REVIEW

Antimicrobial resistance in aquaculture: A global analysis of literature and national action plans

Andrea Caputo¹ | Melba G. Bondad-Reantaso² | Iddya Karunasagar³ | Bin Hao² | Patricia Gaunt⁴ | David Verner-Jeffreys⁵ | Sophie Fridman² | Alejandro Dorado-Garcia⁶

¹ReAct - Action on Antibiotic Resistance, Uppsala University, Uppsala, Sweden
²Fisheries and Aquaculture Division, Food and Agriculture Organization of the United Nations (FAO), Rome, Italy
³Nitte University, Medical Sciences Complex, Deralakatte, Mangaluru, Karnataka, India
⁴Mississippi State University, Starkville, Mississippi, USA
⁵Centre for Environment Fisheries and Aquaculture Science (CEFAS) and FAO Reference Center on AMR, Weymouth, Dorset, UK
⁶Joint FAO/WHO Centre (CODEX Food Standards and Zoonotic Diseases (CJW), Food and Agriculture Organization of the United Nations (FAO), Rome, Italy

Abstract

Since the establishment of a Global Action Plan (GAP) on Antimicrobial Resistance (AMR) (68th World Health Assembly, Geneva, Switzerland, 2015), most members of the World Health Organisation (WHO) have developed and implemented a National Action Plan (NAP) based on a “One Health” approach to AMR. Aquaculture, significant among the food producing sectors, has often been overlooked in AMR governance. We did a systematic review of 95 country NAPs and assessed the inclusion of aquaculture. We also reviewed the scientific literature from 1996 until April 2021 to retrieve data characterising AMR in aquaculture during the last 25 years. In our analysis, 37% of countries did not mention an aquaculture component within their AMR NAP. The South-East Asia Region had the highest implementation rate of AMR-aquaculture programmes. Our literature review indicated that most AMR-aquaculture related studies have taken place in the People’s Republic of China, followed by the United States of America and India. Beta-lactamases, tetracyclines, sulfonamides, macrolides, and fluoroquinolones were the most represented classes of antibiotics, with Vibrio spp. and Aeromonas spp. as the most investigated antimicrobial-resistant bacteria. This review highlighted the gaps in AMR-aquaculture governance and the progress made across WHO members. Countries are encouraged to (i) fulfil their commitments by developing and/or fully implementing the AMR NAP, (ii) further engage in the research, monitoring, and surveillance of antimicrobial usage and AMR within the aquaculture sector, and (iii) collaborate at national and international level for a concerted “One Health” approach.

KEYWORDS

AMR, aquaculture, ARB, ARG, governance, NAP
1 | INTRODUCTION

Following the adoption of the Global Action Plan (GAP) on Antimicrobial Resistance (AMR) during the 68th World Health Assembly in 2015, commitments to support the GAP were obtained from members attending the 83rd General Assembly of the World Organisation for Animal Health (OIE) and the 39th Conference of the Food and Agriculture Organization of the United Nations (FAO). This support included the development of National Action Plans (NAPs) on AMR. Separate resolutions combined AMR actions into (a) the OIE Strategy on AMR and the Prudent Use of Antimicrobials, which supports the four main objectives that include (1) improving awareness and understanding among Member countries, veterinarians, farmers, stakeholders and citizens, (2) strengthening knowledge through monitoring and surveillance systems and research, (3) supporting good governance and capacity building and (4) encouraging implementation of international standards in order to provide a global benchmark for consistent regulation of antimicrobials and to promote their responsible and prudent use, and (b) the FAO Action Plan on AMR (2016–2020) (recently updated to 2021–2025 in 2021), which in turn supports the following five key objectives; (1) to increase stakeholder awareness and engagement in order to foster change, (2) to strengthen surveillance and research, (3) to enable good practices to prevent infections and control the spread of resistance microbes, (4) to promote the responsible use of antimicrobials and (5) to strengthen governance and allocate resources to accelerate and sustain progress.

The convening of the Interagency Coordination Group (IACG) on AMR in May 2017 by the Secretary-General of the United Nations provided guidance on approaches for ensuring sustained global action on AMR. The IACG completed its mandate on the 29th April 2019 upon the delivery of its report to the UN Secretary-General. This report included 14 recommendations for progress, through innovation, collaboration, investment and global governance. The follow-up report to the UN Secretary-General in May 2019 highlighted progress made by members and the Tripartite organisations (FAO, WHO and OIE) in addressing AMR within the guidelines of the GAP. It also called for urgent support and investment to scale up responses to AMR at national, regional and global levels.

