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Review article

Systematic review and meta-analysis of environmental *Vibrio* species – antibiotic resistance

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ABSTRACT

Adequate comprehension of the genomics of microbial resistance to an antimicrobial agent will advance knowledge on the management of associated pathologies and public health safety. However, continued emergences and reemergence of pathogens, including *Vibrio* species, hallmarks a potential knowledge gap. A clear understanding of the process and forecast of the next trend should be in place to nip in the bud, microbial acquisition of resistance to antibiotics. Therefore, this two-decade (1 January 2000 to 31 December 2019) systematic review and meta-analytical study articulated the prevalence and incidence of antibiotics resistance genes in *Vibrio* species isolated from environmental samples. Articles from the Web of Science and PubMed electronic databases was engaged. Heterogeneity of the data and bias were analyzed with random effect model meta-analysis and funnel plot. A total of 1920 *Vibrio* sp. were reported by the ten selected articles included in this study; out of which 32.39% of identified isolates displayed antimicrobial resistance and associated genes. The distribution of antibiotics resistance genes in *Vibrio* sp., reported within six countries was 21% tetracycline (*tet*), and 20% sulphonamide (*sul*) and β-lactamase (*bla*) respectively. The quinolone, tetracycline and sulfonamide resistance genes showed 32.97% (95% CI 0.18–0.53) prevalence while chloramphenicol, macrolides and aminoglycoside resistance genes are expressed in percentages as 28.67% (95% CI 0.15–0.47) and β-lactamase resistance genes 27.93% (95% CI 0.11–0.56) respectively. The *Vibrio* antibiotics resistance genes (*V*-ARG) distribution depicts no regular trend or pattern from the analyzed data. Consequently, more studies would be required to articulate the structure of cohesion in the distribution of the resistance determinants in microbes.

1. Introduction

Cholera is globally distributed and, are caused by *Vibrio cholerae* (Blake, 1993; Didelot et al., 2015; Finkelstein, 1996; Mutreja et al., 2011, 2013). The spread of pathogenic *Vibrio* species which, may have acquired a cocktail of resistant factors to first-line antibiotics, maybe a potential source of disease epidemic with significant morbidities in the foreseeable future. In resource-poor economies, the management of cholera remains a public health challenge that has been exacerbated by poor hygiene, inappropriate use of antibiotics, scant immunization coverage and the unavailability of potable pipe-borne water (El-Fadel et al., 2014; Onohuean et al., 2021a, 2021b; Osunla and Okoh, 2017) The reported treatment failures have been associated with drug resistance, re-infection and a changing disease epidemiology (Van Rie et al., 2005). These factors warrant investigation to update stakeholders with relevant information for public health safety. Globally, antibiotic resistance results in annual human mortality of about 700,000 with expected progression to 10 million by 2050 (Clift, 2019; CDC, 2019). Among the high-income countries, a mortality rate of 25,000 and 23,000 deaths every year due to AMR infections was reported by European Center for Disease

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Prevention and Control (ECDC) and the US Centers for Disease Control and Prevention (CDC, 2019; Centers for Disease Control and Prevention, 2019, 2018). However, in low- and middle-income economies, including India and Thailand, AMR mortality rate has been reported as 58,000 in children and 38,000 adults.

Specific environmental and aquatic niches drive transmission of antimicrobial resistance (AMR) influenced by pathogenic bacteria's persistence in healthcare, agriculture and industrial waste (Fouz et al., 2020; Onohuean et al., 2021a). Egregious prescription practices occasioned by inappropriately trained personnel and self-medication coupled with poor sanitation and personal hygiene in low- and middle-income countries are significant determinants of AMR pathogenesis (Mobarki et al., 2019; Ayukekbong et al., 2017; World Bank, 2016).

Vibrio species are ubiquitous in the environment, especially in aquatic bodies with a unique interactive potency with other pathogens or the free genome in the environment (Kokashvili et al., 2015; Onohuean et al., 2021b; Pruzzo et al., 2005). Genetic interactions leading to the acquisition of plasmids, transposable elements, super-integron and integrating conjugative elements (ICEs) genes may confer antibiotic resistance on *Vibrio* species (Jiang et al., 2017). The need for the estimation of the prevalence, occurrence, and incidence of antibiotic resistance genes cannot be overemphasized and therefore warrant sustained surveillance especially in resource-limited settings. A dart of information abounds on the distribution and origin of antimicrobial resistance genes in the environment. There is scanty literature on *Vibrio* species-ARG from environmental epidemiological studies involving large regions or multiple continents, large populations, and complete epidemiological variables for public awareness and health systems advice. This study is a systematic review and meta-analysis on environmental *Vibrio* species-ARG from a two-decade (January 2000 to December 2019) empirical published data.

2. Materials and methods

Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement (A1 Tabe) (Moher et al., 2016) was applied. Incidence was defined as the presence (occurrence) of antibiotic resistance genes (ARG) in environmental samples tested in the primary studies. At the same time, prevalence (p) meant the number of positive isolates (ps) for ARG from the total sample (ts). Primary studies refer to the published empirical data used in this study. The study population meant the type of ARG present in published research. The most frequent studied ARG considered in this work includes β-lactamase (*bla*), quinolone, tetracycline and sulfonamide resistance genes (*qnr*, *tet*, *sul* and mate). Others included phenicol, macrolides and aminoglycoside resistance genes (*cat* and *floR*, *erm* and *mef*, *aac*, *aphA* and *str*).

2.1. Search strategy

This study's search strategy is to establish and explore the prevalence and incidence of antibiotic resistance genes associated with *Vibrio* species recovered from environmental isolates. To this end, the research question; what is the occurrence of antibiotic resistance genes? As well, the research problem statement describing the incidence and prevalence of antibiotic resistance genes in environmental isolates of *Vibrio* species was articulated. Therefore, either the presence or absence of antibiotic resistance genes was considered possible in the eligible literature.

