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Typology of interventions for antimicrobial use and antimicrobial resistance in aquaculture systems in low- and middle-income countries

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ABSTRACT

Indiscriminate antimicrobial use (AMU) in aquaculture to treat and prevent diseases is common and can lead to the emergence of antimicrobial-resistant micro-organisms, potentially impacting public health and connected ecosystems. This study aimed to develop a typology to classify and characterise interventions to reduce AMU in aquaculture and identify points of action. Seventeen aquaculture and animal health professionals in Asian and African countries were interviewed to gather information on characteristics of interventions in different contexts to develop a typology. Seven types of interventions were defined: (i) legislation and regulations; (ii) industry rules and standards; (iii) voluntary instruments; (iv) commercial technology and alternatives to antimicrobials; (v) on-farm management; (vi) learning and awareness-raising; and (vii) activities with co-benefits. Types were based on intervention function, scope of implementation, implementer, compulsion, strength of the intervention, AMU/antimicrobial resistance (AMR) objective and stakeholder to influence. For each type, examples were described and discussed. The most common interventions to address AMU and AMR were legislative and regulatory frameworks and voluntary instruments, including National Action Plans. Interventions addressing AMU/AMR specifically were scarce. Other interventions focused on indirect effect pathways to AMU and AMR reduction aiming to improve good aquaculture practices, disease prevention and improved management. Monitoring and evaluation of these interventions were found to be rare, only present for interventions driven by development projects and international agencies. The presented typology of existing strategies and interventions addressing AMU/AMR in aquaculture systems can guide evaluation of AMR-sensitive interventions that promote responsible AMU, and informs the design and implementation of future interventions.

1 Introduction

Aquaculture is the fastest growing animal-source food sector in low- and middle-income countries (LMICs) [1]. Seven of the top ten aquaculture producers are LMICs and their contribution to the global trade of aquaculture is growing [2]. Almost 90% of aquaculture production takes place in Asia, where the sector is exposed to production risks linked to farming conditions, disease, as well as environmental and social sustainability of value chains [3–5]. Increased production to meet the demand for aquaculture products has been achieved through intensification of aquaculture systems, which is an important driver for the emergence and spread of infectious diseases [6,7]. As a consequence, indiscriminate antimicrobial use (AMU) to treat or prevent diseases and as growth promoters to increase productivity is common and often compensates for management and biosecurity deficiencies [8].

Indiscriminate AMU in aquaculture has been associated with the development of antimicrobial resistance (AMR) [9–12]. Multiple pathways and hotspots for human exposure to antibiotic residues in aquaculture systems have been described [13,14], where aquatic environments act as a gateway for AMR emergence and spread [15,16]. Antimicrobials are usually applied in feed, potentially leading to the excretion of non-absorbed chemicals from fish into the water, or direct contamination of water if feed is not

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consumed. The active metabolites in sediments can exert selective pressure on bacterial diversity in the aquatic environment and promote AMR development and exchange of plasmids between resistant and non-resistant bacteria. Furthermore, aquaculture facilities are often open systems interconnected with the natural water environment through irrigation or flow of water, producing wastewater discharges and receiving effluences from other systems. Consequently, the use of chemicals and biological products in aquaculture systems has the potential to impact surrounding ecosystems [17–21], as the presence of antibiotic residues in the environment has been demonstrated in several studies [22,23].

Globally, the consumption of antimicrobials in aquaculture has been projected to increase by 33% from the year 2017 to 2030 [24]. These estimates differ greatly between regions and present a wide uncertainty interval owing to lack of reliable data on AMU in this sector. Current AMU estimates, evidence of ecological pathways, and rapid growth of the sector in LMICs highlight the need to develop monitoring and surveillance systems for disease, AMU and AMR in aquaculture, and to understand potential mitigation measures and interventions to address the challenge. Evidence from LMICs shows that AMU (i.e. aquatic health management) is associated with a lack of diagnosis or diagnostic failure, and aquaculture producers, including input suppliers, prioritise treatment over prevention and biosecurity [8]. Therefore, implementing interventions that focus on prevention is considered critical. In LMICs, regulations and their enforcement for the responsible use of antimicrobials are often inefficient or absent, and monitoring and surveillance systems for AMU and AMR are lacking or not systematically implemented [25]. Currently, there is no comprehensive framework to understand the current landscape of interventions in LMICs that could mitigate the risks of AMR in the aquaculture sector.

