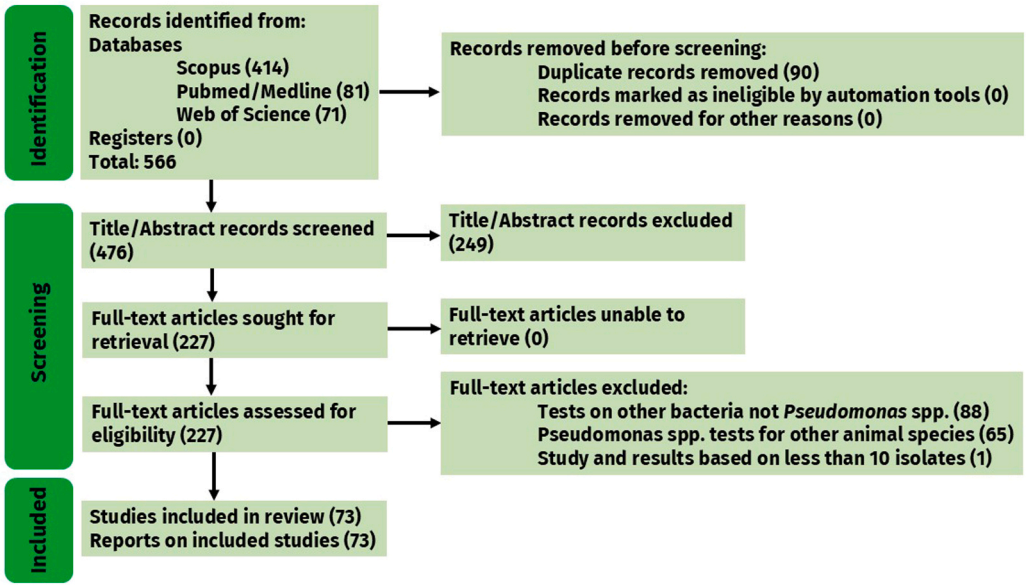

Fig. 1. A PRISMA flow chart summarising the selection strategy for publications providing original data on antibiotic susceptibility of *Pseudomonas* species isolated from dogs.

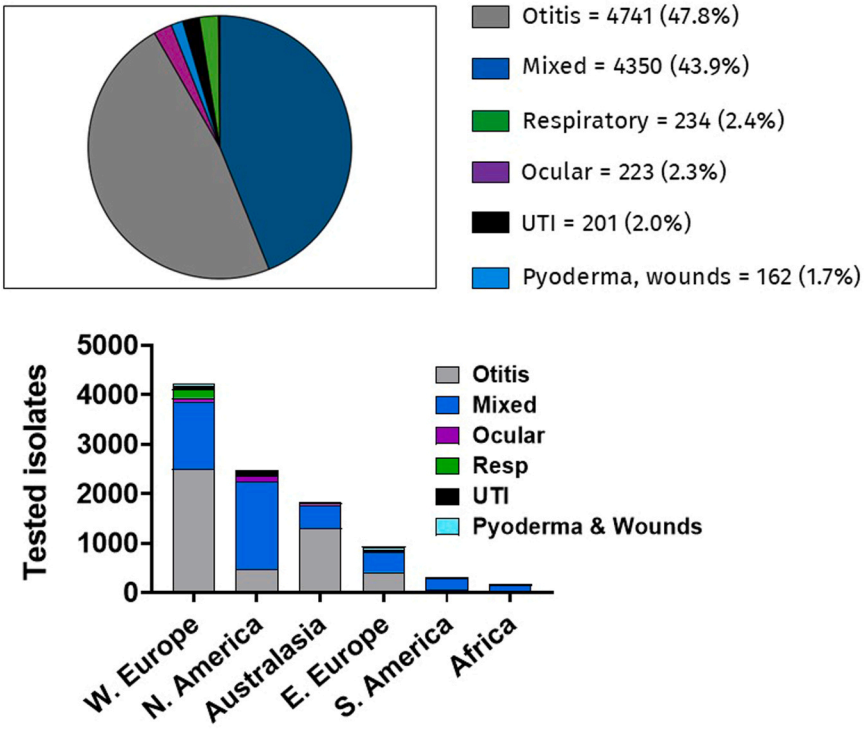

Fig. 2. Proportions of canine *Pseudomonas* species isolates for culture and sensitivity testing stratified by type of infection and represented geographical regions.

of resistance while isolates from cases of otitis tended to have higher pooled proportion of resistance against fluoroquinolones. Among aminoglycosides that are commonly used in veterinary medicine, gentamicin, amikacin, tobramycin and neomycin had the highest number of ASTs. Similarly, for gentamicin, amikacin, tobramycin and neomycin, no differences in proportion of drug-resistant isolates categorised by type of infection were detected (Figs. 6, 7, 8, 9 and Supplemental figure 2). For all other antipseudomonal drug classes including carbapenems, carboxypenicillins, third generation cephalosporins and polymyxins, no differences were detected in the pooled proportion of drug-resistant isolates categorised by type of infection (Supplemental figures 3, 4, 5 and 6).

While data were also categorized by types of infection and the country from which the tested isolates were obtained, significant heterogeneity existed between countries and individual studies for each of the analysed drugs. Detailed analysis revealed no effects on prevalence were attributable to geographical locations. As a general observation however, specific studies in USA (Hewitt et al., 2020), South Africa (Eliasi et al. 2020), Poland (Plokarz et al., 2023), and Japan (Elfadadny et al., 2023) reported relatively high prevalence of resistance (> 85%) against different fluoroquinolones (Supplemental figure 1). Similarly, specific studies in Romania (Degi et al., 2021), Sweden (Pedersen et al., 2007), Brazil (Dos Santos et al., 2019), UK (Goss et al., 2024), USA (Rubin et al., 2008), South Africa (Eliasi et al. 2020), and Canada (Authier et al., 2006) reported relatively high pooled proportion of resistance (> 85%) against different aminoglycosides (Supplemental figure 2). Among other very rarely used antipseudomonal drugs in veterinary medicine e.g., imipenem and meropenem, high pooled proportion of resistance (> 70%) was only reported for isolates from Romania (Degi et al., 2021) (Supplemental figure 3).

Trends in prevalence of resistance categorised by drug class

To retrospectively assess trends in the pooled prevalence of resistance for represented years between 1993 and 2024, only drugs that were represented by at least 5 studies were considered. Time series were analysed using meta-regression with year as moderator using study-level proportions and their variances (Figs. 10 and 11). In all analysed trends, only imipenem showed an increase in the proportion of drug-resistant isolates (Fig. 11). Between 1993 (estimated mean resistance 0.02, 95% CI 0.005, 0.06) and 2012 (estimated mean resistance 0.08, 95% CI 0.05), there was a slow but steady increase in resistance to imipenem within the 95% CI. After 2012, the increase in the prevalence of resistance to imipenem was marked with estimated mean resistance doubling from 0.08 (95% CI 0.06, 0.12) in 2013–0.16 (95% CI 0.09, 0.27) in 2022. Slight upwards trends were observed for other drugs such as enrofloxacin, norfloxacin, orbifloxacin, ticarcillin-clavulanic acid and colistin (Figs. 10 and 11), but there was no evidence to suggest that the prevalence of resistance had changed for these drugs, in the available data.