2.2. Selection criteria

Research articles were retrieved from the PubMed, and title-specific term search in the Web of Science data bases between January 1st 2000 and December 31st 2019. The detail search algorithms or key terms are in the additional information (A2 Text). The datasets where combine on RStudio versions 3.5.1 using bibliometrix R package (Aria and Cuccurullo, 2017), while removal of duplicates and normalization of variables was done using ScientoPy and fBasics R-packages (Ruiz-Rosero et al., 2019).

Inclusion and exclusion criteria were used to select articles relevance to this study.

Studies that report *Vibrio* species antibiotic resistance genes (*Vibrio* species-ARG) in environmental samples were qualified for consideration. Furthermore, studies that fulfilled the following criteria were included:

i) The use of a conventional phenotypic method of isolation of *Vibrio* species from environmental samples.
ii) The genotypic primary Polymerase chain reaction (PCR) methods.
iii) The use of molecular methods for antibiotic resistance genes testing such as whole genome sequencing and MALDI-TOF mass spectrometry.
iv) Availability of full published peer-reviewed articles in English.
v) The total number (population) of samples studied and the number of positive samples for the presence of resistance genes clearly stated in the study.

Excluded articles includes review articles, recovered *Vibrio* species antibiotic resistance genes in artificially contaminated samples, articles such as research thesis, opinion articles, book chapters, non-peer-reviewed, non-clinical or environmental sample sources of and conference abstract, proceeding of which full articles are not readily accessible.

2.3. Retrieval of articles

Articles qualified by inclusion criteria were employed in this study and Metal analysis indices including details of documents were extracted by two investigators independently (OH and AE) and double-checked by third investigator NUU. Afterwards, documents homogeneity or consistency and heterogeneity across studied populations was done and further statistical analysis based on requirements for the study as conceptualized by the investigators.

2.3.1. Assessment for extracted data

Following the inclusion and exclusion criteria, information on the first author names, publication year, *Vibrio* species, antibiotics, antibiotics resistance genes, the total number of samples, number of positive samples, Country of study, sample source studied, study period, study type, experimental methods, antimicrobial resistance breakpoints were identified and extracted from results, discussions, figures and tables in the qualified articles during the studied span.

2.4. Statistical analysis of extracted data

The formula ($p = ps/ts*100$) was used to the calculated percentage of prevalence (%p) of ARG (Tadesse and Tessema, 2014). The study's random-effects meta-analyses weighted was done by estimating the summary effect size (weighted average proportion) to calculate the pooled effect size based on the individual effect sizes and their sampling variances via the argument method = " REML" (using the restricted maximum-likelihood estimator). At 95% confidence intervals to compare the prevalence of ARG in the sample studied. The effects of examined homogeneity or consistency and heterogeneity across studied populations were measured. The Funnel plots for comparison of publication bias was conducted according to asymmetry Egger's test for this purpose. All analysis were two-tailed of p-values < 0.05 level of significance and were conducted in the statistical software R 3.5.1 packages (Balduzzi et al., 2019; Rstudio Team, 2019).

3. Results

3.1. Literature search summary

A total of 891 articles were identified, screening yielded 250 documents, and further reviewing of potentially relevant articles resulted in 83 eligible studies. Lastly, 28 articles were extensively reviewed, while articles that do not clearly state the total number of samples tested and the number of positive samples for the presence of resistance genes were excluded. Therefore only 10 data articles were qualified by criteria eligibility and included in the meta-analysis, as indicated in Figure 1 and Table 1. The ten qualified and included articles on *Vibrio* species-ARG are (Baron et al., 2016; Diep et al., 2015; Faja et al., 2019; Lepuschitz et al., 2019; Letchumanan et al., 2015; Rojas et al., 2011; Shakerian et al., 2017; Shivakumaraswamy et al., 2019; Ye et al., 2016; Zhang et al., 2018). This study revealed the most contaminated environmental samples by pathogen *Vibrio* species-ARG to include water, prawn, fish, shrimps, clam, molluscs, oysters and mussels with most prevalence distributions of different genes in countries such as China and Malaysia (see Table 2).

3.1.1. Culturonomics and diversity

The study observed that cultureomics a global consistent standard methods for isolation, and identification of the various seven ARGs were identified together with their location and region based diversity in the resistant genes cassettes reported (McMillan et al., 2019; Partridge et al., 2018). The resistant genes identified from the papers analysed included [tetracycline (*tet*) and sulfonamide (*sul* and mate), quinolone (*qnr*), β-lactamase (*bla*), chloramphenicol (*cat* and *floR*), macrolides (*erm* and *mef*, *aac*, *aphA*), and aminoglycoside resistance gene (*str*) respectively, Figures 2 and 3).

3.2. Characteristics prevalence of ARG base on eligible studied data

Table 1 below depicts the studies conducted by 10 authors published between 2000 and 2019 from 8 countries is as follow: China (n = 2), Iran (n = 1), Haiti (n = 1), Brazil (n = 1), Southern Vietnam (n = 1), Malaysia (n = 2), Eastern Austria (n = 1), India (n = 1). Risk prevalence of *Vibrio* species-ARG among the classes of antimicrobial found in 1920 isolates, tetracycline (*tet*) 131 (21%) have the highest prevalence follow by sulfonamide (*sul*) 125 (20%) as shown in Figure 3. Polymerase chain reaction (PCR) amplification of specific resistance genes primers was the most commonly used method for the genotypic detection of resistance genes in the isolates included in this study.

Among all the resistance genes reported in the data studied tetracycline (*tet* -21%) and sulfonamide (*sul* and mate -20%) show the highest prevalence compare to quinolone (*qnr*), β-lactamase (*bla*) compared to chloramphenicol (*cat* and *floR*), macrolides (*erm* and *mef*, *aac*, *aphA*), and aminoglycoside resistance gene (*str*).