In May 2018, the Tripartite signed a Memorandum of Understanding (MoU) regarding cooperation to combat health risks at the animal-health-ecosystem interface within the context of a “One Health” approach, identifying AMR as a priority area. A Tripartite work plan for 2019–2020 was developed with five focus areas to be addressed through multi-sectoral collaboration: (1) implementation of the NAP on AMR; (2) awareness and behavioural change; (3) surveillance and monitoring of AMR and antimicrobial use (AMU); (4) stewardship and optimal use of antimicrobial agents; and (5) monitoring and evaluation.

AMR is a global issue; the annual mortality rate due to AMR has been estimated as 1.27 million deaths in 2019, with low- and middle-income countries most affected by the burden. Water and its resources are known to be crucial vectors and reservoirs of AMR. Specifically, the misuse of antibiotics in the aquaculture sector plays a crucial role in AMR dissemination globally, and in documented cases, can lead to dramatic consequences to human, animal and ecosystem health (e.g.,). AMR genes (ARG) in bacteria present in seafood have been previously documented and a recent study in the Netherlands estimated seafood as the most common food source of Escherichia coli containing β-lactam antibiotic resistance genes. As the ever-increasing human population relies more heavily on aquaculture commodities for food security, the spread of AMR and associated infections through seafood represents a major concern for public health. Despite the key role of the aquaculture supply chain and its inclusion within the “One Health” framework, little to no implementation in controlling the spread of AMR has occurred in global aquaculture. This issue, coupled with limited data transparency, could threaten the sustainability of the aquaculture industry with its associated economic impacts.

Considering the global production of aquaculture commodities and its role in providing livelihoods, the prevention of AMR in this sector requires urgent action. The goal of this scoping review is twofold: (i) to analyse gaps and advancements in the implementation of the aquaculture component within the AMR NAPs of all Members, and (ii) to review how AMR is being addressed based on published scientific reports and other literature.

2 | METHODS

In order to achieve objective (i), a review of the governance framework surrounding AMR NAPs in aquaculture (including both government and intergovernmental frameworks) was performed. To achieve objective (ii), a comprehensive search of the literature was conducted where data were shared transparently.

2.1 | Review of AMR NAPs

A review of publicly available literature pertaining to AMR NAPs (as of Monday 6th July 2020) was made in the WHO Library and grouped by WHO’s 2020–2021 survey. This was then selected for further analysis using the following categories: “National AMR action plan developed”; “National AMR action plan approved by the government that reflects GAP objectives, with an operational plan and monitoring arrangements”; and “National AMR action plan has funding sources identified, is being implemented and has relevant sectors involved with a defined monitoring and evaluation process in place”.

To investigate the aquaculture component of the NAPs, each document was scrutinised using the keywords “aquaculture”, “fish”, “marine”, and “ocean”. Three sub-categories were selected to determine the presence or absence of an aquaculture component, as well as its implementation status: (1) “aquaculture component is not mentioned”, where keywords were absent or it did not include defined NAP’s goals or activities; (2) “aquaculture component is discussed”, if any of the keywords were mentioned within the document and it included at least one NAP’s goals or activities related to aquaculture; (3) “aquaculture component is in place”, when the aquaculture/fishery component was part of the goals/actions/timeline of the NAP. The data retrieved were subsequently analysed based on the regional classification of WHO Members (African Region, AFRO; Eastern Mediterranean Region, EMRO; European Region, EURO; Region of the Americas, PAHO; South-East Asia Region, SEARO; Western Pacific Region, WPRO), and subjected to standard statistical
analyses in Microsoft Excel. Documents written in a language that differed from English/Spanish/Italian/Swedish were automatically translated into English (a potential source of misinterpretation due to the translation).

2.2 | Literature review

A scoping review of the literature was performed using two major web-based databases, PubMed.gov and Web of Science. A combination of the keywords “aquaculture”, “antibiotic”, and “antimicrobial” were used as search queries for our review. Results from PubMed were imported to the software EPPI-reviewer (V 4.11.4.0) organised in Web of Science and then imported to Microsoft Excel (2019). A first filtration step was performed based on the title of the paper and its relevance to our review. An additional cut-off was based on the information provided in the abstract of each paper and its conformity to our study. Selection criteria consisted of a specific context (aquaculture/AMR), original data (antibiotics usage/resistant bacteria/resistance genes), food-related specimens (aquaculture commodities), and outcomes (all relevant results related to AMR in aquaculture). Meta-data from the search was extracted and distributed within six categories: “Article Title”, “Journal”, “Authors”, “Publication Year”, “Research Areas” and “Country”. Reviews or papers solely describing alternatives to antibiotics, and/or analyses performed on ornamental fishes were excluded from this search. Standard statistical analyses of the data and plots were performed using Microsoft Excel (2019).