Insights in mechanisms of resistance against fluoroquinolones

Out of all published primary research outputs that met the inclusion criteria for this review, only 9 studies explored putative molecular mechanisms by which *Pseudomonas* spp. isolates show resistance against fluoroquinolones (Tejedor et al., 2003; Rubin et al., 2008; Harada et a., 2012; Lin et al., 2012; Arais et al., 2016; Vingopoulou et al., 2018; Scott et al., 2019; Park et al., 2020; Jangsangthong et al., 2024). None of these studies were designed to determine statistically valid prevalence rates of biomarkers for fluoroquinolone resistance. Collectively, these studies characterised some of the common mutations in Quinolone Resistance-Determining Regions (QRDR) of known molecular targets in DNA gyrases and topoisomerase IV in a total of 131 canine *Pseudomonas* spp. isolates (Fig. 12). In these evaluations, the most common mutations were *gyr*A: Thr83-Ile (43.5%) and Asp87-Asn (6.1%), *par*C: Pro11-Arg (13.7%) and Ser87-Leu (10.7%) and, *gyr*B: Ser468-Phe (4.6%) (Fig. 12).

Discussion

This study presents a systematic review and meta-analysis of global AMR trends in canine *Pseudomonas* spp. infections from peer reviewed

Table 1
Proportion of *Pseudomonas* strains resistant to each antimicrobial, grouped by antibiotic class and individual agents.

Class	Drug	k	Proportion resistant	95% CI		τ^2	I^2(%)
				Lower	Upper		
Aminoglycoside	gentamicin	70	0.15	0.11	0.19	2.07	90
	amikacin	47	0.09	0.07	0.12	0.81	82
	tobramycin	33	0.09	0.05	0.15	1.72	86
	neomycin	12	0.45	0.22	0.69	2.90	90
	streptomycin	4	0.36	0.12	0.71	2.06	92
	kanamycin	3	0.90	0.86	0.93	0.00	0
	framycetin	1	0.04	0.00	0.40		
	netilmicin	1	0.09	0.02	0.29		
	spectinomycin	1	0.97	0.84	1.00		
	Random effect		***0.15***	***0.11***	***0.1519***	***1.01***† ***1.09***‡	
Quinolones	enrofloxacin	62	0.38	0.32	0.44	1.18	95
	ciprofloxacin	46	0.15	0.11	0.21	1.59	88
	marbofloxacin	37	0.21	0.16	0.26	1.16	84
	pradofloxacin	12	0.56	0.49	0.63	0.19	63
	levofloxacin	10	0.19	0.11	0.32	0.93	83
	orbifloxacin	9	0.65	0.48	0.79	1.08	94
	ofloxacin	9	0.22	0.13	0.36	0.67	73
	norfloxacin	6	0.20	0.13	0.28	< 0.01	27
	lomefloxacin	3	0.16	0.05	0.39	0.77	66
	moxifloxacin	3	0.46	0.01	0.98	13.15	90
	Nalidixic acid	3	0.86	0.10	1.00	11.65	97
	gatifloxacin	2	0.12	0.02	0.48	1.51	74
	difloxacin	2	0.30	0.12	0.59	0.66	89
	perfloxacin	1	0.13	0.03	0.41		
	danofloxacin	1	0.19	0.10	0.31		
	sparfloxacin	1	0.03	0.00	0.35		
	Random effect		***0.27***	***0.22***	***0.32***	***0.58***† ***0.80***‡	***94***
Carbapenems	imipenem	38	0.09	0.06	0.13	2.25	87
	meropenem	22	0.06	0.03	0.12	2.19	90
	doripenem	1	0.02	0.00	0.23		
	Random effect		***0.08***	***0.05***	***0.12***	***1.45***† ***0.20***‡	***88***
Cephalosporins	ceftazidime	33	0.06	0.03	0.11	3.13	93
	cefepime	17	0.08	0.03	0.18	3.99	93
	cefpodoxime	5	0.75	0.14	0.98	9.78	88
	ceftriaxone	4	0.30	0.10	0.62	1.50	84
	cefoperazone	2	0.04	0.01	0.26	1.50	59
	Ceftazidime-clavulanic acid	1	0.07	0.03	0.13		
	cefquinome	1	0.55	0.44	0.65		
	Random effect		***0.10***	***0.06***	***0.16***	***1.13***† ***1.80***‡	***93***
Carboxypenicillins	Piperacillin-tazobactam	17	0.05	0.02	0.11	3.42	92
	ticarcillin	14	0.16	0.12	0.23	0.48	60
	aztreonam	13	0.13	0.06	0.24	1.44	89
	piperacillin	10	0.08	0.02	0.25	3.78	96
	Ticarcillin-clavulanic acid	6	0.21	0.13	0.31	0.30	68
	carbenicillin	2	0.19	0.11	0.31	0.12	37
	Random effect		***0.12***	***0.08***	***0.18***	***0.93***† ***0.80***‡	***92***
Polymyxins	polymyxin B	22	0.14	0.06	0.29	4.30	94
	colistin	5	0.09	0.02	0.38	3.54	89
	Random effect		***0.12***	***0.05***	***0.24***	***3.77***† ***0.07***‡	***93***

† = Autor effect; ‡ = Author/Drug effect; k = Number of studies; CI = Confidence Interval; τ^2 = Tau squared; I^2(%) = Percentage Heterogeneity

primary research articles, while existing reviews in this field have focussed on narrowly defined geographical regions (Nielsen et al. 2022), or specific types of infections caused by *Pseudomonas* spp. such as UTIs (Pereira et al. 2025). In all studies that met the inclusion criteria, geographical representation skewed towards Western Europe, North America and Australia in Australasia. Other regions including Eastern Europe, South America, Africa and other parts of Australasia were represented by less than 10% of tested isolates. This distribution pattern underscores the need to improve surveillance of AMR in canine infections in all global regions and particularly the Low- and Middle-Income countries in Africa, South America and Asia where the implementation of antibiotic stewardship programs remains a bigger challenge (Cox et al. 2017; Shamas et al. 2023). Most of the tested isolates were from clinical cases of otitis externa (48%) or undifferentiated mixed infections including otitis, pyoderma, wounds, ocular, urinary tract and respiratory (52%). This designation of a high proportion of isolates as mixed infections when determining prevalence of AMR is not optimal given that different routes of drug administration are used in treating different types of infection. Topical application of antibiotics for cases such as otitis externa and superficial wounds can achieve high and sustained concentrations of the drug at the site of infection compared to parenteral administration of antibiotics for deeper, systemic infections (Lipsky and Hoey, 2009). Thus, the application of antibiotics topically when warranted may minimise exposure of bacteria to sub-therapeutic concentrations and this may reduce the selection for AMR. In this review, however, no differences in the prevalence of AMR

