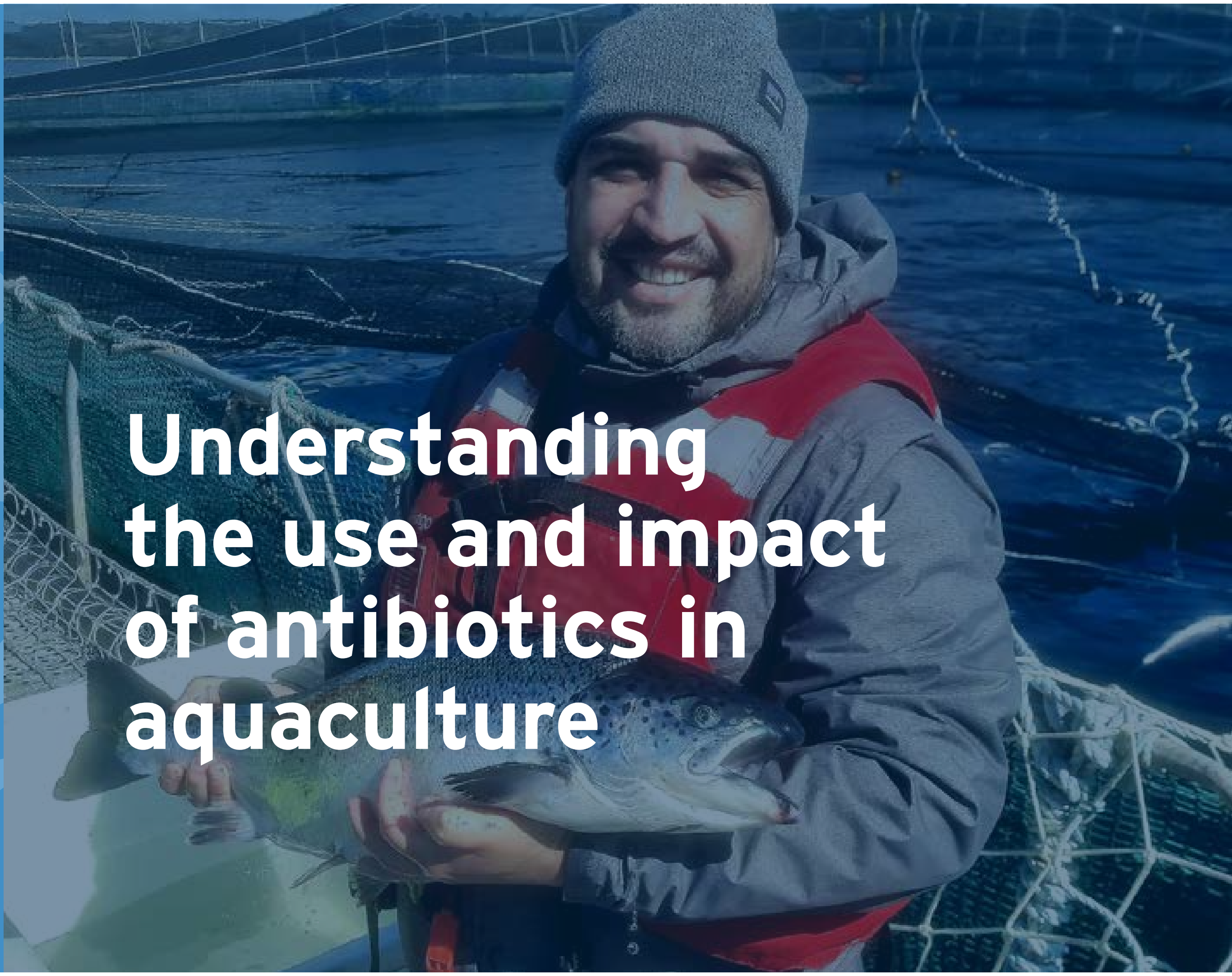
Monterey Bay Aquarium



Understanding the use and impact of antibiotics in aquaculture

A workshop series of the Antimicrobial assessment on Global Aquaculture Production (AGAP)

SEAFOOD SUSTAINABILITY SERIES | VOLUME 1 | 2023

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ACRONYMS

AGAP	Antimicrobial assessment on Global Aquaculture Production
AMR	Antimicrobial resistance
FAO	Food and Agriculture Organization of the United Nations
WHO	World Health Organization

Contents

Purpose

This report addresses the state of antimicrobial use in aquaculture, focusing on knowledge gaps, establishing ecological and human health impact indicators, and developing the basis to standardize impact assessment methodology under the One Health approach. While the scope aimed to cover the entire value chain of aquaculture products, the focus was kept on finfish and crustacean aquaculture of all scales in various production systems and environments (e.g., marine net pens, hatcheries, brackish water ponds, and freshwater cages). In these types of aquaculture, antimicrobial use is often described as excessive.

Remarks

Relevant information about the impact of antimicrobials in aquatic ecosystems was identified. This includes: that cyanobacteria are the most affected organisms; the disruption of biogeochemical cycles and the recycling of essential nutrients that considerably affect ecosystem services (e.g., nitrogen); and that there is relevant information missing regarding the effects on other aquatic organisms. In addition, it was noted that there is a need for pollution assessments and methods for this evaluation.

The main findings regarding socioeconomic drivers and behaviors are related to the need for more robust and transparent regulatory frameworks to guide farmers. Particularly at the small-scale level — these producers currently lack access to and understanding of certification schemes and disease risk management. Therefore, they operate under a lower level of technical knowledge, reflected in their antimicrobial use practices. There is a need for training on antimicrobial use and access to veterinary and extension services to educate governments, producers, and investors to work together to reduce antimicrobial use to enhance animal health and well-being, and food safety.