3 | RESULTS AND DISCUSSION

3.1 | Review of AMR NAPs

A total of 95 NAPs were analysed (until 5 March 2022) and the results are illustrated in Figure 1. Of the top 15 world aquaculture producers (Figure 1, Insert 1), 60% (9/15; i.e., People’s Republic of China (subsequently referred to as China in this paper), India, Indonesia, Viet Nam, Norway, Myanmar, Philippines, Japan and the Republic of Korea) had the aquaculture component integrated within the AMR NAP, 20% (3/15; i.e., Bangladesh, Chile and Thailand) mentioned aquaculture within the AMR NAP, and 20% (3/15; i.e., Egypt, Brazil and Ecuador) did not acknowledge aquaculture within the AMR NAP (Note that Ecuador did not have an AMR NAP when the study was conducted).

Globally, 63% (61/95) of the NAPs acknowledged aquaculture as a crucial food value chain to be surveyed for the purpose of AMR containment, while the remaining 37% (34/95) did not (Figure 1, Insert 2). In the SEARO, WPRO and EMRO Regions (Figure 1, Insert 3), the aquaculture component of their NAP had been implemented recently, reflecting the importance of aquaculture for livelihoods in these regions. It should be noted that some countries, although not ranking among the top aquaculture producers globally, are displaying a proactive approach and have an aquaculture component in place, for example, Peru, Tanzania and Saudi Arabia.

As for the EMRO Region, one of the countries that emerged from our analysis is Sudan, which, despite being a minor producing country,
has developed an AMR NAP that includes the aquaculture sector by involving competent authorities such as the Ministry of Livestock, Fisheries and Rangelands. The FAO support has been crucial to the development of Sudan’s AMR NAP, mostly via the FAO Blue Growth Initiative (BGI) and the FAO-World Bank-African Development Bank ‘African Package for Climate-Resilient Ocean Economies’ partnership. The example of Sudan’s AMR NAP could be a model for other aquaculture producing-countries such as Egypt (the world’s 6th largest producer; Figure 1, Insert 1), where the aquaculture sector is not mentioned in their NAP and recent studies reported multi-drug resistant pathogens in aquaculture isolates.  

Within the PAHO Region, neither Brazil (the world’s 13th largest producer; Figure 1, Insert 1) where ~3.5 million people are involved in the aquaculture sector (FAO, 2019a), nor Ecuador (the world’s 15th largest producer; Figure 1, Insert 1), have an aquaculture component within the NAP which is currently under development. Members of the WHO EURO Region, with some notable exceptions, that is, Norway, which is currently the 7th largest producer globally, and the United Kingdom have the fewest mentions of aquaculture in their AMR NAPs. However, the European Union Guidelines for the Prudent Use of Antimicrobials in Veterinary Medicine and the good example set by some countries including Croatia should be considered. Most of the analysed countries have developed an extensive Animal Health section within their NAP, reflecting a “One Health” approach. However, specific guidelines for the aquaculture sector are not indicated, in contrast to livestock and poultry. Of the analysed EURO countries, 32% (8/25) do not mention “One Health” within their NAP. Among these countries is Greece, the 6th largest European aquaculture producer. Some minor producing countries, such as Switzerland, have well-developed aquaculture NAPs, as they are significant importers. Switzerland imports the majority of its aquaculture commodities, ranking 10th in Europe for volume imported (accounting for ~8.5% of world seafood trade), producing ~2.3% of seafood consumed internally. A regulative framework to control imported seafood products is essential for curbing the spread of AMR. As for the other WHO regions, 13% (2/16) of the EMRO countries and 20% (6/20) of the WPRO Region do not acknowledge “One Health” within their NAP. All AFRO, PAHO, and SEARO countries included in our analyses have developed their NAPs based on a “One Health” approach, following WHO GAP recommendations. Since not all NAPs followed a “One Health” approach, countries should consider the inclusion of all relevant sectors in the development or updating of their NAPs.