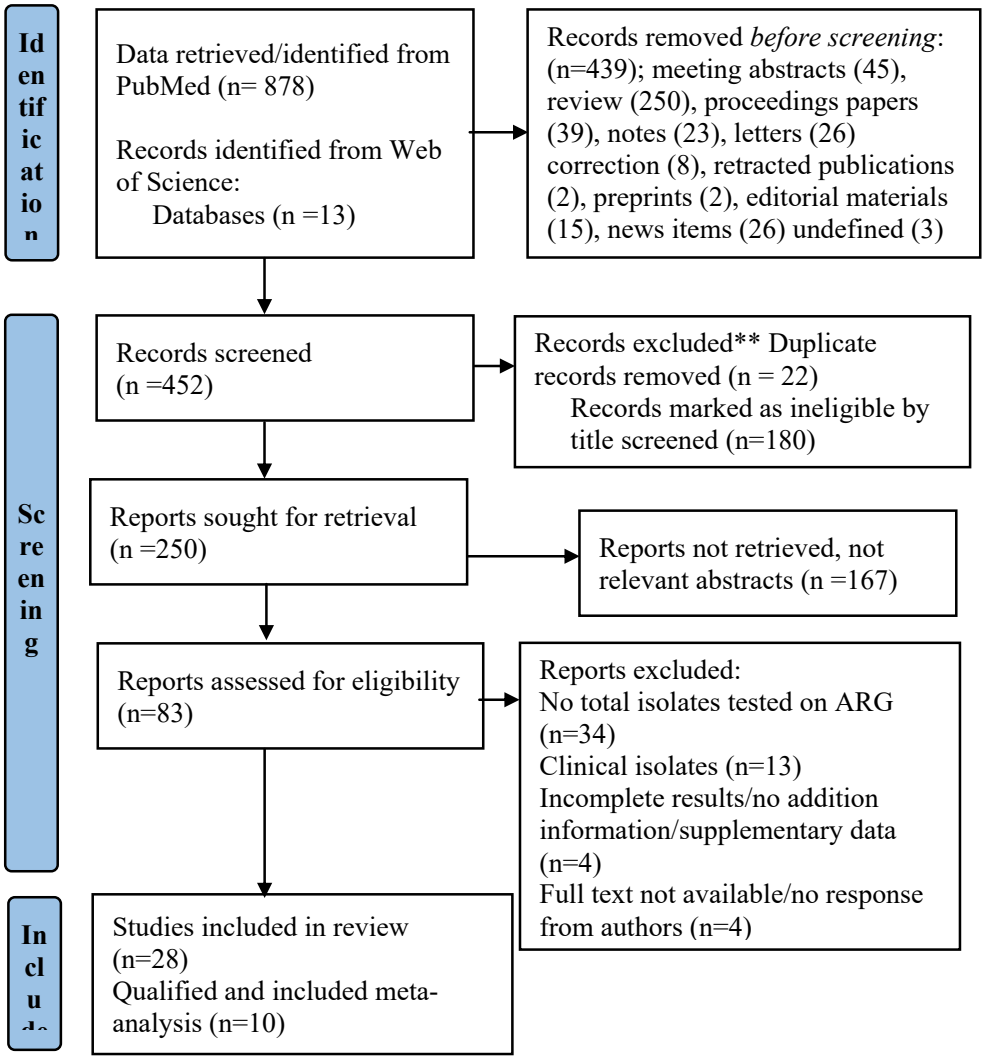

Figure 1. Study selection flowchart.

Table 1. Descriptive summary of qualified studies (n = 10).

s/n	Authors and PY	*Vibrio* species	antibiotics	ARG	ts	ps	%P	Country	SS	study period
1	Shakerian et al. (2017)	*Vibrio* species	Not mention	*str*A	31	9	29.03	Iran	Prawn	Feb–Aug 2015
				*tet*S	31	7	22.58			
				*erm*B	31	10	32.26			
				*sul*2	31	4	12.90			
2	Ye et al. (2016)	*V. algino*	cephalosporin	bla_{PER-1}	5	2	40.00	China	Foods	June 2014–Aug 2015
			cephalosporin	bla_{CMY-2}	5	1	20.00			
			cephalosporin	bla_{VEB-1}	5	2	40.00			
3	Zhang et al. (2018)	*Vibrio* species	quinolone	*qnr*VC5	39	18	46.15	China	Foods	2015–2016
			quinolone	*qnr*VC4	39	10	25.64			
			quinolone	*qnr*VC6	39	5	12.82			
			quinolone	*qnr*VC1	39	2	5.13			
			quinolone	*qnr*VC7	39	1	2.56			
4	Baron et al. (2016)	*V.cholerae* non-O1/non-O139	streptomycin	*str*A	50	3	6.00	Haiti	Water	Jul-12
			streptomycin	*str*B	50	11	22.00			
			sulfonamide	*sul*1	50	41	82.00			
			sulfonamide	*sul*2	50	3	6.00			
			erythromycin	*erm*A/B	50	45	90.00			
			erythromycin	*mef*A	50	1	2.00			
5	Rojas et al. (2011)	*V. para*	β-lactamase	$bla_{TEM-116}$	19	19	100.00	Brazil	oysters & mussels	Feb 89 – Jan 90
6	Diep et al. (2015)	*V. chol*, Non-O1, non O139	penicillins, cephalosporin & carbapenem	bla_{NDM-1}	3	3	100.00	Southern Vietnam	Environmental	2010–2013
7	Letchumanan et al. (2015)	*V. para*	chloramphenicol	*cat*A2	8	8	100.00	Malaysia	shrimp	Jan 2014–June 2014
			kanamycin	*aph*A-3	52	15	28.85			
8	Lepuschitz et al. (2019)	*V. chol*	tetracycline	*tet* (34)	54	46	85.19	Eastern Austria	Lake	May' 11- Oct '12
			beta-lactam, Ampicillin	bla_{CARB7}	54	7	12.96			
			Beta-lactam	bla_{CARB9}	54	2	3.70			
			Phenicol	*cat*B9	54	3	5.56			
			sulfonamide and bicyclomycin	*Bicyclomycin /MATE*	54	46	85.19			
			MATE	*Multidrug and toxic compound extrusion*	54	19	35.19			
9	Shivakumaraswamy et al. (2019)	*Vibrio* species	tetracycline	*tet*A, *tet*B, *tet*C, *tet*D, *tet*E, *tet*G, *tet*M & *tet*S	58	45	77.59	India	Fish, oyster, clam, olluscs	2011–2014
			co-trimoxazole	*sul genes*	38	12	31.58			
			ampicillin	bla_{TEM}	125	8	6.40			
			cefotaxime	bla_{CTX-M}	62	5	8.06			
			chloramphenicol	*cat*1, *cat*2 *and cml*A	15	5	33.33			
			nalidixic acid	*qnr*A, *qnr*B *or qnr*S	71	9	12.68			
10	Faja et al. (2019)	*V. para*	Not mention	*aac(3)-lla*	73	12	16.44	Malaysia	Seawater & fish	
				*bla*P1	73	39	53.42			
				*erm*B	73	15	20.55			
				floR	73	16	21.92			
				*qnr*A	73	14	19.18			
				*str*B	73	59	80.82			
				*tet*A	73	40	54.79			