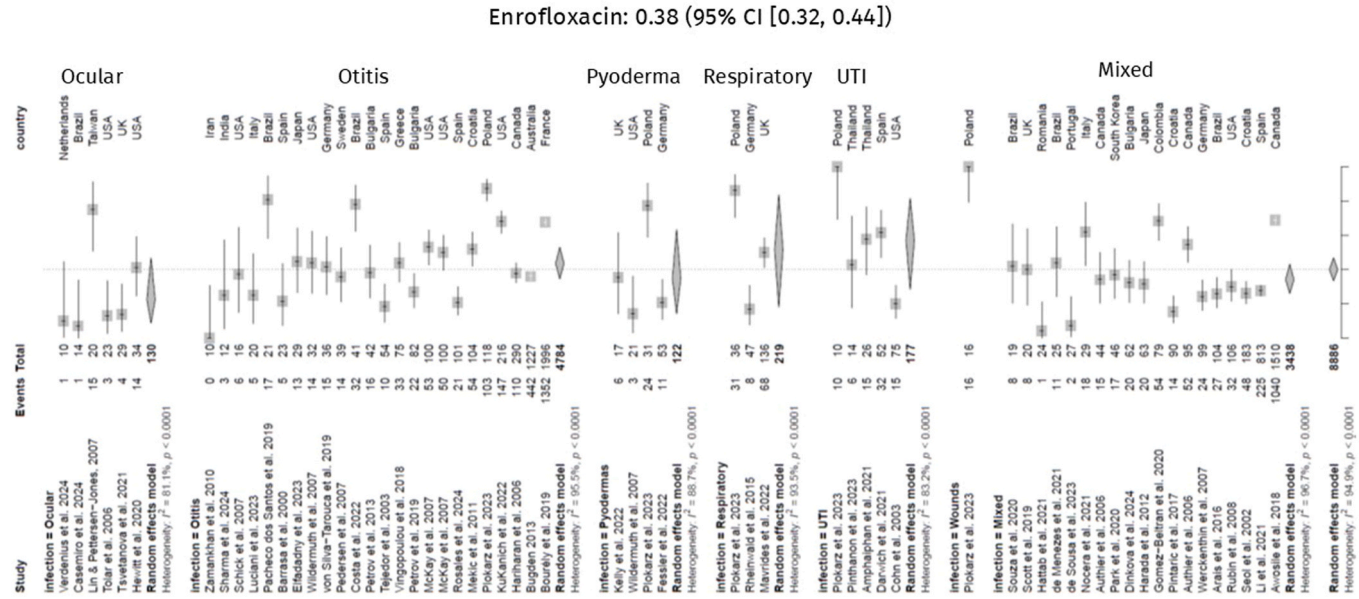

Fig. 3. The proportion of enrofloxacin resistant canine *Pseudomonas* isolates grouped by type of infection, represented geographical regions and individual studies.

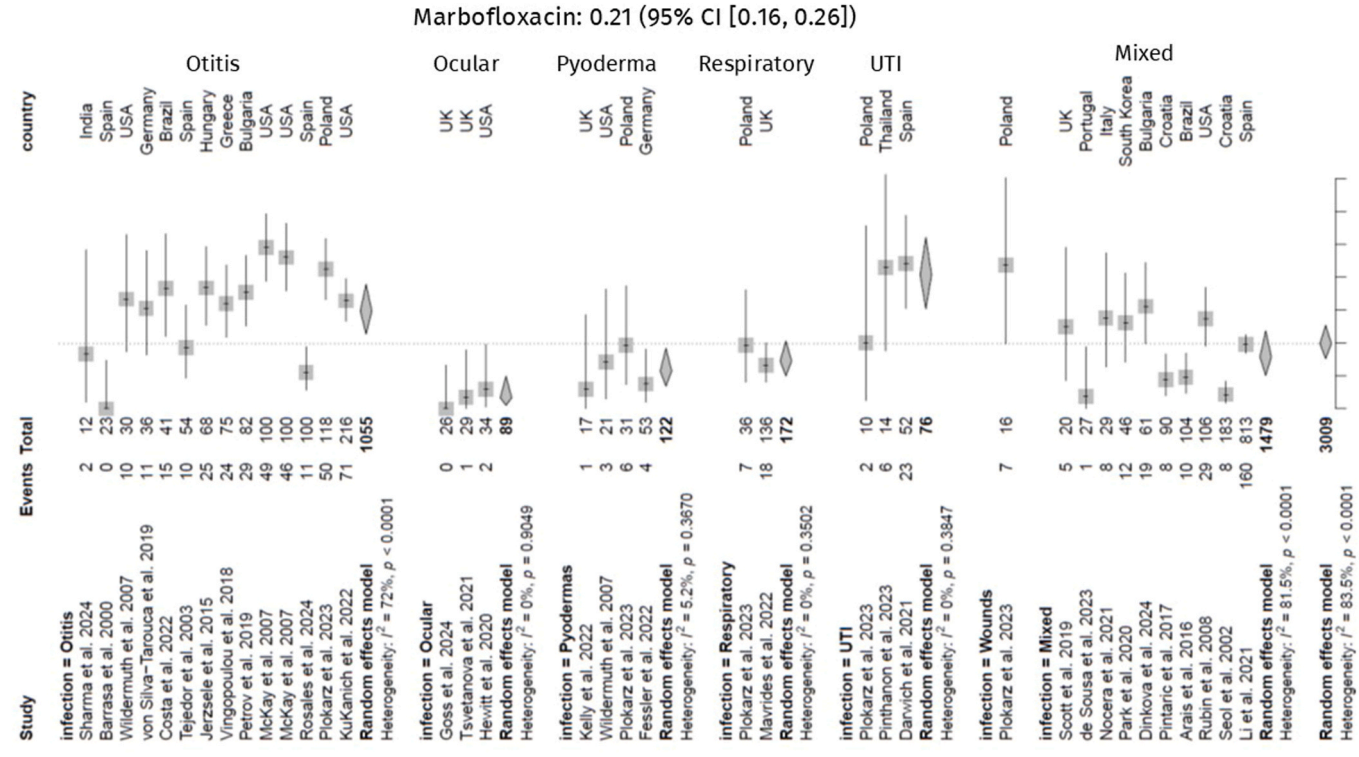

Fig. 4. The proportion of marbofloxacin resistant canine *Pseudomonas* isolates grouped by type of infection, represented geographical regions and individual studies.

were detected when pathogenic *Pseudomonas* spp. isolates were stratified by type of infection. Based on our observations, we recommend the adoption of a standardised approach that stratifies data by specific pathogen, type of infection and treatment history for AMR surveillance reports.

Fluoroquinolones occupy a critical but vulnerable position in veterinary practice. Their favourable pharmacokinetic profile (Toutain et al. 2021), multiple routes of administration and practicality for home treatment have made them the mainstay of therapy for canine *Pseudomonas* infections. This led us to postulate that pathogenic *Pseudomonas spp.*, exhibited higher prevalence of resistance against this antimicrobial class in ASTs *in vitro*. We show that approximately one in four *Pseudomonas* isolates were resistant to at least one fluoroquinolone, but there was no evidence to suggest that the prevalence of resistance against this antimicrobial class was trending upwards over time. These data should be interpreted cautiously, given substantial between-study heterogeneity and overlapping confidence intervals, possibly due to differences in geographical locations or jurisdictions and types of infections. In addition, the detailed clinical history and the treatment regimen received by individual dogs prior to isolating *Pseudomonas* spp. for ASTs were not