The Antimicrobial assessment on Global Aquaculture Production initiative established relevant networking and collaboration opportunities with global institutions and experts, proposing an initial risk assessment framework that aquaculture stakeholders can utilize to better estimate the potential environmental impacts associated with antibiotic use at the farm and regional levels.

Executive summary

Aquaculture production is crucial in providing food to the growing human population and is projected to increase rapidly through 2030. But aquaculture producers face a significant challenge derived from the intensification of aquaculture activity in the context of climate change. The main challenges include sustainable raw materials sources, decreased seabed and watercourses impacts, and managing bacterial diseases. Prevention and control of bacteria include using antimicrobials, which can potentially cause environmental and human health impacts. Antibiotics are one of the most convenient and cost-effective tools, with few alternatives available to control bacterial diseases.

Marine net pen salmon enclosure in Chile. Photo by the Monterey Bay Aquarium.

The Monterey Bay Aquarium and the World Bank aimed to address the state of antimicrobial use in aquaculture, establishing the basis to identify ecological impact indicators, characterizing the social drivers of the use and misuse of antimicrobials, and developing the basis for a standardized methodology to measure the ecological impact under the One Health approach. To accomplish these aims, a series of workshops were conducted supported by recognized researchers of diverse fields, covering the following areas: 1) antimicrobial ecological impacts in aquaculture, 2) the socioeconomic perspective, 3) antimicrobial resistance role in aquaculture, and 4) identifying monitoring tools that can be adapted and implemented across sectors and countries. The meetings focused on identifying the knowledge gaps and strengthening the antimicrobial impacts assessment methodology by establishing the basis to distinguish ecological impact indicators and thresholds. Experts attended the workshops and shared experiences regarding effective antimicrobial use governance, socioeconomic considerations, and monitoring approaches. The overall process produced a series of recommendations related to antimicrobial resistance and aquaculture on the need to further explore the environmental impact of antimicrobial use in aquaculture, socioeconomic drivers, and methodological aspects.

The Antimicrobial assessment on Global Aquaculture Production series' results allowed the establishment of an initial risk assessment framework that aquaculture stakeholders could utilize to better estimate the potential environmental impacts associated with antibiotic use at the farm and regional levels. The framework allows assessments on the type and degree of expected impacts from antimicrobial use in a specific socioecological, regional, and farm-based context. In addition, the risk framework and accompanying standardized sampling protocols may be used on the ground in projects to establish baselines of current impacts, decrease antimicrobial use, and increase the well-being and health of animals, humans, and ecosystems — useful for NGOs, benefactors, governments, and the aquaculture industry, among others.

Introduction

The international community has recognized the aquaculture industry through the United Nations 2030 Agenda for Sustainable Development, highlighting its contribution to food security. Aquaculture production is crucial in providing food to the growing human population and is projected to increase rapidly through 2030.

Bacterial disease presents a significant challenge to aquaculture producers globally. Control methods include using antimicrobials, often without knowing the potential environmental and human health impacts. Antimicrobials include antifungals, antiseptics, antibiotics, and other agents used to eliminate microorganisms. Antibiotics are the most common chemicals used in aquaculture.

Antimicrobials are overused and misused (e.g., growth promotion); not all of the chemical is used, and it stays in the environment where it can reach non-target organisms and contribute to antimicrobial resistance (AMR); (Rigos and Troisi 2005; Rodgers and Furones 2009). Notably, there is a need to better understand the different uses given to antimicrobials and the role that aquaculture production plays in developing AMR, a global health concern (Hendriksen et al. 2019). The World Health Organization (WHO) has estimated that curing AMR-related diseases could cause global economic losses worth $100 trillion by 2050.

Antimicrobials are widely used in shrimp and fish farms to prevent and treat diseases. In shrimp farms, antimicrobials are commonly used in hatcheries to treat diseases such as hepatopancreatic necrosis disease, which has been associated with Vibrio parahaemolyticus. In fish aquaculture, antibiotics are the most frequent method to manage common diseases that affect animal health and welfare and cause substantial losses, such as Piscirickettsia salmonis and Renibacterium salmoninarum in salmon farms and to treat Edwarsiella species in tilapia farms. Antibiotics are widely used without adequate preventive tools such as vaccines or preventive sanitation management.

It is well known that antimicrobials introduced to the environment: persist in water and sediment, contaminate non-target organisms, cause AMR, potentially accumulate throughout the food chain, stay in the environment, and cause detrimental effects on the ecosystem, as well as impact markets and consumers — as the final products can contain antimicrobial residuals. From the broad spectrum of antimicrobials, the antibiotics amoxicillin and ciprofloxacin are part of a "watch list" of emerging pollutants that affect the aquatic environment. Others, such as tetracyclines — the most commonly used in animals and humans, and oxytetracycline — widely used in aquaculture, lead to antibiotic resistant bacteria. However, the occurrence and consequences of antimicrobials in the environment are still unclear, and it has become a worldwide concern.

The presence of antimicrobials in the environment depends on the drug's pharmacokinetic profile; for instance, some antimicrobials have poor bioavailability after oral administration. Given the impact of antibiotics in terrestrial and aquatic environments, it is essential to understand antibiotic degradation. For example, fluoroquinolones are not easy to degrade due to their high stability and persistence in the environment. Therefore, there is a need for better policies for antimicrobial use, misuse, and discharge (Lulijwa et al. 2019).

There are no global standards for assessing the ecological impact of antimicrobial use in aquaculture. The Food and Agriculture Organization of the United Nations (FAO) states there is a lack of surveillance monitoring systems, harmonization of sampling, testing methods, and available data that could compare programs across regions. FAO has published guidelines for AMR monitoring and surveillance in agriculture for some Asian countries that have been gradually implemented. The guidelines proposed sampling methods for AMR monitoring and surveillance, target population and pathogens (determined by each country), and surveillance approach (diseased/infected aquatic species) for the Asia region.