PY = Publication years, ARG = antibiotics resistance genes, ts = total samples, ps = positive samples, %P = percentage prevalence, SS = sample sources studied, algino = *alginolyticus*, para = *parahaemolyticus*, chol. = *cholerae*, AMR = antimicrobial resistance.
Note: All study considered were cross-sectional, experimental method = PCR, AMR breakpoint = CLSI.

β-lactamase (*bla*) is distributed in six countries, and it was the only resistance gene found in Brazil. Six out of the seven resistance genes prevalence in this study was present in the environmental samples recover from Malaysia except for *sul* (sulfonamide) and streptomycin (*str*) been highly distributed. The result show tetracycline (*tet*) prevalence in India, Eastern Austria and Malaysia. There is a prevalence of sulfonamide (*sul*) in Eastern Austria and Haiti. Highest occurrence of erythromycin (*erm*) resistance genes in Haiti while quinolone resistance gene is the significant prevalence in China and little prevalence of β-lactamase (*bla*).

3.2.1. *Meta-analysis of prevalence of β-lactamase resistance genes positive in Vibrio species isolates extracted in the studied data*

Vibrio species-ARG was present in 622 (32.39%) isolates from the total of 1920 *Vibrio* species environmental isolates seen the papers analyzed. The meta-analysis of prevalence and incidence of β-lactamase resistance genes positive in *Vibrio* species isolates done on the data study of 88 (21.73%) resistance genes isolates out of 405 ps of *Vibrio* species-ARG, has a pooled estimate proportion of 27.93% (0.11–0.56) with heterogeneity significance of ($Q = 83.99$, $p > 0.001$) (Figure 4).

Table 2. The Prevalence and meta-analysis statistics of *Vibrio* species-ARG identified in the studied data.

df	Sample	esp 95 % CI	Heterogeneity			esp	Variance
			Q value	p value	I^2		
9	β-lactamase resistance genes	27.93 (0.11–0.56)	83.99	0.001	91.01	0.59	0.95
15	quinolone, tetracycline and sulfonamide resistance genes	32.97 (0.18–0.53)	214.29	0.001	94.89	0.71	0.42
14	Phenicol, macrolides and aminoglycoside resistance genes	28.67 (0.15–0.47)	151.45	0.001	93.36	0.91	0.41

df = degree of freedom; esp = estimate summary proportion/effect estimate; Q-statistic = Cochran's test; I^2 = inverse variance index; es = Standard error.

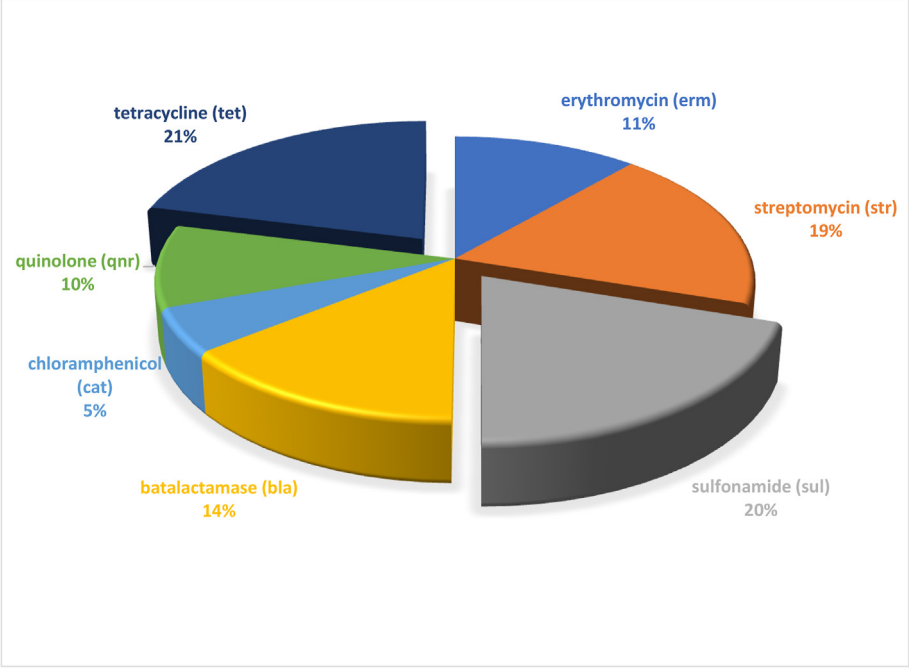

Figure 2. Prevalence of *Vibrio* species-ARG from the studied data.