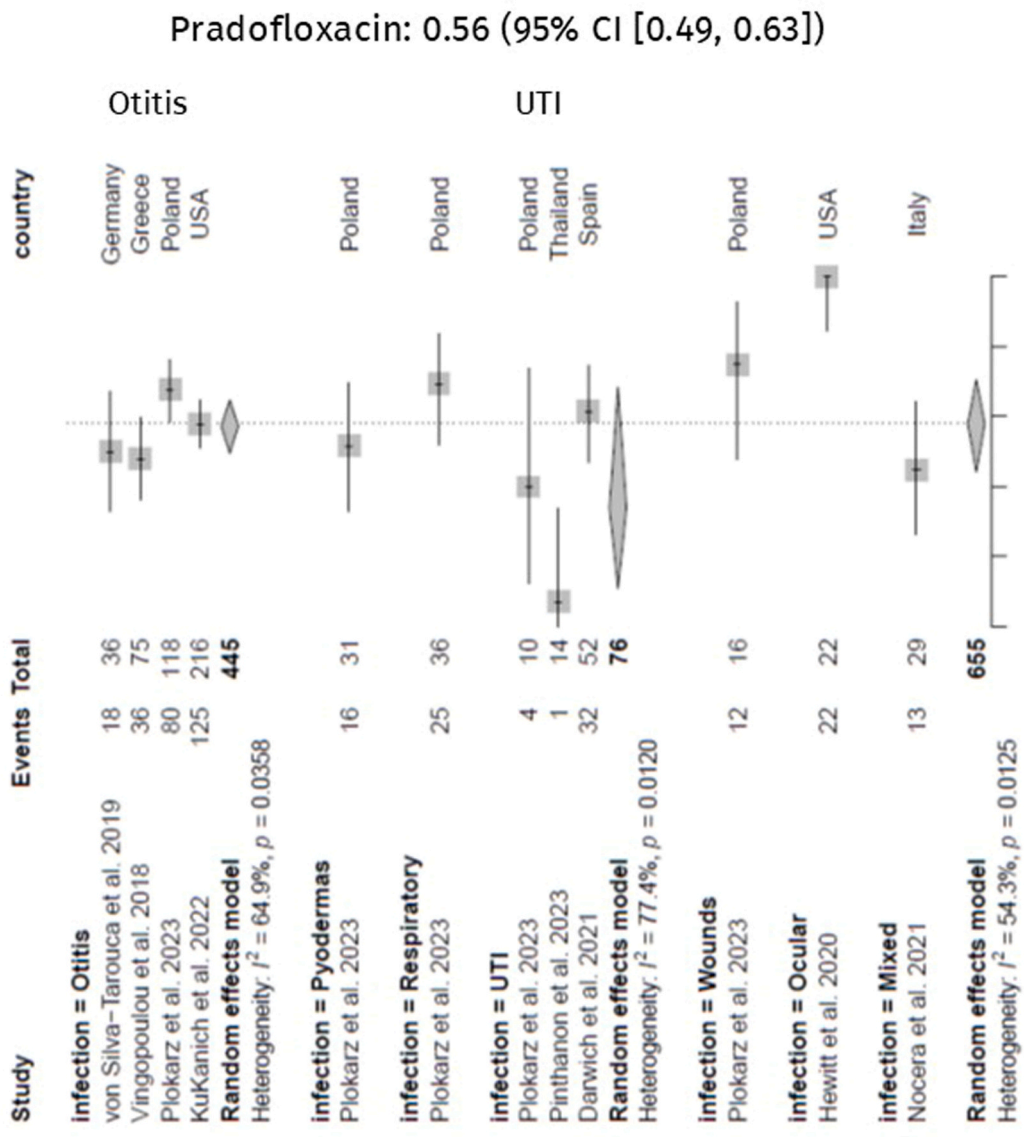

Fig. 5. The proportion of pradofloxacin resistant canine *Pseudomonas* isolates grouped by type of infection, represented geographical regions and individual studies.

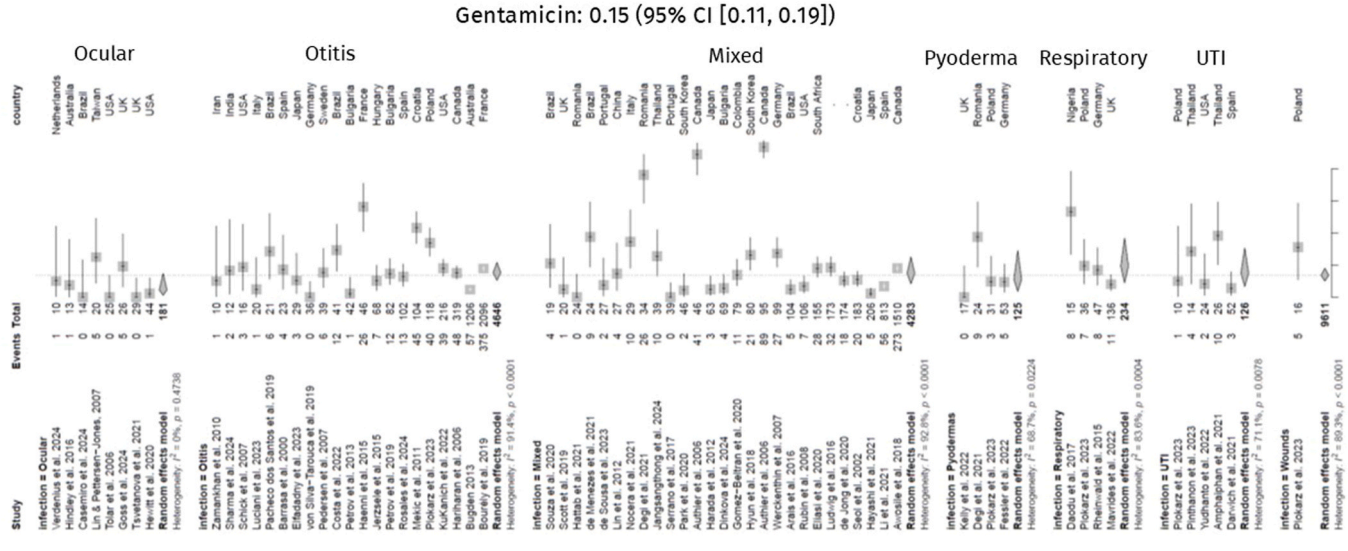

Fig. 6. The proportion of gentamicin resistant canine *Pseudomonas* isolates grouped by type of infection, represented geographical regions and individual studies.

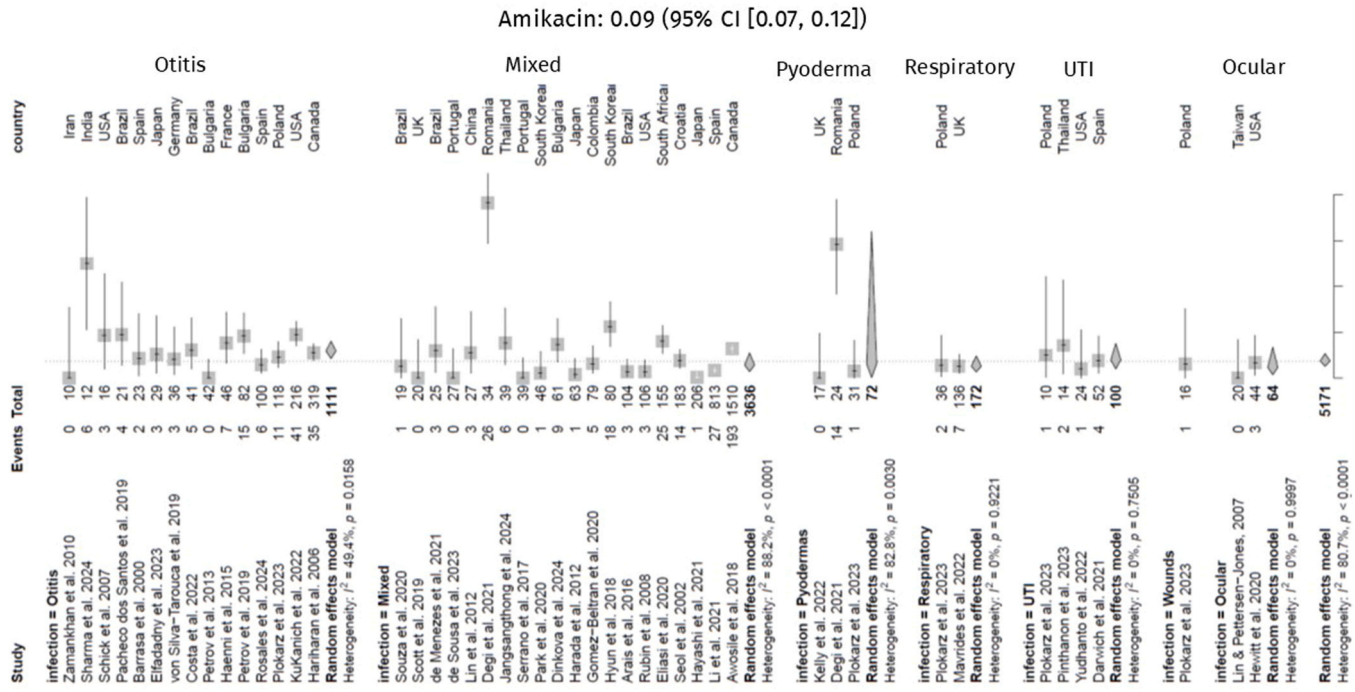

Fig. 7. The proportion of amikacin resistant canine *Pseudomonas* isolates grouped by type of infection, represented geographical regions and individual studies.