This study aimed to classify and characterise interventions applied in aquaculture systems to address AMR in selected LMICs. The objectives of this study were (i) to generate a typology of interventions to address AMU and AMR in aquaculture and (ii) to describe the characteristics of existing interventions.

2 Methods

2.1. General overview

To develop and apply the typology, the steps in Fig. 1 were followed.

2.2. Conceptualisation

In this study, an intervention was defined as any form of action designed to address a challenge aiming to obtain a desired change in the system (reduction of AMU and AMR). This encompassed policies (i.e. actions on the part of responsible authorities that enable or support interventions), instruments, programmes and projects. Different frameworks were consulted to identify relevant elements of an intervention: (i) the International Classification of Health Interventions[1] (ICHI) that characterises an intervention by target population, action and means of implementation; (ii) the intervention function and policy categories based on the desired behaviour of the stakeholder [26]; (iii) the Nuffield ladder of interventions that categorises interventions by virtue of their relative intrusiveness in people's lives [27]; and (iv) choice- and non-choice-based interventions to animal health compensation and biosecurity [28]. Based on these, the elements to be investigated were: interventions (action); target population or stakeholder; objective of the intervention; stakeholders involved; delivery mechanism; compulsion; and strength of the interventions (Fig. 2). These formed the basis for the development of the interview guide (Supplementary File 1). In addition, the literature review included a search on methods to conduct a typology analysis. We considered information provided on any intervention in the systems that can lead to a reduction of AMU and AMR in aquaculture systems.

2.3. Study participants and data collection

The aim of the interviews was to obtain information to characterise interventions and to understand the context that can influence their implementation and effectiveness. Initial scoping discussions with experts in the aquaculture field guided the selection of countries and identification of professionals with knowledge in the sector. Country selection was based on aquaculture being a big contributor to GDP or a rapidly growing contributor to food security, diversity of aquaculture systems, AMU, and potential AMU and AMR interventions. It included Asian countries, where aquaculture value chains have undergone decades of transformation, and African countries, where domestic commercial aquaculture is well established or is emerging as a key contributor to domestic food security, with potential for intensification and increasing use of antimicrobials. The selection of professionals was purposive, following a snowball process. First, established collaborators in international and academic institutions with experience in the aquaculture sector and knowledge about AMU/AMR and interventions were contacted and interviewed. Second, other national experts in public and private institutions in Egypt, Zambia, Uganda, Kenya, Bangladesh and Vietnam were interviewed. The interviewees provided information about countries of their professional experience. Interviews were conducted in English using online meeting applications and face to face; hand-written notes were taken throughout the process. Ethical approval for the interviews was granted by the Royal Veterinary College's Ethics Committee. Before each interview, an overview introduction to the study was provided by email and consent was obtained. Discussions covered the policy landscape in each setting as well as past, current and future activities to address the AMU challenge. During the interviews different themes emerged, including the problem of AMU in different settings, perceived drivers of AMU, and challenges for aquatic health and management, and for aquaculture in general. Participants shared relevant documentation and sources of information, such as scientific studies, reports and other online sources that could contain information on interventions and policies, during and after the interview.

2.4. Data editing, analytical process and typology development

Interview notes were screened to identify information on interventions and variables for analysis. Table 1 shows the variables used to create typologies, and the categories for each variable. These variables reflected the elements in Fig. 2, and other variables were added based on information obtained. For example, *intervention function* was categorised as 'restricting' when the intervention is designed to limit or restrain a particular behaviour, such as imposing bans or regulating and limiting AMU, or as 'enabling' for those interventions promoting desirable behaviours that can lead to a reduction in AMU/AMR risks, such as by providing structural changes, resources and information that can facilitate that behaviour. The *scope* refers to the reach of the implementation; it was categorised as 'international', 'national', 'sub-national' or 'local'. *Implementers* reflected the stakeholder involved. *Compulsion* was categorised as compulsory (e.g. policies such as regulations and industry requirements) or as voluntary when participa-

[1] Defines intervention as 'an act performed for, with or on behalf of a person or a population whose purpose is to assess, improve, maintain, promote or modify health, functioning or health conditions'. [https://mitel.dimi.uniud.it/ichi/docs]