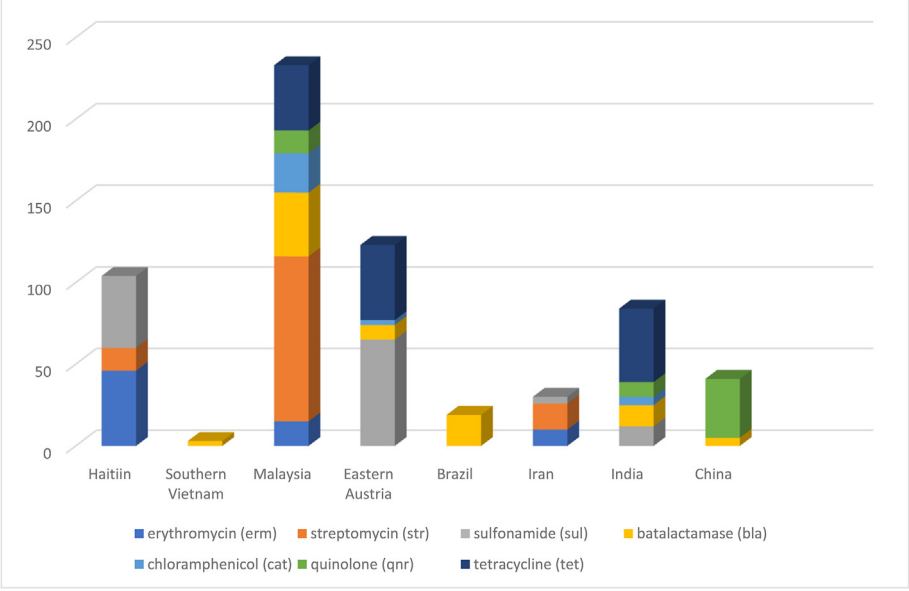

Figure 3. Countries distributions of *Vibrio* species-ARG from the studied data.

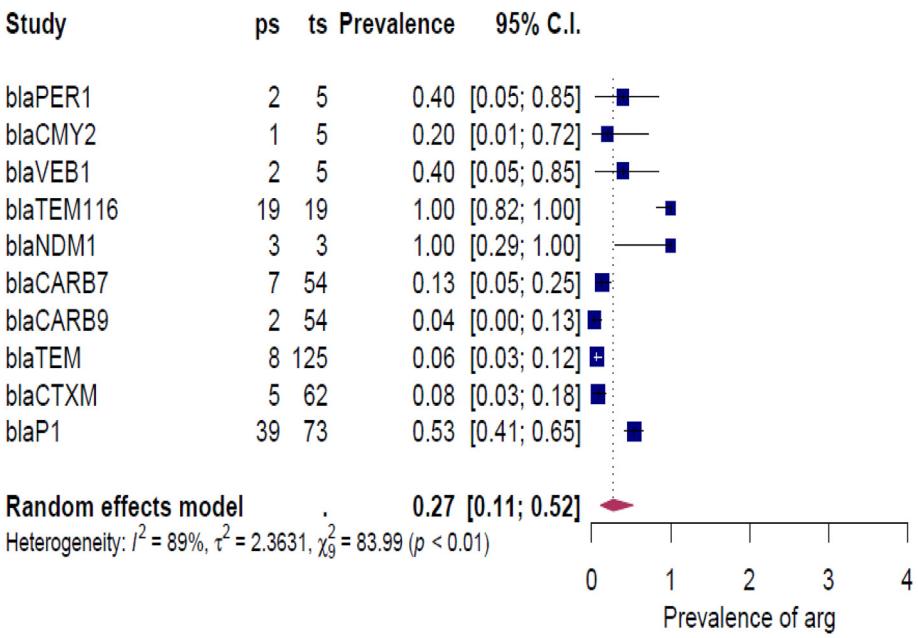

Figure 4. Forest plots of the prevalence of β-lactamase resistance genes positive in *Vibrio* species isolate for random-effects model meta-analyses. (The confidence interval at 95% and random effect estimates of *Vibrio* species-ARG with size squares proportional to the weight assigned to the study in the meta-analysis).

Observed pooled heterogenicity significance of beta lactamase ARG may highlight the interplay between aquatic and terrestrial factors that defines the diversity and microevolution of resistance in the ecosystem.

The plot's diagonal line indicates 95 % confidence interval and the vertical line indicates the summary prevalence rate resulting from the random-effect model meta-analysis.

3.2.2. Meta-analysis of prevalence of quinolone, tetracycline and sulfonamide resistance genes positives in Vibrio species isolates extracted in the studied data

The meta-analysis of prevalence and incidence of quinolone, tetracycline and sulfonamide resistance genes positive in *Vibrio* species isolates done on the data study of 315 (39.33%) ps resistance genes isolates out of 801 ts of *Vibrio* species-ARG, has a pooled estimate proportion of 32.97% (0.18–0.53) with heterogeneity significant of (Q = 214.29, p > 0.001).

3.2.3. Meta-analysis of prevalence of phenicol, macrolides and aminoglycoside resistance genes positives in Vibrio species isolates extracted from the studied data

The meta-analysis of prevalence and incidence of quinolone, tetracycline and sulfonamide resistance genes positive in *Vibrio* species isolates done on the data study of 219 (30.67%) ps resistance genes isolates out of 714 ts of *Vibrio* species-ARG, has a pooled estimate proportion of 28.67% (0.15–0.47) with heterogeneity significant of (Q = 151.49, p > 0.001).