3.2 | Literature review

A total of 876 scientific papers were analysed, from 1989 until 15th April 2021. A sub-group of 511 papers was selected based on relevance to our study, narrowing the time span from 1996–2021. Among the 365 non-included papers, 98% (358/365) investigated alternatives to antibiotics in aquaculture. Of these alternatives, included were probiotics (44%), bacteriophages (37%) and vaccines (9%).

3.2.1 | Country-based analysis

Within the selected sub-group of papers, the first analysis was based on the country or region where the studies were performed; an overview TreeMap of the number of studies per country/region is illustrated in Figure 2. Sixty-one different countries from all WHO regions were involved in aquaculture studies, investigating the usage of antibiotics and bacterial AMR in multiple environmental compartments, that is, water, sediment, biofilms, feed and organisms. China, the top aquaculture producer with 60% of global aquaculture production, scored highest on the list, with 115 studies performed in the last 25 years. This information was consistent with a recent review analysis where China had the most studies on AMR in aquaculture and “related environments”. China is one of the few countries that had implemented a variety of techniques, from standard microbiological analyses (e.g., minimal inhibitory concentration [MIC] tests) to advanced proteomics studies. Second on this list of countries was the United States of America with 32 studies, closely followed by India, the second top aquaculture producer with 8% of global production,
with 27 studies investigating AMR issues related to aquaculture. In the EURO region, the countries with the highest number of papers were Spain and Italy, with 15 and 14 publications respectively. As for the EMRO region, Egypt ranked highest with seven publications; in the AFRO region, South Africa was at the top, with five publications.

The language criteria of our literature research were limited to English-written papers. Because a large percentage of relevant literature was published in Chinese, an additional screening of Chinese literature was performed through the CNKI database (https://www.cnki.net/) by searching the combination of words “antibiotic” and “aquaculture” and “AMR” in both abstract and full text. According to the search results, there are 4059 relevant studies performed in the last 15 years including various aspects such as antibiotic residues detection, AMR development and risk assessment, AMR ecological impact, AMR genes, antibiotic drug use, alternatives to antibiotics, AMR monitoring, AMR containment policy and NAPs. The latter highlights the importance of adopting a common language for sharing knowledge, especially when it comes to science, allowing for a broader outreach and a faster technological advancement.

3.2.2 | Journal-based analysis

A further outcome of our review was the identification of the type of scientific journal where the articles were published. The majority of the articles analysed were published in broad-scope journals (e.g., Frontiers in Microbiology, 10.4%; PLOS ONE, 9.1%; Science of the Total Environment, 8%) rather than niche journals (e.g., Diseases of Aquatic Organisms, 5.6%; Aquaculture, 3.9%; or Microbial Drug Resistance, 1.3%). These results might suggest that the choice of scientific journal can be affected by trends, such as publishing in the same journal as major experts (even if independent of the study’s aim), or choosing the journal’s impact factor over its scope or audience. Additionally, many studies are rejected for publication by niche journals because they fail to use appropriate testing methodologies and interpretive criteria, hence directing the author/s to a different choice of journal.

3.2.3 | Methodology-based analysis

The rapidly growing aquaculture sector relies heavily on the use of antimicrobials to combat infectious bacterial diseases that threaten production, thus contributing to the AMR reservoir. Although researchers have been studying AMR in the aquaculture sector for more than 50 years, there has been a reported increase in evidence relating to AMR in aquaculture over the last decade.21–24 However, research approaches have changed over the years as a function of both the usage of new antibiotics, as well as the increasing awareness of microorganisms resistant to drugs, making some antibiotic treatments ineffective.25 In addition, with the establishment of a GAP for AMR, the WHO has set objectives and guidelines for AMR monitoring and surveillance which have prompted studies to characterise multiple AMR parameters. The types of methodologies used have evolved to take advantage of both advances in technology (such as the use of whole genome sequencing) and the development of harmonised reporting systems (e.g., Global AMR Surveillance System (GLASS)).26,27 As early as the 1970s, researchers were identifying multidrug-resistant R plasmids in the aquaculture environment.29–32 Advancement of molecular techniques then allowed for a genetic characterisation of resistant fish pathogens and the establishment of a direct causality to the development of antibiotic resistance.33 It was not until 2015 that one of the first ARB-strains’ genomes was sequenced (Aeromonas salmonicida sp. strain CBA100).34 This represented a milestone for the upcoming genomics and proteomics studies of aquaculture zoonotic pathogens (35). In parallel, clinical studies developed microbiological tests for determining the susceptibility of fish pathogens to antimicrobials (i.e., antimicrobial susceptibility test, AST). The latter, still in use today, allows for preliminary evidence on the appropriate prescription of a specific medication.35 However, a lack of harmonisation among laboratories, particularly in interpretative criteria, such as the use of different break points and epidemiological cut-off values (ECVs), created misinterpretations and an overall slowdown of the global data collection.36 Additional common methodologies emerged in our scoping review that were biophysical analyses (mostly liquid chromatography), ecological analyses (e.g., salmonid resistance response to ecological stressors), modelling and social-sciences.37 Hence, our analyses highlighted the importance of both using up-to-date technologies as well as a multi-sectorial approach that would allow for a comprehensive picture of AMR issues. Current and future monitoring/surveillance programmes should integrate analyses that detect antimicrobial residues in the environment and characterise the microbial community, providing a tool for the rapid detection of AMR hotspots and ad hoc interventions.