Although several different methodologies have been tested, their results have been context-specific and have limited applicability across species, regions, or production systems. There is a global need to establish standard methodologies and tools to understand the impact of antimicrobial use in aquaculture, as FAO (2019) suggested. The methodology development is not the only area that benefits from further research. While there is a general understanding of what drives the use and misuse of antimicrobials in aquaculture, there are critical data gaps in antimicrobial usage (amount and type) across sectors and how they are distributed among big producer countries. There is a lack of records, analysis, metrics, and governmental actions to obtain this information and a need for scientific studies to assess the impacts of antimicrobial use on the ecosystem.

A novel study published by Alvarado-Flores et al. (2021) compiled scientific evidence on different chemicals used in fish farms, such as antibiotics, anesthetics, disinfectants, and antiparasitics, the exposure, and the potential environmental effects. They evaluated 21 active principles used in freshwater fish farming. The results revealed that 12 of the active principles showed high ecological risk to aquatic organisms, with 19 active chemical compounds having a high risk to at least one trophic level.

The world is currently concentrating on controlling the plastic contamination crisis as the most pressing visible environmental issue, inland and in the ocean. Necessary global actions have reduced contamination by banning certain plastics and promoting recycling. In contrast, little is known about antimicrobial pollution derived from anthropogenic activity, including urbanization and aquaculture. It is important to gather relevant knowledge to understand antimicrobial impact on ecosystems to be able to take appropriate actions to reduce and ban antimicrobial use.

Hendriksen et al. (2019) suggested metagenomics as an effective method for determining AMR occurrences in human populations. This technique uses short-read next-generation sequencing data that brings numerous benefits, such as identifying bacterial species and quantifying thousands of transmissible resistance genes simultaneously in one sample, among others.

Antimicrobial exposure for long periods generates resistance. Plasmids can hold antibiotic resistant genes that can be transferred to other aquatic bacteria or fish pathogens. DNA extraction is used to identify the occurrence and dissemination of antibiotic resistant genes. Other scientific studies based their research on quantitative real-time PCR (qRT-PCR), RNA isolation, and bacterial DNA extraction through standard techniques such as HPLC or ELISA tests for antibiotic detection in the various matrices.

Identifying the problem and searching for a solution

Due to the lack of information and the gaps previously stated, the World Bank, in collaboration with the Monterey Bay Aquarium, created the Antimicrobial assessment on Global Aquaculture Production (AGAP) initiative. A series of workshops were conducted to better understand: 1) the role aquaculture production plays in the impact of antimicrobials on the environment, 2) the drivers of its use and misuse in aquaculture, particularly at the smallholder level, and 3) the need to standardize the assessment of the ecological impact of antibiotic use in aquaculture in a way that can be adapted to country- and production-specific contexts.

There is global concern about the interconnectivity between antimicrobial use, AMR, and animal and human health. Therefore, it is essential to incorporate the One Health approach as the most appropriate strategy to address the issues.

> "One Health is an integrated, unifying approach that aims to sustainably balance and optimize the health of people, animals and ecosystems. It recognizes the health of humans, domestic and wild animals, plants, and the wider environment (including ecosystems) are closely linked and inter-dependent." WHO (2021)

The AGAP initiative focused on the state of antimicrobial use: addressing knowledge gaps, establishing ecological, socioeconomic, and human health impact indicators, and developing a standardized impact assessment methodology under the One Health approach. The workshops were opportunities to discuss the knowledge gaps with the attending experts, which strengthened the antimicrobial impact assessment methodology by establishing ecological indicators and thresholds. The experts shared experiences regarding effective antimicrobial governance, socioeconomic considerations, and monitoring approaches in aquaculture. The results allow the development of a future action plan, including fieldwork on selected aquaculture-relevant countries, and include suggestions to NGOs, society, governments, and the aquaculture industry.

The AGAP initiative covered the entire value chain of aquaculture products, focusing on finfish and crustacean aquaculture of all scales in various production systems and environments (e.g., marine net pens, hatcheries, brackish water ponds, and freshwater cages). In these types of aquaculture, antimicrobial use is often described as excessive. The workshops leveraged the expertise in each session to produce material that, together with a literature review, is the basis for two published outputs.

Objectives

- Assess existing knowledge gaps on antimicrobial use in aquaculture
- Identify ecological measurable impact indicators and thresholds
- Identify existing socioeconomic factors, effective governance mechanisms, and monitoring tools to be implemented across sectors
- Assess the relationship between the use of antibiotics in aquaculture and antibiotic resistance
- Identify antimicrobial monitoring tools that can be adapted and implemented across sectors and countries
- Prospect methods to perform laboratory and field tests or pilots, considering different scenarios (e.g., production and antibiotics), assess AMR, and improve aquaculture sustainability

The process

An extensive range of literature and current publications were reviewed to evaluate the preliminary information available, the main issues, and the existing knowledge gaps. As a result, four main topics were selected for discussion: ecological impacts of antimicrobials, socioeconomic drivers of use and misuse of antimicrobials, AMR, and methodological recommendations for measuring impacts.

A group of 55 experts selected across different fields worldwide were invited for an individual interview to: 1) gather information, 2) identify central issues, and 3) suggest and recommend guidelines for assessing questions related to impact threshold, drivers, economics, and methodology to assess the impact at different levels under the One Health approach. The experts were then invited to be part of the four thematic discussion panels according to their areas of expertise. The areas of expertise cover ecology, microbiology, economics, aquaculture, antibiotic resistance, and other environmental sciences.