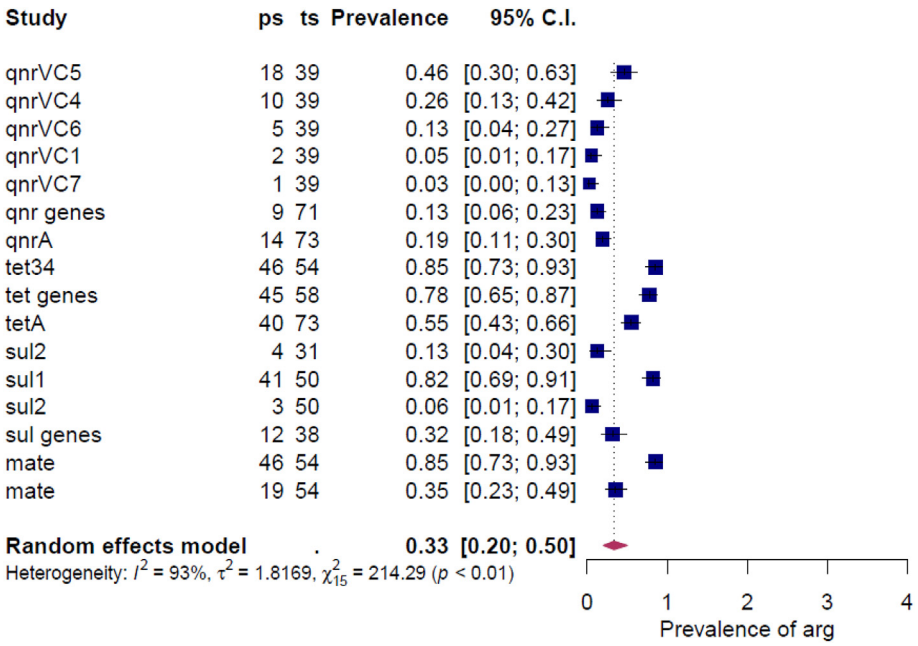

Figure 5. Forest plots of the prevalence of quinolone, tetracycline and sulfonamide resistance genes positive in *Vibrio* species isolates for random-effects model meta-analyses. (The confidence interval at 95% and random effect estimates of *Vibrio* species-ARG with size squares proportional to the weight assigned to the study in the meta-analysis).

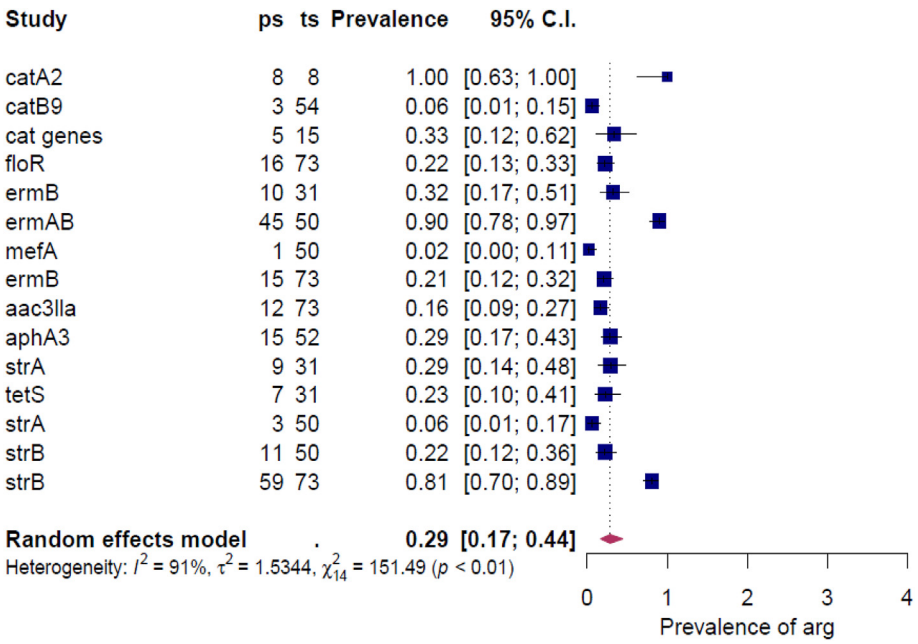

Figure 6. Forest plots of prevalence of phenicol, macrolides and aminoglycoside resistance genes positive in *Vibrio* species isolates for random-effects model meta-analyses. (The confidence interval at 95% and random effect estimates of *Vibrio* species-ARG with size squares proportional to the weight assigned to the study in the meta-analysis).

4. Discussion

Acquisition of *Vibrio* species-ARG is a public health threat responsible for developing severe gastroenteritis, septicemia, *Vibrio* infections, and re-occurrence of outbreaks. Here, we present three antibiotic resistance genes prevalence among environmental *Vibrio* species-ARG. Group1; β-lactamase resistance genes, group 2; quinolone, tetracycline and sulfonamide, group 3; phenicol, macrolides and aminoglycoside resistance genes Seven resistance genes were found as shown in Figure 2 indicating tetracycline (*tet*) 21% and sulfonamide 20% being the most prevalence compared to chloramphenicol (*cat*) 5%. The excessive and uncontrolled use of antibiotics in treating human disease and many agricultural practices are linked to the increase of ARGs. Antibiotic resistance develops in bacteria by various methods, which can be passed on to non-resistant bacteria via DNA or other genetic elements such as integrons, transposons, and bacteriophages. The occurrence of resistance *Vibrio* strains and other resistance bacteria in the environment and its transmission across the food chain to the consumer have an indirect relationship. However, the extent to which the food chain contributes to global antibiotic resistance is unknown. We were not surprised about observing this pattern of resistance genes because of changing disease epidemiology of infections agents and lack of sustained surveillance in limited-resource settings. Chloramphenicol have been withdrawn from routine prescription lists due to bone marrow aplasia's side effect and lack of prescription drugs leading to use of sublethal doses of medications all may explain observed resistance. The 5% resistance may be due to topical application in wound infections or eyes and ear drops. Tetracycline (*tet*) been 21% resistance was not surprising because it is highly resisted by many bacteria (Gao et al., 2012; Nguyen et al., 2014; Roberts, 2003) due to its low efficacy, doxycycline had been used instead. Sulfonamide (*sul*) 20% are routinely used to manage HIV, TB, malaria, pneumonia, and febrile illness (Hsu et al., 2014; Xu et al., 2015).