3.2.4 | Areas of research-based analysis

An additional result of our systematic review highlighted the major areas of research that have investigated the AMR issue in aquaculture over the last 25 years; an overview TreeMap summarising the main areas of research that have investigated AMR in aquaculture from 1996–2020 is illustrated in Figure 3. Considering the scope of our research, it is not surprising that the two major areas of research were “fisheries” and “microbiology” (with 117 and 105 studies, respectively). Nonetheless, other sectors have also been investigating the AMR-aquaculture topic, such as veterinary science, environmental sciences, and biotechnology. These results emphasise the investments of multiple fields of research in order to solve the AMR issue in aquaculture. However, they may highlight the lack of either funding or action for certain disciplines such as public health, which is known to be at risk if effective measures on the AMR-disrupted aquaculture supply chains are not implemented immediately.

3.2.5 | AMU-based analysis

Indirect data on the usage of antibiotics were retrieved in our literature review. Most common classes of antibiotics were represented as
well as their respective resistance genes. Generally, data on the use of antibiotics for food-producing animals are based on sales data (e.g., mg of active pharmaceutical ingredient/population correction unit) and/or surveys targeting stakeholders involved in the production, sales, use and application of veterinary products. However, in the United States of America, the FDA states that sales and distribution data only reflect the total quantity of antimicrobial drug product that enters the market and does not represent how much or in what way these drugs are ultimately used. Nevertheless, the over-the-counter sale of antibiotics is still occurring in several developing and developed countries, making the traceability of the active pharmaceutical ingredients problematic.

In our analyses, five classes of antibiotics stood out: beta-lactamases (194/511 studies), tetracyclines (131/511 studies), sulfonamides (66/511 studies), macrolides (61/511 studies), and fluoroquinolones (61/511 studies) (Table 1). As for the ARGs, the sulfonamide-resistant gene sul1 was detected in 6% of the studies, the tetracycline-resistant gene tetM in 4% of the studies, the beta-lactamase-resistant gene blaCTX and the fluoroquinolone-resistant gene qnrS in 3% of the studies and, lastly, the erythromycin-resistant gene emB in 2% of the studies (Table 1).

This information was consistent with a previous survey reporting on the availability of antibiotics in aquaculture, where tetracyclines, sulfonamides and beta-lactamases were among the most recorded. Florfenicol is a member of the phenicol class of antibiotics which is not among the five largest classes of antibiotics reported here, but has been widely used in terrestrial and aquatic veterinary medicine for a number of years. It has gained popularity in all major aquaculture-producing countries and was reported used in ~10% (52/511) of the studies.

Furthermore, we analysed the studies that focused their attention on colistin. This is now an antibiotic of last resort for treatment of cystic fibrosis and other conditions in human medicine, but has otherwise been widely used in veterinary medicine since the 1950s. Colistin has largely been used for the prevention and treatment of infectious diseases, and in some Asian countries (e.g., China, Japan, India, and Viet Nam) to stimulate the growth of young animals. The misuse of this antibiotic, mostly as a growth promoter, caused a severe spreading of colistin-resistance along the supply chain, reaching the human microbiota. Despite its ban in most aquaculture-producing countries, colistin residues and/or resistance genes (i.e., mcr 1–4) are still found. In our study, only 3.3% (6/181) of the analysed papers reported colistin detected in the samples. Within this 3.3%, countries that stand out are China and India, leaders in global