State of antimicrobial use in aquaculture: main findings

From the discussion, a theoretical framework was produced (fig. 1) showing the ecological impact of antimicrobials used in aquaculture, a review of the occurrence, ecotoxicological effects, and a risk assessment.

The impact of antimicrobials on the aquatic ecosystem is a complex problem to solve, and there is limited information regarding the ecological effects. In this context, separating the impacts generated in fresh water and the marine environment is essential — given the different exposure routes, scenarios, and species potentially affected.

Effective surveillance is needed to enhance AMR, specifically: identifying the problem, monitoring progress toward goals, and understanding the adverse effects and toxicity leading to microbial resistance. Antimicrobials mainly affect microorganisms, but we also need to know how this disruption can affect other organisms. Bacteria studies in the laboratory differ from environmental impact assessments; therefore, it is difficult to extrapolate to real environmental situations.

Currently, there are conceptual assessment frameworks that can be applied to measure possible effects. However, different scales and scenarios must be incorporated into the evaluation. As a result, conducting field tests or pilots is needed to obtain valuable data. The expected persistence and effects in the environment vary according to the chemical structure of the antibiotics. Therefore, case studies in areas where antimicrobials are highly used are needed to better understand the impacts.

The risk of antimicrobial dispersion to humans is potentially higher in fresh water than in marine ecosystems due to differences in the volumes of antimicrobials in the water and the access humans have to fresh water, leading to greater contact probability. Pollution assessments by monitoring sediment and water column changes at high-dispersive sites are complex. There is a need for policies and regulatory structures to promote antimicrobial safe use and optimal efficacy. When policies and regulations are unavailable, a prospective risk assessment framework for antibiotics should be incorporated into country policies. Currently, in some countries in the European Union, the USA, and Japan, these studies already exist in early stages. Nevertheless, more discussion is needed, and harmonizing risk assessment methods would be beneficial.

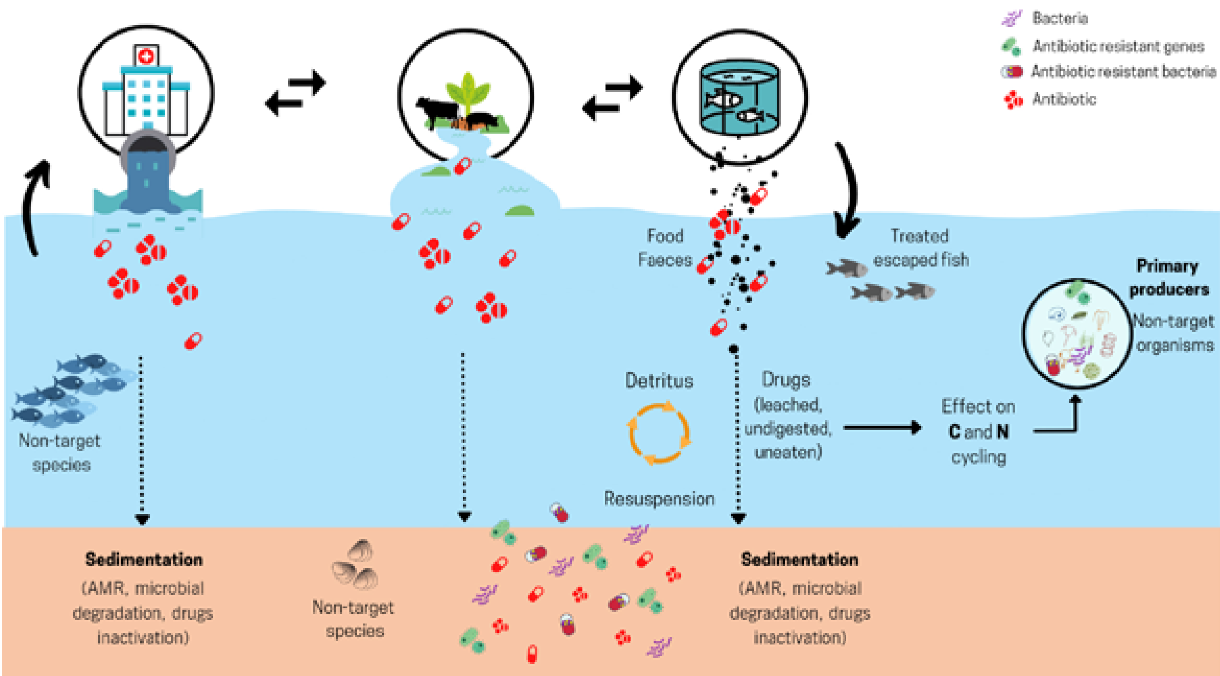

Figure 1. The theoretical framework of potential antimicrobial spread in aquatic ecosystems. Adapted from Danner et al. (2019) and Rigos and Troisi (2005).

Socioeconomic drivers and their interaction on aquaculture society

Antimicrobial use, misuse, and overuse are not purely technical issues; other concerns for understanding socioeconomic drivers such as marketing, production, food safety, prescription, and its interaction with aquaculture society for effective governance must be covered. The discussion around socioeconomic drivers and effective governance mechanisms of antimicrobial use followed three main objectives: 1) identify the use, misuse, and overuse of antimicrobials under different aquaculture production systems, 2) identify socioeconomic drivers for antimicrobial use in aquaculture production systems, and 3) assess existing knowledge gaps.

Some main findings to foster sustainable changes in behaviors related to antimicrobial use were identified and covered diverse areas of the socioeconomics perspective. If we compare aquaculture with land-based production such as poultry or pigs, aquaculture has a lower proportion of antibiotic use, including growth promoters. It is important to note that there is considerable inaccuracy in antibiotic use data since the source is business sales, not users (i.e., farmers).