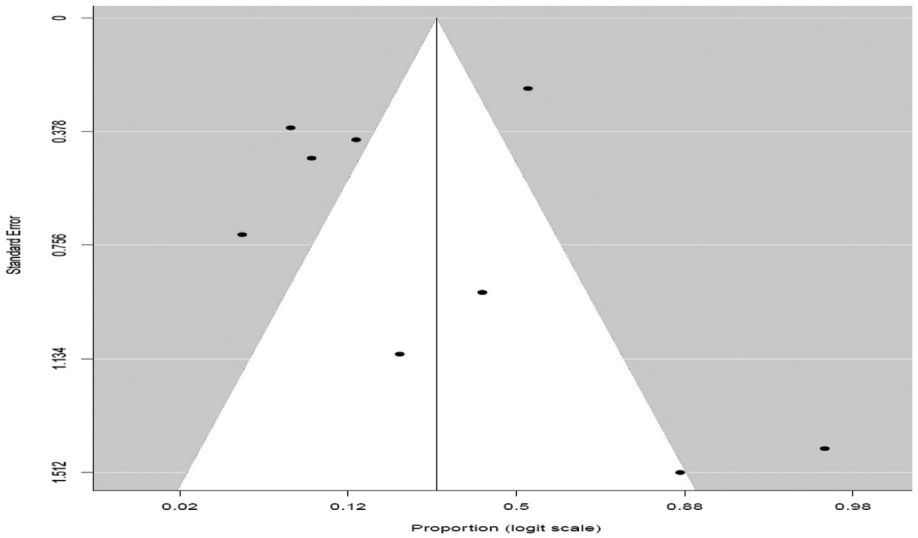

Figure 7. Bias assessment is revealed by funnel plot of prevalence of β-lactamase resistance genes positive in *Vibrio* species isolates.

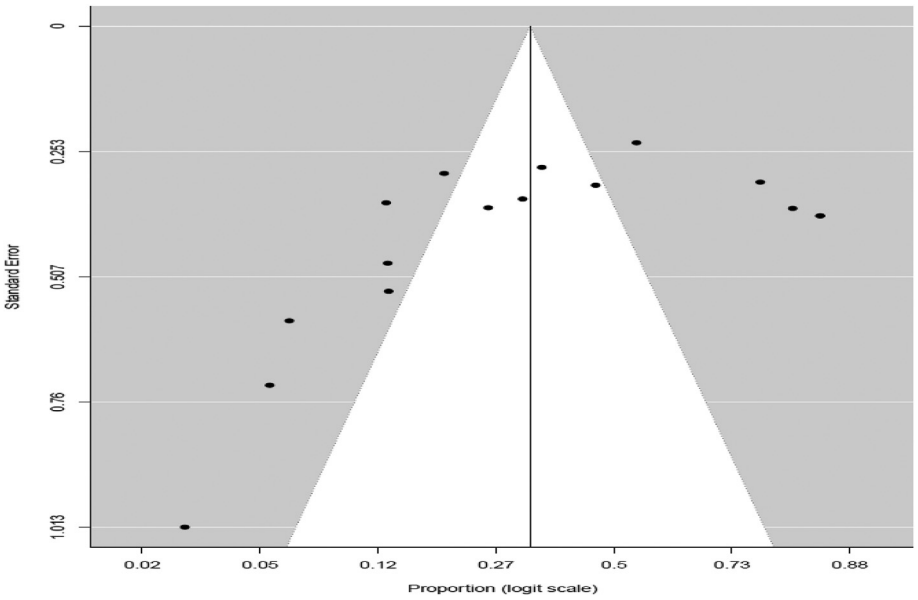

Figure 8. Bias assessment is shown by funnel plot of prevalence of quinolone, tetracycline and sulfonamide resistance genes positive in *Vibrio* species isolates. The plot's diagonal line indicates 95 % confidence interval and the vertical line indicates the summary prevalence rate resulting from the random-effect model meta-analysis.

In Figure 2, Malaysia harbour 3 out of the 7 *Vibrio* species-ARG; β-lactamase (*bla*), streptomycin (*str*), chloramphenicol (*cat*). The prevalence of streptomycin (*str*) and chloramphenicol (*cat*) resistance genes in the Malaysian study population may be due to aquaculture, livestock and economic reason (HAIAP, 2013; Kathleen et al., 2016). It could also be that there are stringent antibiotics policies in Malaysia (Fatokun, 2014; Hassali et al., 2017) that put away drugs that have a side effect from the general public despite its implications. Report of streptomycin resistance genes is a signal danger in T.B management. The results also show an incidence of quinolone (*qnr*) and β-lactamase (*bla*) resistance genes in China. In 2010, China was the world's second-largest user of antibiotics, accounting for 57 % of the growth in the healthcare industries of BRICS countries (Cui et al., 2017). At the same time, China's rapid economic expansion has resulted in a rise in travel and migration, which has exacerbated the country's AMR problem. However, in 2016, the National Antimicrobial Resistance Action Plan (2016–2020) was released by Chinse authority, thereby creating opportunities to address the challenge of antibiotics and antimicrobial resistance in China (Xiao, 2018). Despite the implementation of several policies, the statewide use of surveillance networks, and the establishment of a national committee, there is still misuse of drugs. According to the National Surveillance Report of Adverse Drug Reactions from 2015, allopathic (Western) medicines accounted for 81.2 % of all adverse drug reaction reports, with anti-infectives accounting for 44.9 % and antimicrobial infusions accounting for 61.3 % (Cui et al., 2017). Nevertheless, the observed resistance genes of quinolone and β-lactamase in China could be associated with the routine used of Quinolone (*qnr*) in the control of Chinese herbal natural (Heeb et al., 2011; Li et al., 2012) drugs during development. Also, quinolone and β-lactamase are the most commonly used drugs in many field trials for agricultural and veterinary products in many countries, including China (Qu et al., 2018; Xiao et al., 2017). Environmental antibiotics content ultimately ends up with humans. On the other hand, least ARG detection depicts resistance in those countries; therefore, police and service providers should take note.