---

**TABLE 1** List of modal antibiotics and antimicrobial resistance genes (ARGs) studied between 1996 and 2021 in the aquaculture sector. Percentage and mode (in parenthesis) of the classes of modal antibiotics and ARGs

<table>
<thead>
<tr>
<th>Antibiotic classes</th>
<th>Beta-lactamase</th>
<th>Tetracycline</th>
<th>Sulfonamide</th>
<th>Macrolide</th>
<th>Fluoroquinolone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modal bacteria</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ampicillin</td>
<td>38% (194/511)</td>
<td>26% (131/511)</td>
<td>13% (66/511)</td>
<td>12% (61/511)</td>
<td>12% (61/511)</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>8% (40/511)</td>
<td>8% (43/511)</td>
<td>5% (24/511)</td>
<td>7% (37/511)</td>
<td>4% (19/511)</td>
</tr>
<tr>
<td>Sulfonamide</td>
<td>6% (32/511)</td>
<td>6% (32/511)</td>
<td>6% (32/511)</td>
<td>6% (32/511)</td>
<td>6% (32/511)</td>
</tr>
<tr>
<td>Macrolide</td>
<td>12% (61/511)</td>
<td>12% (61/511)</td>
<td>12% (61/511)</td>
<td>12% (61/511)</td>
<td>12% (61/511)</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td>12% (61/511)</td>
<td>12% (61/511)</td>
<td>12% (61/511)</td>
<td>12% (61/511)</td>
<td>12% (61/511)</td>
</tr>
</tbody>
</table>

**FIGURE 3** TreeMap summarising the main areas of research that have investigated AMR in aquaculture from 1996–2020.
Considering that the Chinese Ministry of Agriculture banned colistin as a feed additive for growth promotion in animals in 2017, followed by India in 2019, a decrease of colistin-resistant isolates should hopefully be detected in the coming years. Other commonly banned antibiotics in aquaculture that were detected in our literature search were chloramphenicol (in 12% of the studies), sulfonamides (in 9% of the studies, which excludes approved sulfadimethoxine, sulfabromomethazine and sulfaethoxy-pyridazine) and fluoroquinolones (in 4% of the studies).

3.2.6 | ARB-based analysis

The last part of our analyses focused on the antimicrobial-resistant bacteria (ARB) and associated diseases. The development of antibiotic resistance in fish pathogens has been known for five decades, along with the consequences to public health.28,48–50 Nevertheless, the effects of globalisation, coupled with insufficient data, incongruent measurements and the continuous evolution of novel strains, have made associations between the misuse of antibiotics in aquaculture and the presence of resistant pathogens in the human microbiota difficult to detect and trace.

In our review, 43 different bacterial genera were found. The most frequent ARB investigated belonged to *Vibrio* spp. (25%) and *Aeromonas* spp. (18%), followed by the Enterobacteriaceae *Escherichia coli* (7%) (Figure 4). Additionally, our analysis reflected the most common diseases affecting aquaculture species, such as furunculosis, which is caused by the bacterium *Aeromonas salmonicida*, and vibriosis, with both diseases causing severe haemorrhages and organ swelling in fishes. Vaccinations against furunculosis have been one of the major drivers of Norway’s success in reducing the usage of antimicrobials in aquaculture.51 While *A. salmonicida* is non-pathogenic in humans, growing optimally at temperatures between 22 and 25°C and not surviving temperatures higher than 34.5°C, conversely, species such as *Vibrio damsela* and *V. vulnificus* are able to grow at a wide temperature range (20°C to >40°C) and can cause severe infections in fishes and humans, thus representing a threat to public health.

Human infections caused by members of Enterobacteriaceae such as *Salmonella* from contaminated seafood were commonly reported in the literature review, mostly found in undercooked aquaculture commodities harvested from faecal-contaminated waters. Immediate signs of human infections reported were diarrhoea and high fever. The FAO/WHO Codex Alimentarius provides recommendations to protect the health of consumers and to avoid the spread of infectious diseases. *Flavobacterium psychrophilum* a pathogenic bacterium belonging to the family Flavobacteriaceae, is mostly known for being the causative agent of Bacterial Cold-Water Disease (BCWD). It is common among salmonids and causes discoloration of the skin and ulcerations that may penetrate muscular layers, leading to high mortality rates, however, this organism is not of zoonotic significance.

Bacterial diseases are also known to affect shrimp, for example, Acute Hepatopancreatic Necrosis Disease (AHPND) caused by a strain of *Vibrio parahaemolyticus*, causing severe production and financial losses. However, in our literature review directed at ARB in crustaceans, we found few results, highlighting the need for further research and intervention in this field.