It was noted that small- and large-scale producers in developing countries are often not trained or regulated on antimicrobial use. They often get easy access to products and sell products containing antimicrobials that are not identified as such. As a result, they are not appropriately applied. Additionally, there are poor cost-effective alternative tools for managing disease or subsidies for small-scale farms to implement good practices in aquatic animal health. This coincides with insufficient aquatic health professionals, as occurs in parts of Asia and Africa.

The role of aquaculture in antibiotic resistance development

The workshops explored the relationship between the use of antimicrobials in aquaculture and AMR development under the One Health approach with three main objectives:

1. Identify the role of antimicrobial consumption in aquaculture in the rise of AMR under different production scenarios, including the transfer to humans

2. Identify methodologies to incorporate in monitoring and surveillance programs

3. Assess existing knowledge gaps

The panel detected that it is still challenging to identify if aquaculture is a source or a vehicle of AMR, for example, generation or proliferation. Nevertheless, it does not mean that it is not happening. Therefore, questions remain on the relative magnitude of AMR contributions from aquaculture compared with other land-based animal growing systems, such as pig farms or poultry, and with human medicine.

Sanitation is critical in reducing bacterial infections and other consequences, e.g., using chemotherapeutics or lost revenue. Sanitary conditions should be prioritized to avoid the use of antimicrobials and complemented with regulations — the best method to control and reduce antimicrobial use in land-based animal farms. However, antimicrobial use in aquaculture production is hard to control, especially in an open system.

Another relevant factor is certification. Currently, some certification schemes such as the Aquaculture Stewardship Council, Best Aquaculture Practices, and GLOBALG.A.P. guarantee the product's quality and sustainability, and mandatory certification could reduce antimicrobial use. However, the percentage of certified sustainable products is significantly lower in aquaculture goods than in other sectors. There is little opportunity to differentiate products through pricing, and small-scale producers cannot access certification. In fisheries, organic produce is more expensive because large federal programs do not support it, while land-based agriculture does have support therefore corn, soy, and other cash crops are cheaper for the consumer.

People's practices and behavior, irrespective of the food farmed, challenge profit against health (Polianciuc et al. 2020). For example, a recent study by Shao et al. (2021) revealed that there is little regulation on purchasing antimicrobials in China. In other Asian countries, farmers directly applied active antimicrobial compounds to feed and water with inappropriate dosages, meaning they have direct contact with the chemicals. Consequently, this leads to direct health issues, such as allergies.

It was summarized that there is no model for risk assessment to address the exposure of AMR in the different nodes of the One Health approach (ecosystems, animals, and humans). However, Denmark is an interesting case study of how this could advance. The country has well-connected data with 3 to 4 antimicrobial classes — susceptibility data and pathogen type is well documented, which is not the case for other antimicrobial consumer countries (Personal comm. Anders Dalsgaard).

Methodologies for measuring the impact of antimicrobial use in aquaculture

While discussing the methodology, monitoring, and surveillance for assessing the impacts of antimicrobial use in aquaculture at different levels, some questions were pointed out: what should be measured, how to measure it, and at which point the productive landscape should be estimated, what surveillance elements should be considered, is there information already available that we should take into consideration, how to establish the frequency of sampling, analysis, or monitoring, and what are the appropriate methods of analysis and sampling?

Significant gaps exist in assessing antimicrobials in ecosystems, as there are no known antimicrobial concentrations in the natural environment. What makes it more difficult is that chemicals stay in the environment, and antimicrobials can travel from freshwater systems and reach coastal areas, where it is known that chemicals then persist in sediments, contrary to what happens in the water.

Suggestions arose to extrapolate models from terrestrial animals to create a baseline. Yet, as no database is available to use models in aquaculture systems, it is, therefore, necessary to begin trials to get the essential data to run models (trials could be done in the field or a mesocosm).

There are early experiments with microcosms in Thailand where antimicrobial concentrations were evaluated from 10 to 100 mg/L. However, more knowledge is needed to consolidate the data. A recent investigation conducted by González-Gaya et al. (2022) evaluated the effects of aquaculture and antibiotics in marine ecosystems. The study showed the moderate persistence of flumequine and oxytetracycline in marine sediments and how uptake by macrofauna and benthic environment contamination and residual concentrations of antibiotics contribute to a selection of resistant genes. This investigation could be used as a basis to propose pilot studies.

Gaps and challenges

Significant knowledge gaps were identified through the development of the AGAP initiative. Gaps identified in the ecological impact approach could be divided into four fundamental areas: methodological and technical, regulatory, socioeconomic, and the role of AMR in aquaculture (Table 1).

Salmon site in Chile. Photo by the Monterey Bay Aquarium.

TABLE 1. THE MAIN GAPS IDENTIFIED THROUGH THE DEVELOPMENT OF THE AGAP INITIATIVE

Antimicrobial use and ecological impacts: methodological and technical
There is no standardized methodology to measure impacts in the field — the current methodology is costly and thus prohibitive
Passive monitoring of antimicrobials in the environment
Cumulative impact modeling (e.g., chronic discharge or multiple point sources)
Establishment of impact thresholds and lack of validated framework by which to establish those thresholds
Validated models are necessary to measure impacts and provide recommendations to stakeholders
Antimicrobial use and ecological impacts: regulatory aspects
Lack of internationally agreed and validated Environmental Quality Standards (both ecotoxicological and antimicrobial resistance) for antimicrobial discharge
Lack of standard risk assessment methodology applicable to developing countries
Specific protection goals for ecosystem and human protection should be delineated
Social and economic gaps identified
Wild fish issues: there is not enough information about antibiotic impacts on wild fisheries
Lack of knowledge on how the disruption of macrobiotics may affect other organisms
Behavioral drivers and the level of trust in different aquaculture systems
Farm neighbors' knowledge about antimicrobial management among farms can mitigate control and effects. However, there is currently no information available
Gaps identified in the role of antimicrobial resistance on aquaculture
Although new scientific research has come out, there are still significant antimicrobial resistance knowledge gaps
Understanding the relative magnitude of aquaculture in comparison with other land-based animal growing systems and antimicrobial (over-) consumption by humans
How to determine aquaculture systems boundaries
Improving knowledge of the role of antimicrobial resistance and the steps to reach this goal
Find out how to categorize systems in terms of risk
Gathering more detailed information about antibiotic resistance genes to develop methodologies