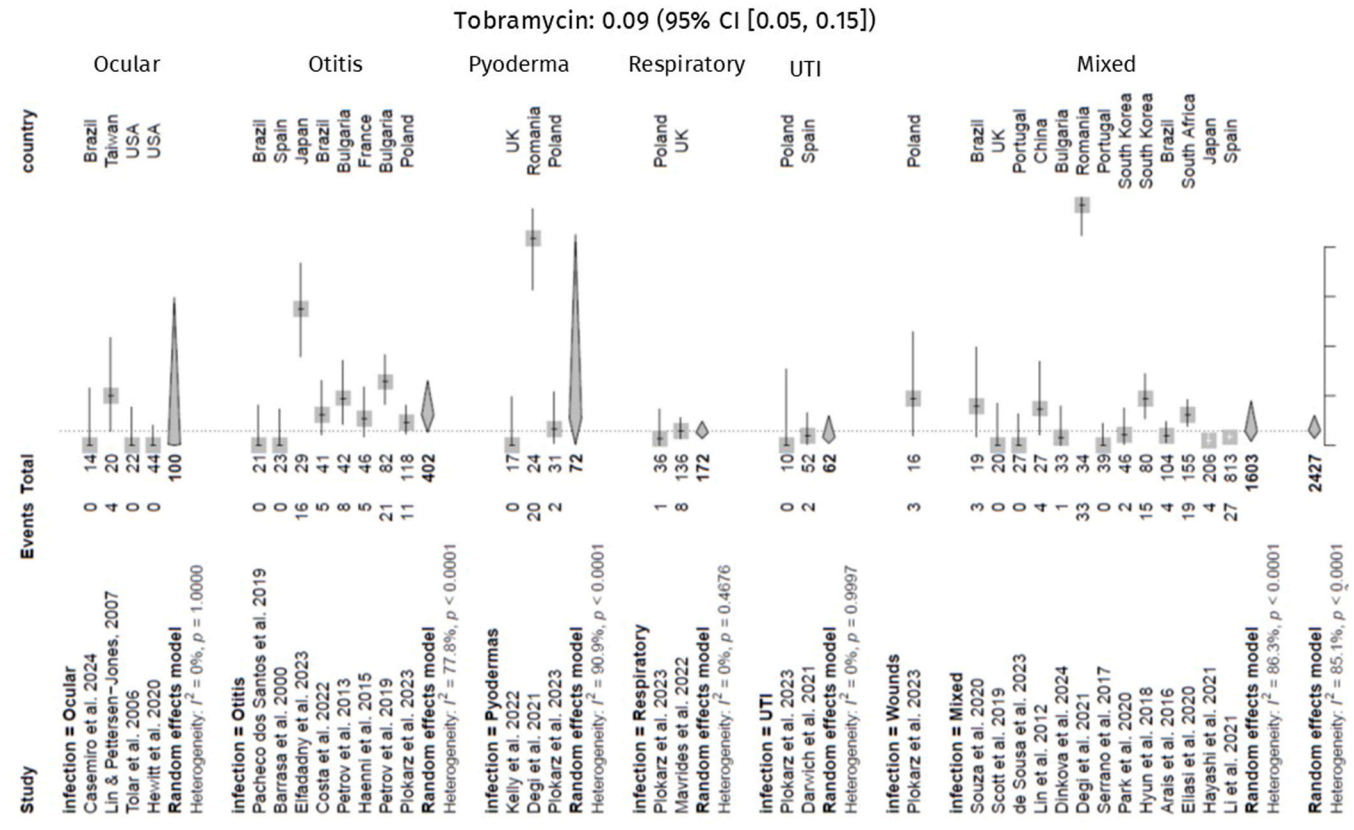

Fig. 8. The proportion of tobramycin resistant canine *Pseudomonas* isolates grouped by type of infection, represented geographical regions and individual studies.

reported in the analysed publications. In animals with prior exposure to one or multiple antibiotics, tested isolates *in vitro* may have been pre-selected for resistance, and this would contribute to variability. Similar levels of variability in prevalence of resistance to anti-pseudomonal drugs were observed by Pereira et al. (2025).

For better insight on specific antibiotics within the different antimicrobial classes, meta-analysis was further stratified by specific drug and type of infection. Among fluoroquinolones that are extensively used in veterinary medicine, pradofloxacin and enrofloxacin had the highest prevalence of resistance; these were higher than those for marbofloxacin