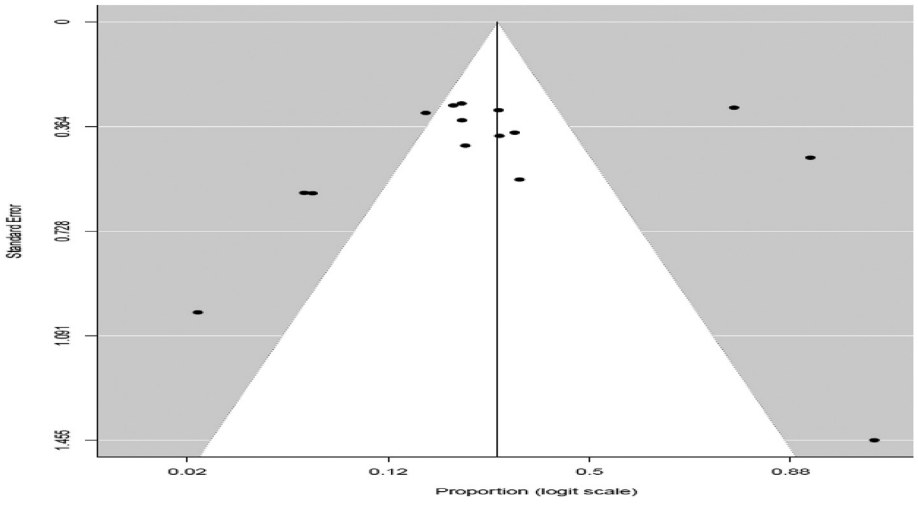

Figure 9. Bias assessment is shown by funnel plot of prevalence of quinolone, tetracycline and sulfonamide resistance genes positive in *Vibrio* species isolates. The plot's diagonal line indicates 95 % confidence interval and the vertical line indicates the summary prevalence rate resulting from the random-effect model meta-analysis.

As shown in Table 1, many research studies have been reported on environmental *Vibrio* species susceptibility and antibiogram profile, but very few studies report the detailed information on resistance genes required for the meta-analysis. Other several studies failed to provide the information needed to advance this subject's knowledge and were not included in this study. Hence, out of 891 publications, only 10 (1.12%) meet the minimum requirement described in the data assessment quality above. Authors are advised to improve the quality and publishers to work with authors in this regard.

The forest plots, shown in Figure 4, 5, 6, shows that the red diamond is located at the centre of the line of no difference (Balduzzi et al., 2019; Ganeshkumar and Gopalakrishnan, 2013; Hak et al., 2018). Therefore, there is no statistically significant difference in the meta-analysis of studied data. Thus, the prevalence of *Vibrio* species-ARG is not dependent on any of the experimental factors.

The asymmetric funnel plots are shown in Figure 7, 8 and 9 imply possible publication bias due to the small size of the include articles and experimental method. Finally, it is recommended that improved research design, standardize study procedures and reporting to improve comparability and comprehensiveness in future meta-analyses studies in this field.

4.1. Research limitations

In this study, we encounter some limitations, and here we try to highlight a few of them. Firstly, the use of small data sets is due to the failure of published articles to qualify for the exclusion criteria. Secondly, there was heterogeneity of studies included which may be due to study design, experimental method and other sampling factors, making it hard to achieve steady meta-analysis results notwithstanding the use of a standardized analysis process. Thirdly, we did not analyze outliers in this study.

5. Conclusion

This study's observations point a high incidence and prevalence rate of quinolone, tetracycline and sulfonamide resistance genes in *Vibrio* species isolates recovered from environmental samples. This may pose a public health threat and failure to the therapeutic management of severe vibriosis; hence, more studies are needed to investigate resistance genes' genotypic distribution. However, this study is an experimental new data develop analysis tool for AMR genes, and a platform for regional and international surveillance for monitoring of ARG could serve to mitigate the public threat of therapeutic failed to resistance.

Furthermore, understanding the molecular mechanism of resistance genes will provide a new intervention strategy to emerge and remerge environmental pathogens.

To limit the distribution of *Vibrio* species-ARG, it is of urgent essential to optimizes the rational of antibiotic usage at regional and national levels in limited-resource settings to ensure quality and effective health care management of *Vibrio* infections.

Declarations

Author contribution statement

All authors listed have significantly contributed to the development and the writing of this article.

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Data availability statement

Data will be made available on request.

Declaration of interests statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

Appendix

Additional Materials

A1 Table. Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) Statement.

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3 - 6
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6

(*continued on next page*)

A1 Table (*continued*)

Section/topic	#	Checklist item	Reported on page #
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	No registration
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	7
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7-8
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	A1 Text
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6 - 8
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6 -8
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	13
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	13
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	13
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	17, 19, 21
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9, Figure 1.
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	10 – 12, Figures 2, 3
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Figures 7, 8, 9
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Figures 2, 4, 5, 6
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Figures 2, 4, 5, 6
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Fig 7, 8, 9
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Figure 2, 3
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	21-23
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	23
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	23 - 24
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	24

(A2 Text). The detail search algorithms or key terms.

Search keywords/algorithm (vibrio species antibiotic resistance genes): PubMed

(("vibrio"[MeSH Terms] OR "vibrio"[All Fields] OR ("vibrio"[All Fields] AND "species"[All Fields]) OR "vibrio species"[All Fields]) AND ("anti-bacterial agents"[Pharmacological Action] OR "anti-bacterial agents"[MeSH Terms] OR ("anti-bacterial"[All Fields] AND "agents"[All Fields]) OR "anti-bacterial agents"[All Fields] OR "antibiotics"[All Fields]) AND resistance[All Fields] AND ("genes"[MeSH Terms] OR "genes"[All Fields] OR signatures [All Fields]OR determinates)) AND 2000[PDAT] : 2019[PDAT]

Search keywords/algorithm (vibrio species antibiotic resistance genes): Web of science

("vibrio"[MeSH Terms] OR "vibrio"[All Fields] OR ("vibrio"[All Fields] AND "species"[All Fields]) OR "vibrio species"[All Fields]) AND anti-bacterial [All Fields] OR antibiotics OR Antibiotic agents OR resistance [All Fields] AND ("genes"[MeSH Terms] OR "genes"[All Fields] OR signatures [All Fields] resistance determinates [All Fields])

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