Recommendations

This section summarizes the advice, suggestions, and improvements that resulted from the process. It is presented in two main sections. The first section, **"Recommendations from the workshop series"** contains suggestions provided by experts from the four workshops covering ecological perspective, socioeconomic drivers, the role of aquaculture, and the methodological elements. The second section, **"Time to take One Health action: ocean, animal, and human health"** provides advice from experts and key messages for stakeholders.

Recommendations from the workshop series

Ecological perspective

Other indirect impacts on ecosystems must be evaluated and considered for environmental assessments, such as ecological processes mediated by environmental bacteria, escaped fish moving away, and benthic fauna affected by antimicrobial precipitation. There is agreement that ecological evaluation criteria for antimicrobials should be incorporated into country policies. As there is no clear information regarding the ecological effects caused by antimicrobials, separating the impacts generated in fresh water and the marine environment is suggested.

Information on the antimicrobial type used, quantities, use patterns, and emissions are vital in measuring ecological impacts, and since the evaluation framework exists, it is recommended to do a field test or pilot assessment to obtain valuable data and measure impacts.

Environmental Quality Standards (ecotoxicological and AMR) for environment and emissions can be used as guidance in aquaculture. Existing methods for deriving Environmental Quality Standards and Environmental Risk Assessments are sufficient to reduce the risk of undesired toxicities, AMR, and improve aquaculture sustainability. Although, the current Environmental Risk Assessment used for drug approval is insufficient to assess environmental risk.

Socioeconomic drivers

Several recommendations and actions were suggested to improve the knowledge base of socioeconomic drivers of the use and misuse of antimicrobials. It is important to understand the regulatory frameworks in different countries and production scales, and take stock of existing tools that could be leveraged to address the identified socioeconomic drivers of antimicrobial use.

One of the main observations was that each country's legal framework must be considered to assess whether new aquatic animal health regulation is required, which is not valid in most cases. Regulatory guidelines are required as legal tools to regulate the commercialization and use of antibiotics — many countries do not have such regulatory frameworks in place. Considering alternatives for bacterial disease control instead of blanket bans would be more effective in reducing antimicrobial use and promoting good practices. Different sources supply antibiotics, so labeling products could be a solution for providing information and promoting standardization.

More investment in technology is recommended to control diseases, especially technology that is environmentally friendly and ecologically compatible with production. It is recommended to improve diagnostic tools, predictors, alternatives to antimicrobials, and limited-spectrum antibiotics for specific diseases. It is imperative to assess these tools and focus them while considering segmentation of the producers and targeted markets, and implementing them differently in small-scale versus large-scale productions. Few tools for disease management at the small scale exist; in-country extension services could be an essential element to improve access to aquatic animal health tools considering that small-scale aquaculture facilities are often remotely located.

Drivers of antibiotic use may be related to risk management. It is important to understand these risks maintaining a whole value chain perspective (value chain analysis and vulnerability). For example, hazard analysis and critical control point thinking are used to identify issues (e.g., drugs, resistance, or diseases), risk sources, hotspots, and risk practices. Therefore, it is recommended to consider the value chain.

The role of aquaculture for AMR

Allowing classes of antimicrobials for which resistance is more likely to happen via point mutation instead of genes that are more easily mobilized (or known to be already present on plasmids) is favored. This would limit the real potential for co-selection of resistance against antimicrobials, which is essential in human medicine on plasmids or integrons. Thus, gathering more information on the theme to assess AMR and treat every class of antibiotics independently and specifically is suggested.

The hazard identification for AMR risk needs to be considered based on the overall abundance, which becomes an "AMR hazard" when it comprises microorganisms and the determinants of resistance. The World Organization for Animal Health defines a hazard as a resistant microorganism or resistance determinant that emerges from using a specific *antimicrobial agent* in *aquatic animals*. Thus, it could also be considered AMR in non-pathogenic bacteria. A recommendation from the discussion would be to gather more information to answer relevant questions regarding this issue.

Issues vary when approached from a consumer, producer, or processor lens; and, as such, must be approached with all due consideration. Whenever possible, the solution is to reduce antimicrobial use. From a One Health perspective, integrating (from human health water quality perspectives) and developing a standard set-up from human to animal regulations are critical and required for managing control.

Methodological elements for measuring impacts

From the methodological perspective, some aspects need to be covered to answer questions about the main gaps in the relationship between humans and antimicrobial use in aquaculture, such as: the steps to reach those gaps, prioritize factors as first steps, and methodological elements that need to be incorporated into monitoring and surveillance programs.

Some surveillance elements were suggested, such as trophic web, benthic respiration, primary production, oxidative stress, environmental DNA, deposition, oxygenation, and metagenomics and metabarcoding as testing methods.

Regarding monitoring sites, some areas were recommended, such as fjords, areas affected by urbanization, away from anthropogenic impacts, high-intensity aquaculture, and marine protected areas as reference sites. In the case of salmon aquaculture areas, monitoring performance could be carried on before or after production. Suggested trials for assessing antimicrobial impacts should be carried out on specific sites; however, it is critical to determine the capacity of the ecosystem to handle antimicrobials.