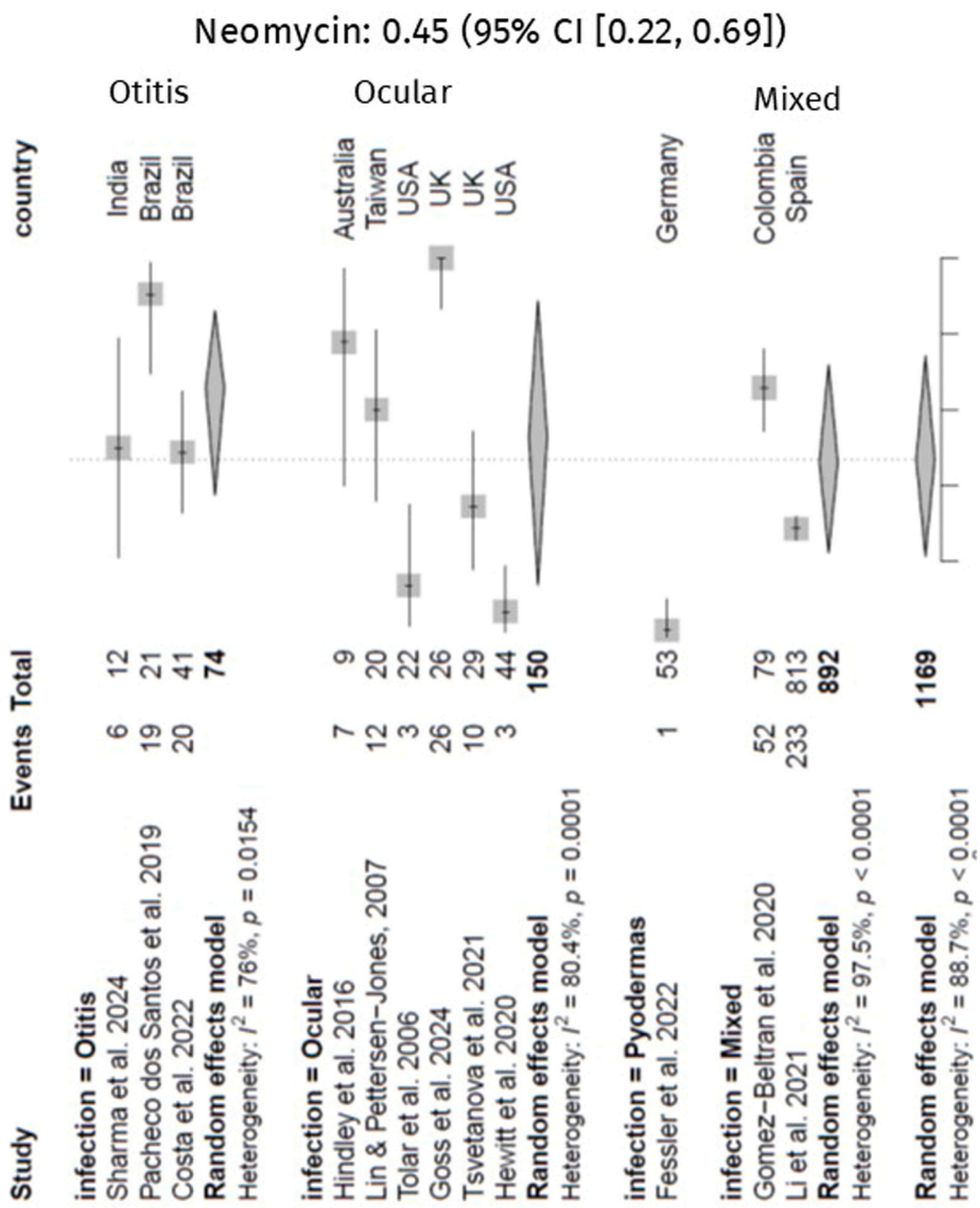

Fig. 9. The proportion of neomycin resistant canine *Pseudomonas* isolates grouped by type of infection, represented geographical regions and individual studies.

with similar results when isolates were stratified by type of infection. This suggests that differences in the pooled proportion of resistance among specific fluoroquinolones was accounted for by more than just differences resulting from topical or systemic drug administration. Compared to marbofloxacin and pradofloxacin, enrofloxacin is an older drug that has had a longer and broader clinical usage, which may contribute to high selection for resistance (Joosten et al. 2020; De Marchi et al. 2024). In addition, it is known that more lipophilic fluoroquinolones such as enrofloxacin are better substrates and more affected by efflux pumps encoded in the *mex*AB-*opr*M operon described for PA, than the less lipophilic drug such as ciprofloxacin and marbofloxacin (Tejedor et al. 2003; Harada et al. 2012). Furthermore, the main mechanisms of fluoroquinolone resistance in Gram-negative bacteria involve mutations in the QRDR of target enzymes (DNA gyrase and topoisomerase IV), expression of plasmid-mediated quinolone resistance genes (PMQR) and the modification of efflux pumps and porins (Robicsek et al. 2006; Kherroubi et al. 2024). In the QRDR, gene mutations in *gyr*A, *gyr*B, *par*C and *par*E are the most frequently detected (Ostrer et al. 2019). However, the primary QRDR target may vary for specific drugs and bacterial species, leading to differences in susceptibility profiles among fluoroquinolones. A study by Vingopoulou et al. (2018), showed that out of four PA isolates that were resistant to pradofloxacin but susceptible to enrofloxacin and marbofloxacin, three had wild-type *gyr*A and *par*C and one had a single substitution (*gyr*A: Val73-Gly) that had not been identified prior to this publication. These observations may lend explanations to some conclusions in our meta-analysis, but detailed mechanistic evaluations were beyond the scope of this review. Among the limited number of studies that genotyped fluoroquinolone resistant *Pseudomonas* spp. isolates in this review however, *gyr*A mutations were the most frequent with gyrA: Thr83-Ile representing 43.5% of genotyped isolates. This result is consistent with previous reports showing a relatively higher frequency of the gyrA: Thr83-Ile mutation in canine and human PA isolates (Yonezawa et al. 1995; Rubin et al. 2008; Tam et al. 2010; Harada et al. 2012; Salma et al. 2013; Arais et al. 2016). The data in this meta-analysis indicate that among commonly screened antipseudomonal drugs in AST,

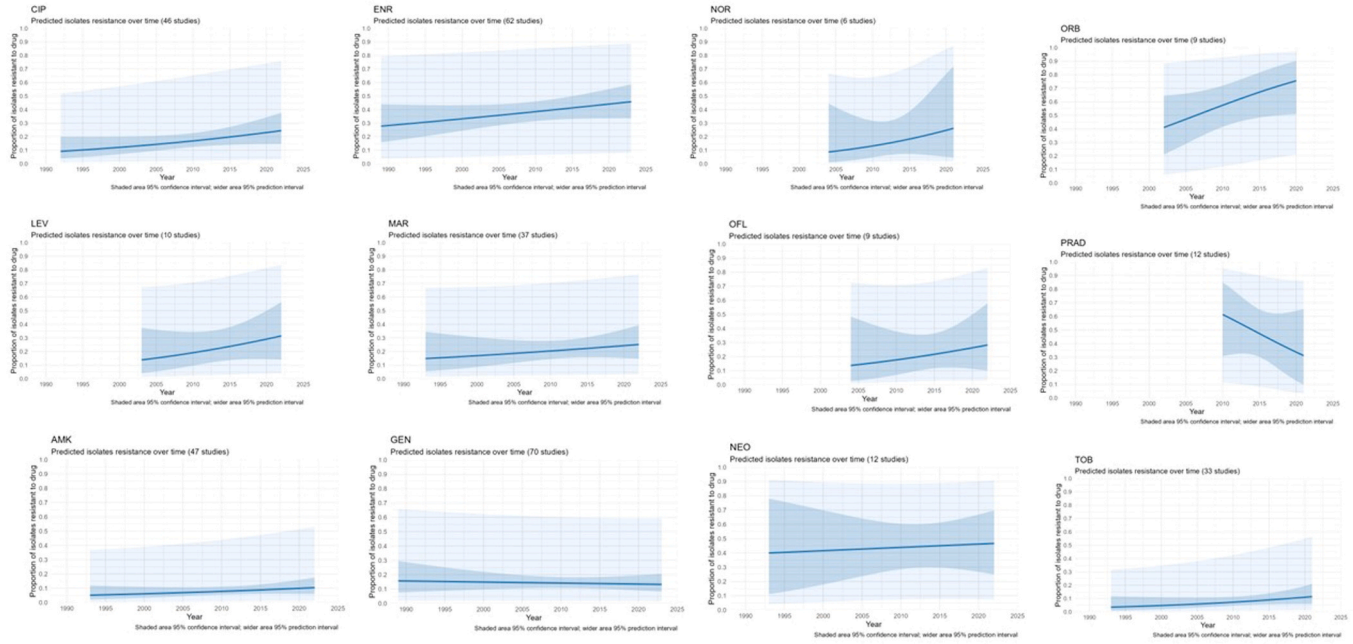

Fig. 10. Trends over time in the proportion of resistant canine *Pseudomonas* strains to quinolones, aminoglycosides. The darker shading is for the 95% confidence interval of the estimated weighted mean proportion of resistance. The lighter shading is the 95% prediction interval if a new study was added to the existing data. Abbreviations: amikacin, AMK; ciprofloxacin, CIP; enrofloxacin, ENR; gentamicin, GEN; levofloxacin, LEV; marbofloxacin, MAR; neomycin, NEO; norfloxacin, NOR; ofloxacin, OFL; orbifloxacin, ORB; pradofloxacin, PRAD; tobramycin, TOB.