4 | DISCUSSION AND CONCLUSIONS

This report reviews government frameworks and the available scientific data surrounding AMR in the aquaculture supply chain. While most WHO Members have developed an AMR NAP compliant with the “One Health” perspective, almost 40% do not acknowledge...
aquaculture as a critical component where AMR should be further investigated and contained along the entire supply chain (from the seed source to aquaculture facility to the consumer). Responsibilities in the aquaculture supply chain should be shared among regulators, farmers, veterinarians, aquatic health and aquaculture specialists, retailers and consumers. In particular, leading countries in aquaculture production and export should be aware of and follow the WHO goals listed within the GAP on AMR, as well as support the implementation of the FAO action plan and OIE strategy on AMR as previously mentioned. Ultimately, aquaculture represents only one portion of the entire food system, therefore an integrated “One Health” approach is essential to combat multiple sources of AMR.

There are a number of initiatives, tools, guidance and references that can aid in increasing understanding and raising awareness of AMR in aquaculture as well as assisting in knowledge sharing. In 2017, the FAO implemented a project ‘Strengthening capacities, policies, and national action plans on the prudent and responsible use of antimicrobials in fisheries’ whose objectives were to develop and/or enhance knowledge, skills and capacity of the participating Competent Authorities (CA) on fisheries and aquaculture and to facilitate the development and implementation of policies and NAPs on judicious antimicrobial usage. This resulted in the development of specific guidance on the development of NAPs for AMR in aquaculture. In addition, in support of the 1995 FAO’s Code of Conduct for Responsible Fisheries (CCRF), the FAO’s technical guidelines ‘Recommendations for prudent and responsible use of veterinary medicines in aquaculture’ directly addresses issues relating to the judicious use of veterinary medicines in aquaculture production and guidance on their usage targeted towards government agencies, the private sector and aquatic animal health professionals. Further guidance on the recording of antimicrobial usage in aquaculture and the surveillance and monitoring of AMR in bacteria isolated from aquatic animals aims to strengthen the capacity of national laboratories and enhance monitoring of AMR.

The importance and need for a “One Health” integrated action plan has been recently discussed by Wernli et al. which proposes a “One Health” online platform as an educational tool, as well as fully accessible database. Furthermore, from an aquaculture perspective, Stentiford et al. highlighted how integrating scientific evidence with policymaking is crucial for a sustainable aquaculture sector. The implementation of such initiatives might guide developed countries towards fulfilling their AMR NAP goals, as well as help less developed countries, move towards such goals. The overall usage of antibiotics in aquaculture should be minimised and recommendations for responsible use followed. In addition, the example set by major producing countries such as Norway should be reproduced, which, in less than 30 years, has reduced the use of antimicrobials in fish farming by more than 47 metric tonnes (MT), yet is leading the world in the production and export of aquaculture commodities.

China, the largest global aquaculture producer stands out from our analyses as the country where most aquaculture studies have been performed and advanced technologies adopted. However, China has recently recorded cases of animal-transferred colistin-resistant pathogens in humans suggesting that further implementation of an AMR NAP is needed along with an integrated surveillance system. India, with support from FAO, has established the Indian Network of Fisheries and Animal AMR (INFAAR) in 2018 to document AMR in different production systems, describe the spread of resistant bacterial strains and resistance genes, identify trends in resistance and generate hypotheses about sources and reservoirs of resistant bacteria through a structured national surveillance. Other positive examples are represented by China, Malaysia, the Philippines, Singapore and Viet Nam, where FAO’s aid in developing their NAPs is reflected in the implementation of AMR-aquaculture stewardship.

In the EURO region, the monitoring of antibiotics for farmed animals was implemented in 2009, when the European Medicines Agency (EMA) established a surveillance programme (The European Surveillance of Veterinary Antibiotic Consumption, ESVAC). However, as highlighted in this review, prophylactic use of antibiotics still occurs in some countries (especially for poultry and pigs). As a result, new legislation, approved by the European Parliament on 25th October 2018 banning preventive mass medication in animals, has been implemented on 28 January 2022, aimed at reinforcing a prudent use of antibiotics in animals and the overall containment of AMR. As for the Asian continent, the Association of Southeast Asian Nations (ASEAN) recently renewed its initiative of supporting member countries in fighting AMR from a “One Health” perspective, including the aquaculture sector. Similarly, in the Southern African Development Community (SADC), AMR represents a high-priority risk that needs to be mitigated, yet targeted interventions are still in development.