Time to take One Health action: ocean, animal, and human health

Actions to minimize the impacts of antimicrobial use are urgent and necessary from a One Health perspective. Ensuring the health of animals, humans, and the environment must be integrated and prioritized among stakeholders, including the public, private, and academic sectors. Although some countries have made progress in implementing regulatory and voluntary actions to reduce impacts, significant gaps remain in many countries where aquaculture is a significant economic activity or where the foundations for sustainable aquaculture are being laid. Because of the impacts of climate change, tackling disease control through sustainable tools is imperative to ensure animal welfare, food security, food safety, and ecosystem health.

Based on the results of these reports, the recommendations are based on five pillars: **T**raining, **I**nvestment, **M**onitoring, **E**valuation, and **R**estriction (**T.I.M.E.R**). Specifically, for governments, farmers, investors, and scientists, the recommendations are summarized below.

Governments

1. Implement or strengthen the regulation for creating a registry of antimicrobial use at the producer level. Implement a data collection system on antimicrobials according to production type and technology access. Increase the transparency and availability of data on antimicrobial use for adequate analysis and creation of indicators to establish actions for continuous improvement.
2. Restrict access to antibiotics by producers, regulating the informal sale of medicines.
3. Demand the proper labeling of veterinary products considering their indications for use, precautions, and final disposal.
4. Increase official veterinary services, especially among small farmers, to implement disease prevention management plans.
5. Increase training for official entities and farmers on the efficient and responsible use of antimicrobials. Participate in intergovernmental bodies to exchange experiences related to the use of antibiotics, initiatives for good practice, food safety, and ecosystem impacts.
6. Encourage communication and awareness of the efficient and responsible use of antimicrobials to the different stakeholders of the supply chain.
7. Create incentives to reduce the use of antibiotics at the farm level. This should include subsidies to small farmers to access veterinary services, certifications, and production with low consumption of antibiotics.
8. Encourage and fund science to establish doses, withdrawal periods, and specific maximum residue limits in antibiotics use.
9. Incorporate ecological evaluation in the registration of antibiotics used in aquaculture.
10. Implement programs to monitor the consumption and impact of antibiotics drugs in aquaculture.

Farmers

1. Record the use of antibiotics and the efficacy results each time an antibiotic treatment is carried out, facilitating traceability between different production stages.
2. Train field personnel in the early identification of diseases and the proper use of antibiotics, including their final disposal.
3. Acquire medicines in authorized places and duly registered, avoiding informal sources of commercialization.
4. Comply with the dosage and periods of safeguards established for the antibiotics according to the diagnosis and culture system. If this information does not exist, antibiotic suppliers must generate this information.

5. Whenever possible, incorporate diagnostic and technological tools for disease prevention with a regional perspective. Remotely incorporate diagnostics and technical support when farms are in remote areas.
6. Participate in gradual and collective actions to reduce the consumption of antimicrobials.
7. Facilitate access to data and facilities to scientific institutions to increase knowledge to reduce the impact of antimicrobial use or other initiatives aimed at improving their use.

Scientists

1. In collaboration with governments and producers, design and implement standard methodologies for estimating the impacts associated with antibiotics, including acceptable ecosystem limits, the definition of hazards, and risks considering different protection subjects (animal, ecosystem, and human).
2. Creation of metrics and models that allow establishing the cumulative impacts of the use of antimicrobials and mitigating their effects.
3. Validation of species-specific doses, retention periods, and maximum residue limits.
4. Creation and maintenance of field measurement data repositories of antimicrobials and their impacts, including baselines.
5. Understand the contribution of aquaculture to the phenomenon of AMR, suggesting limits for each node under different scenarios.

Investors and donors

1. Support and finance preventive solutions to diseases, mainly those related to vaccination, genetics, and early diagnosis of diseases, especially those applied to small farmers.
2. Discourage investment in producers that do not meet the requirements for proper use of antibiotics, segmenting according to size and type of producer.
3. Invest in connectivity technologies for farming sites to enable remote diagnostics, training, and technical assistance.
4. Support initiatives and science that aim to reduce the impact of antimicrobials, favoring a collective perspective under the principles of One Health.

Taking action: the Chilean case

Chile has witnessed a massive increase in farmed salmon, resulting in an increase in fish susceptibility to diseases. Based on available data, the country reached the highest antimicrobial consumption per harvested ton worldwide[1]. In 2016, Chile took actions to reduce antimicrobials currently approved in the salmon industry from six to four (florfenicol, oxytetracycline, erythromycin, and tilmicosin). The same year, Chile began an official program to certify marine salmon farms as antimicrobial-free and created a voluntary certification in farms with low use of antibiotics. In 2019, an agreement between the Monterey Bay Aquarium and the Chilean industry created the Chilean Salmon Antibiotic Reduction Program, which is a broader collaboration initiative to improve practices, and where the salmon industry aims to reduce antibiotics use by 50 percent by 2025.

[1] Miranda et al. (2018)

Final thoughts

Understanding the ecological effects of antimicrobial use in aquaculture involves finding suitable, measurable indicators and appropriate thresholds to assess impacts on aquatic ecosystems. This is challenging as there is a lack of information.

The most affected organisms in aquatic environments are bacteria and cyanobacteria in sediments and in the water column. Carbon and nitrogen cycling could be affected, but there is limited information on this subject. There is also not enough information about environmental or ecological impacts on other aquatic organisms (e.g., macrofauna). Therefore, pollution assessments are needed, including information regarding monitoring plans on water, sediments, and ideally on some organisms such as wild fish, escaped fish, and shellfish that should be considered. Fresh water and marine water must be treated separately as they are different systems, and specific environmental conditions could be found.