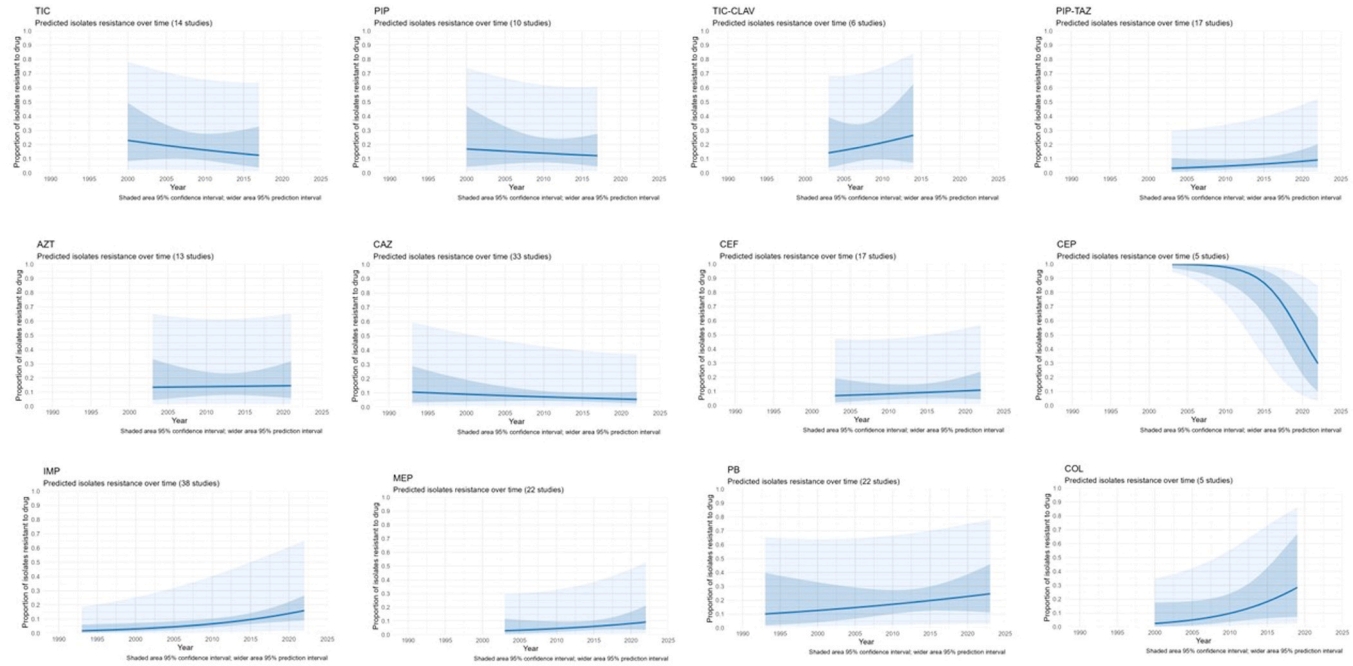

Fig. 11. Trends over time in the proportion of resistant canine *Pseudomonas* strains to extended spectrum beta-lactams, third generation cephalosporins, polymyxins and carbapenems. The darker shading is for the 95% confidence interval of the estimated weighted mean proportion of resistance. The lighter shading is the 95% prediction interval if a new study was added to the existing data. Abbreviations: aztreonam, AZT; ceftazidime, CAZ; cefepime, CEF; Cefpodoxime, CEP; colistin, COL; imipenem, IMP; meropenem, MEP; polymyxin B, PB; piperacillin, PIP; piperacillin-tazobactam, PIP-TAZ; ticarcillin, TIC; ticarcillin-clavulanic acid, TIC-Clav.

fluroquinolones had the highest prevalence of resistance against pathogenic *Pseudomonas* spp. isolates, with high intra-class differences for specific drugs. To avoid over reliance on fluoroquinolones and change the observed trends, culture and AST combined with pharmacokinetic considerations should be used as the basis for selecting enrofloxacin, marbofloxacin or pradofloxacin against infections caused by pathogenic *Pseudomonas* spp. in dogs.

Aminoglycosides, such as gentamicin, are a good choice for pathogenic *Pseudomonas* infections in companion animals and these are usually considered for topical application and some systemic therapy where appropriate. Compared to fluoroquinolones, a lower level of resistance to aminoglycosides was recorded with 12% pooled proportion of

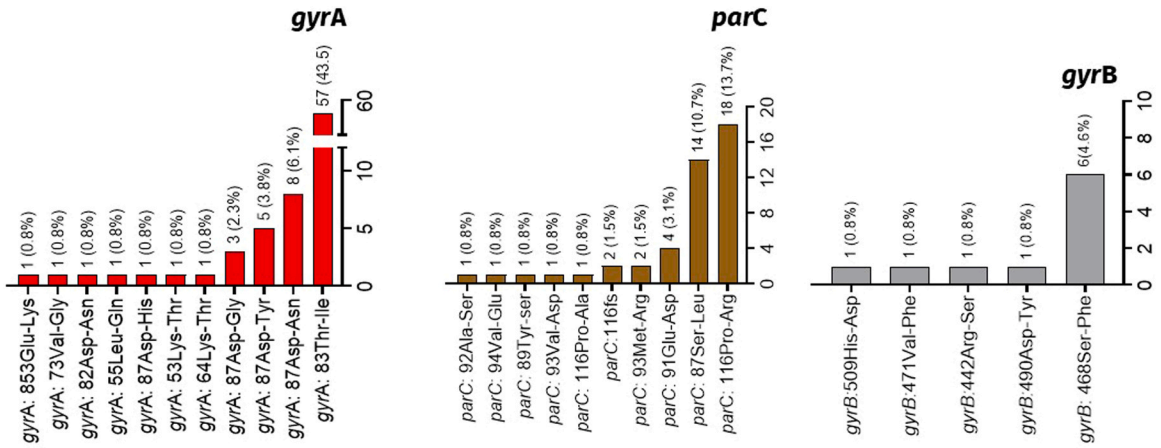

Fig. 12. Studies characterising some of the common mutations in the molecular targets for fluoroquinolones including DNA gyrases and topoisomerase IV in a total of 131 canine *Pseudomonas* spp. isolates.

resistance in AST. While resistance to both fluoroquinolones and aminoglycosides may be driven by overexpression of different drug efflux pumps, observed differences in prevalence of resistance in the current study are more likely attributable to differences in other mechanisms. This notion is supported by previous work which showed that fluoroquinolone resistance in PA isolates was predominantly due to simple mutations in the QRDR, while resistance to aminoglycoside may require the acquisition of aminoglycoside modifying enzymes mainly (acetyltransferases, nucleotidyltransferases, phosphotransferases), or mutations in ribosomal binding sites (Thirumalmuthu et al. 2019; Boushra et al. 2024). In addition, it has also been shown that the acquisition of these genetic determinants of resistance to aminoglycosides by PA isolates is costly to bacterial fitness leading to slow growth rates (Thirumalmuthu et al. 2019). For clinical applications in veterinary medicine, aminoglycosides are used less commonly compared to flurquinolones, and this may lower the selection for resistance. Aminoglycosides are generally safe for topical applications and there are several commercial formulations for topical ear drops and eye ointments. However, systemic administration of aminoglycosides is limited because of their narrow safety margin due to their ability to accumulate in kidneys, cause nephrotoxicity and a risk for fatal renal failure (Clark, 1977). Our analyses here also show that among specific aminoglycosides, neomycin had a higher prevalence of resistance compared to gentamicin, amikacin and tobramycin. For companion animal medicine in most jurisdictions, neomycin is predominantly used in topical formulations for ocular and ear infections and very rarely, to target dysbiosis in the gastrointestinal system. This implies that selection for resistance against neomycin via systemic exposure is limited, but PA is known to rapidly acquire adaptive resistance against neomycin (Uemura et al. 2017). Overall, the meta-analysis presented here show that aminoglycosides such as gentamicin, amikacin and tobramycin remain effective antipseudomonal drugs for canine infections. We caution however, that unusually high rates of resistance to aminoglycoside were reported in a few individual studies from Canada, India and Romania (Authier et al. 2006; Zamankhan et al. 2010; Degi et al. 2021). Bacterial culture and AST should continue to guide the selection of aminoglycosides against pathogenic *Pseudomonas* spp. infections.