In conclusion, there is a discrepancy between the distribution of funds and the number of studies performed, and there is a clear need for future programmes in regions where aquaculture is vital for food security, for example in the AFRO and EMRO regions. Therefore, we encourage governments to sponsor national and international initiatives to promote AMR stewardship, thus avoiding a potential deadlock caused by limited external funding. Awareness campaigns, so far focused on a limited number of countries, should expand the pace of scientific advancement, while channelling knowledge to both small and large-scale producers throughout the entire value chain. Finally, the paucity of data available from multiple sources clearly highlights (a) the need for further research investments in this area, and (b) the need to standardise methodologies and data collection.

Further research is needed to get a better understanding of the source of AMR in aquatic organisms. For example, techniques like Next Generation Sequencing (NGS) would provide more information on tracing the source of the microorganism carrying AMR and also understanding the association between mobile genetic elements and gene cassettes and the AMR genes. Though expensive to carry out, NGS could help understand the direction of gene flow, for example, from aquatic organisms to human or animal pathogens or vice versa.

Increased data collection is conducive towards creating more science-based policies, which ultimately will allow for (1) sound target setting, (2) concerted monitoring and surveillance systems, and (3) targeted interventions to contain the spread of AMR via the aquaculture value chain.
Countries are encouraged to (1) fulfil their commitments by developing and/or fully implementing the AMR NAP, (2) engage in research, monitoring, and surveillance of antimicrobial usage and AMR within the aquaculture sector, and (3) collaborate at national and international level for a concerted “One Health” approach.

Not the least, when developing or renewing a NAP, governments should make sure that funding sources are available and assigned to specific activities throughout the NAP mandate. In relation to this issue, WHO has recently made available a Costing and Budgeting tool (https://www.who.int/teams/surveillance-prevention-control-AMR/who-amr-costing-and-budgeting-tool) that should be conducive towards identifying resources already available for AMR activities, as well as budgeting for new costs. Additionally, responsible authorities should be assigned for each of such activities and made accountable for their implementation.

AUTHOR CONTRIBUTIONS
Andrea Caputo: Conceptualization; data curation; formal analysis; investigation; methodology; validation; visualization; writing – original draft; writing – review and editing. Melba G. Bondad-Reantaso: Conceptualization; formal analysis; funding acquisition; methodology; project administration; resources; supervision; validation; writing – original draft; writing – review and editing. Idyda Karunasagar: Investigation; validation; writing – original draft; writing – review and editing. Bin Hao: Investigation; methodology; writing – original draft; writing – review and editing. Patricia Gaunt: Investigation; methodology; writing – original draft; writing – review and editing. David Verner-Jeffreys: Investigation; methodology; writing – original draft; writing – review and editing. Sophie Fridman: Investigation; writing – original draft; writing – review and editing. Alejandro Dorado-Garcia: Investigation; writing – review and editing.

ACKNOWLEDGEMENTS
This study was undertaken under the auspices of two projects being implemented by FAO, namely: GCP/GLO/979/NOR: Improving Biosecurity Governance and Legal Framework for Efficient and Sustainable Aquaculture Production and GCP/GLO/352/NOR: Responsible use of fisheries and aquaculture resources for sustainable development, both funded by the Norwegian Agency for Development Cooperation (Norad). We also acknowledge the support from Regular Programme funds under FAO’s strategic framework on better production and two relevant programme priority areas, that is, “Blue Transformation” and “One Health”.

DATA AVAILABILITY STATEMENT
Data derived from public domain resources.

ORCID
Andrea Caputo https://orcid.org/0000-0002-7353-9168
Melba G. Bondad-Reantaso https://orcid.org/0000-0002-2380-3549
Idyda Karunasagar https://orcid.org/0000-0001-8783-1269
Bin Hao https://orcid.org/0000-0002-5284-7946
Patricia Gaunt https://orcid.org/0000-0001-8360-304X

REFERENCES
52. FAO. FAO Project FMM/RAS/298/MUL: Strengthening capacities, policies and national action plans on prudent and responsible use of antimicrobials in fisheries: Final Workshop, Concorde Hotel, Singapore, 12–14 December, 2017; Rome.


**SUPPORTING INFORMATION**

Additional supporting information can be found online in the Supporting Information section at the end of this article.