The information about antimicrobial quantities, patterns, and emissions is essential for managing purposes to measure antimicrobial ecological impacts. In the case of regulatory knowledge, there is a lack of information regarding ecotoxicology and AMR in discharge. Indeed, there is current information on Environmental Quality Standards for environment and emissions that could be used as guidance in aquaculture. However, the current Environmental Risk Assessment for drug approval is insufficient to assess environmental risk, particularly in developing nations where it does not exist. Hence, ecological evaluation criteria for antimicrobials should be incorporated into country policies.

Regarding socioeconomic drivers and behaviors, the workshops acknowledged the complexity of the issue and a clear need to develop research and the knowledge base further to identify critical drivers and the actions to control them. The main findings relate to the need for more robust and more precise regulatory frameworks to guide farmers, particularly small-scale farms, as it is these producers who currently lack access and understanding of certification schemes and disease risk management. They, therefore, operate under a lower level of technical knowledge, which is reflected in their practices in antimicrobial use.

Extension services should play a critical role in the enforcement of regulations, in strengthening good practices in the use of antimicrobials, and in developing and implementing better monitoring tools for risk management. Interventions would likely benefit from the producer and market segmentation, as different scales and target markets (i.e., domestic or international) determine drivers, risks, and thus the potential impact of different measures and actions.

Further, implementing a ban on highly critical products could yield little to no results. Instead, an approach based on improving communication — thus trust — between regulators and producers, for which extension services might be instrumental, should strengthen support received by small-scale producers, resulting in better disease management practices and a clearer understanding of antimicrobials as a productive tool, thus reducing their unnecessary use.

Overall, the AGAP initiative established relevant networking and collaboration opportunities with global institutions and experts. The workshops covered some areas of concern for antimicrobial use in aquaculture — such as impacts on the aquatic ecosystem — but others were not addressed. There is still no detailed understanding of ecological impact nor the level of impact acceptability. Among identified gaps, there are still some limitations regarding well-documented information, solid knowledge associated with antimicrobial use, and good connection data. For example, the risks for the spread of resistant bacteria from aquaculture in aquatic systems to people living in the vicinity of the production need to be better understood.

References

Alvarado-Flores, C., Encina-Montoya, F., Tucca, F., Vega-Aguayo, R., Nimptsch, J., Oberti, C., Carmona, E.R., Luders, C. 2021. "Assessing the ecological risk of active principles used currently by freshwater fish farms." *Sci Total Environ* 775, 144716.

Danner, M.C., Robertson, A., Behrends, V., Reiss, J. 2019. "Antibiotic pollution in surface freshwaters: Occurrence and effects." *Sci Total Environ* 664, 793-804.

FAO, 2019. *Monitoring and surveillance of antimicrobial resistance in bacteria from healthy food animals intended for consumption. Regional Antimicrobial Resistance Monitoring and Surveillance Guidelines – Volume 1.* Bangkok, p. 84.

González-Gaya, B., García-Bueno, N., Buelow, E., Marin, A., Rico, A. 2022. "Effects of aquaculture waste feed and antibiotics on marine benthic ecosystems in the Mediterranean Sea." *Sci Total Environ* 806, 151190.

Hendriksen, R.S., Munk, P., Njage, P., van Bunnik, B., McNally, L., Lukjancenko, O., Roder, T., Nieuwenhuijse, D., Pedersen, S.K., Kjeldgaard, J., Kaas, R.S., Clausen, P., Vogt, J.K., Leekitcharoenphon, P., van de Schans, M.G.M., Zuidema, T., de Roda Husman, A.M., Rasmussen, S., Petersen, B., Global Sewage Surveillance project consortium, Amid, C., Cochrane, G., Sicheritz-Ponten, T., Schmitt, H., Alvarez, J.R.M., Aidara-Kane, A., Pamp, S.J., Lund, O., Hald, T., Woolhouse, M., Koopmans, M.P., Vigre, H., Petersen, T.N., Aarestrup, F.M. 2019. "Global monitoring of antimicrobial resistance based on metagenomics analyses of urban sewage." *Nat Commun* 10, 1124.

Lulijwa, R., Rupia, E.J., Alfaro, A.C. 2019. "Antibiotic use in aquaculture, policies and regulation, health and environmental risks: a review of the top 15 major producers." *Reviews in Aquaculture* 12, 640-663.

Miranda, C.D., Godoy, F.A., Lee, M.R. 2018. "Current Status of the Use of Antibiotics and the Antimicrobial Resistance in the Chilean Salmon Farms." *Front Microbiol* 9, 1284. https://doi.org/10.3389/fmicb.2018.01284

Polianciuc, S.I., Gurzău, A.E., Kiss, B., Ştefan, M.G., Loghin, F. 2020. "Antibiotics in the environment: causes and consequences." *Medicine and Pharmacy Reports* 93, 10.

Rigos, G., Troisi, G.M. 2005. "Antibacterial Agents in Mediterranean Finfish Farming: A Synopsis of Drug Pharmacokinetics in Important Euryhaline Fish Species and Possible Environmental Implications." *Reviews in Fish Biology and Fisheries* 15, 53-73.

Rodgers, C., Furones, M. 2009. "Antimicrobial agents in aquaculture: practices, needs and issues", In: *The use of veterinary drugs and vaccines in Mediterranean aquaculture.* CIHEAM: Zaragoza, Spain, pp. 41-59.

Shao, Y., Wang, Y., Yuan, Y., Xie, Y. 2021. "A systematic review on antibiotics misuse in livestock and aquaculture and regulation implications in China." *Sci Total Environ* 798, 149205.

WHO, 2021. *Tripartite and UNEP support OHHLEP's definition of "One Health".* https://www.who.int/news/item/01-12-2021-tripartite-and-unep-support-ohhlep-s-definition-of-one-health [accessed on the 30th April 2022].

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