Antipseudomonal beta-lactams are safe and effective drugs but, their high value in the treatment of life-threatening infections in people restricts their legal use in animals for most jurisdictions. The use of antipseudomonal beta-lactam drugs in companion animals is also restricted by unfavourable pharmacokinetic profiles characterised by poor absorption and shorter elimination half-lives, and this creates a need for shorter dosing intervals that are not suitable for out of hospital veterinary patients. Collectively, these factors may account for the low selection for resistance in pathogenic canine *Pseudomonas* spp. isolates seen in our analyses. We show that in the beta-lactam group, carbapenems (imipenem and meropenem) had the lowest levels of resistance (6–9%) in canine *Pseudomonas* spp. isolates. Despite this low prevalence overall, trend analysis indicates that the proportion of imipenem resistant isolates increased markedly between 1993 and 2022. This upward trend in imipenem resistance among pathogenic canine *Pseudomonas* isolates is troubling because as resistance rises and spread, clinicians will increasingly have very limited therapeutic options for multi-drug-resistant strains. It is worth noting however, that these evaluations of imipenem in canine *Pseudomonas* isolates do contrast markedly with evaluations of human PA isolates. Recent studies indicate that carbapenem resistance in human PA isolates is on a rise with much higher prevalence rates ranging from 15% to 40% depending on geographical region, hospital settings where isolates are obtained, and the patient population (Arowolo et al., 2023; Ramatla et al., 2025; Jayathilaka et al. 2025). In another example for potentiated beta-lactams, piperacillin-tazobactam is a preferred treatment option for people with infections caused by beta-lactamase producing PA. and as a result, resistance to piperacillin-tazobactam among human PA isolates is a growing concern with surveillance reports showing a prevalence of 14–17% in the USA, 23% in Greece, and 22–36% in Lebanon (Centre for Disease Control and Prevention, 2025) (https//www.cdc.gov); Nduagu et al. 2024; Eid et al. 2025). In the current study, we show that the prevalence of resistance to piperacillin-tazobactam in canine *Pseudomonas* spp. isolates was only 5%. This may be ascribed to the fact that this antimicrobial formulation is not registered for use in dogs but can be used extra-label provided the selection is supported by AST, and when fluoroquinolones or aminoglycosides are not effective or unsuitable. In addition, veterinarians face stricter requirements when prescribing piperacillin-tazobactam and must take full responsibility for the proper administration and management of treatment regimen. These stewardship approaches together with continued surveillance are encouraged, and especially in countries such as Romania and Brazil that had high rates of resistance to beta-lactam drugs in canine *Pseudomonas* spp. isolates (Degi et al. 2021; Costa et al. 2022). Collectively, these observations indicate that for humans and dogs, different detailed epidemiological drivers may be involved in propagating drug resistance for infections caused by *Pseudomonas* spp.

There are some limitations to this study, and these must be considered when interpreting our results. In many of the publications that met the inclusion criteria, members of *Pseudomonas* genus were not identified to species level. PA is the most pathogenic and most antimicrobial resistant in the genus. Whilst PA is likely to be the dominant species in publications that did not specify species, other *Pseudomonas* species such as *Ectopseudomonas mendocina* (formerly *Pseudomonas mendocina*), *Pseudomonas fluorescens, Pseudomonas putida* group and *Stutzerimonas*

stutzeri (formerly *Pseudomonas stutzeri*) may have been included. Whilst these pseudomonads can develop multidrug resistance, it is less common than drug resistance in PA. In addition, *Pseudomonas* isolates were only reported as susceptible or resistant, because majority (67%) of AST in included studies used the agar disk diffusion method instead of the tested MIC range with specific breakpoints. Furthermore, there are no CLSI approved breakpoints for canine otitis externa, and most studies use breakpoints for systemic administrations. We show that there was no consistency in reporting in publications for CLSI guidelines with respect to year and/or edition, and tested drug (Supplemental Table 1). The designation of canine *Pseudomonas* spp. isolates as resistant or susceptible was based on CLSI guidelines at the time of publication for each of the included studies, and this included veterinary and human CLSI documents, and in some cases no relevant information was provided (Supplemental Table 1). For topical applications of concentration dependent antibiotics, these factors make it difficult to accurately detect subtle resistance levels that could be overridden by increasing doses. Furthermore, for fluoroquinolones of veterinary importance including enrofloxacin and marbofloxacin, earlier CLSI guidelines were replaced by updated versions that accounted for pharmacokinetics and pharmacodynamics data, and clinical outcome data (Papich et al. 2023; CLSI, 2023; CLSI, 2021). For instance, prior to 2023, enrofloxacin breakpoints for *Pseudomonas aeruginosa* in dogs were susceptible (S), $\leq$ 0.5 μg/mL, intermediate (I) 1–2 μg/mL, and resistant (R) $\geq$ 4 μg/mL (CLSI, 2021). In 2023, the relevant breakpoints were revised to S $\leq$ 0.06 μg/mL for a dose of 5 mg/kg, 0.12 μg/mL for a dose of 10 mg/kg, 0.25 μg/mL for a high dose of 20 mg/kg, and R $\geq$ 0.5 μg/mL, and breakpoints of 0.12 and 0.25 μg/mL represented a new susceptible-dose dependent category (CLSI, 2023). Based on these changes, it possible this study underestimates prevalence rates for fluoroquinolone resistance in work published prior to 2024. These new guidelines should be considered in all future surveillance reports.

Conclusion

This review and meta-analysis provide a comprehensive evaluation of AMR in *Pseudomonas* spp. associated with canine infections. Across 9911 *Pseudomonas* spp. isolates from 73 studies spanning over three decades and multiple continents, several consistent patterns emerge that have important implications for veterinary practice, antimicrobial stewardship, and public health. The findings collectively demonstrate that the highest prevalence of resistance in canine *Pseudomonas* spp. was against fluoroquinolones while resistance to aminoglycosides and anti-pseudomonal β-lactams remains comparatively lower. Although the observed trends are complicated by substantial variation between studies, infection types and geographical regions, the overall signal remains clear, that fluoroquinolones now face a substantial resistance burden in canine *Pseudomonas* infections, and this must be factored into empirical prescribing decisions. Effective antimicrobial stewardship is essential to preserve the utility of remaining treatment options against pathogenic canine *Pseudomonas* spp. infections. Stricter adherence to updated fluoroquinolone dosing guidelines is recommended.

CRediT authorship contribution statement

Jacqueline Picard: Writing – review & editing, Validation, Methodology, Investigation, Formal analysis, Data curation. **Michael Crowe:** Writing – review & editing, Validation, Methodology, Investigation, Formal analysis, Data curation. **Robert Kinobe:** Writing – review & editing, Writing – original draft, Validation, Supervision, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Isabella Fitzgerald:** Writing – review & editing, Writing – original draft, Validation, Methodology, Investigation, Data curation. **Yaoqin Hong:** Writing – review & editing, Validation, Methodology, Investigation, Formal analysis, Data curation.

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Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors used Grammarly to improve readability and language. After using this tool, all authors reviewed and edited the content to meet their specific needs. All included scientific concepts, content, conclusions and interpretations were generated by authors. Authors take full responsibility for the content of this research article.

Declaration of Competing Interest

All authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tvjl.2026.106690.

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