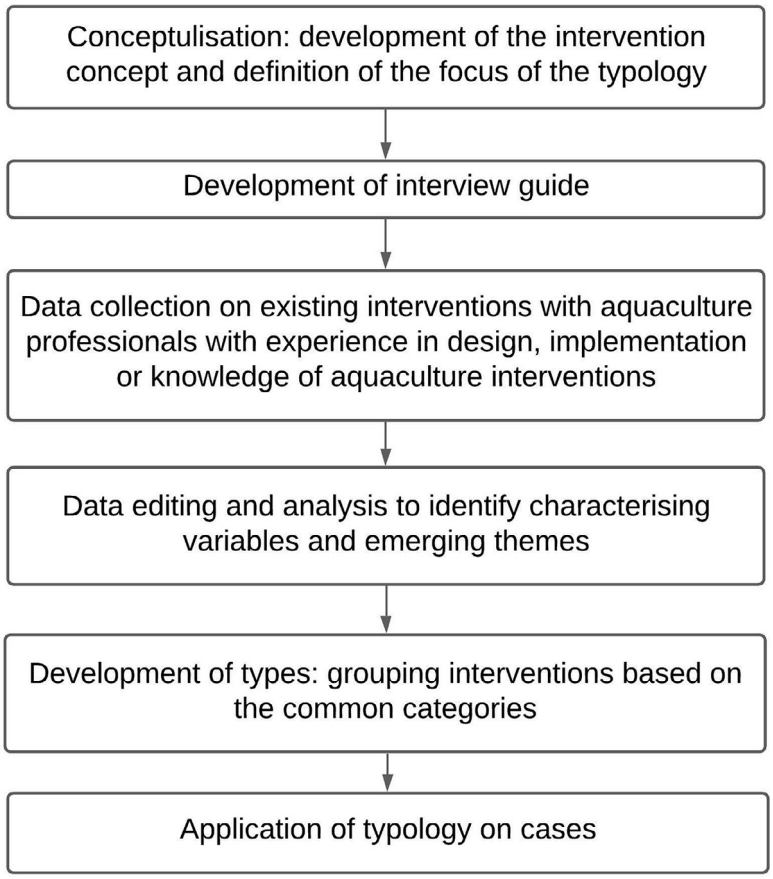

Fig. 1. Overview of the methodological process.

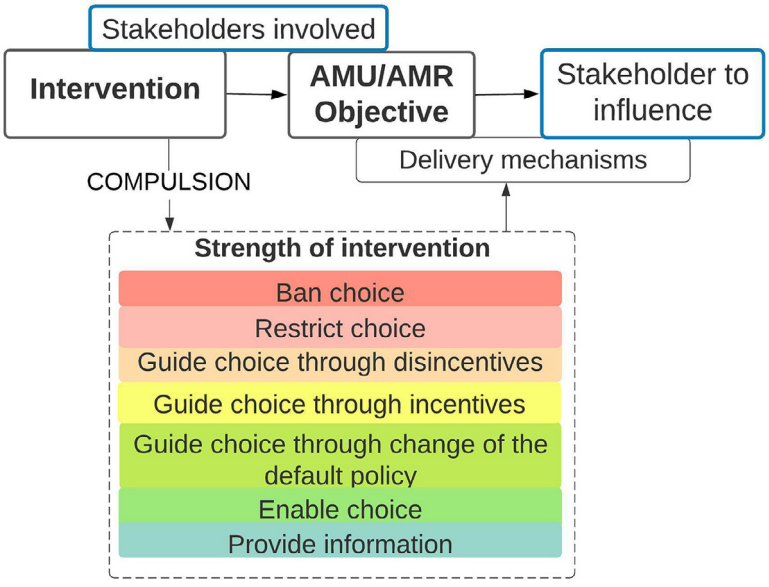

Fig. 2. Elements of the intervention investigated. AMU, antimicrobial use; AMR, antimicrobial resistance.

tion, enrolment or engagement was optional. The *strength of the intervention* was categorised following the grades proposed by the Nuffield ladder of interventions [27]. The *effect path* was classified as 'direct effect' when aimed at addressing AMU/AMR reduction or promoting responsible and adequate use; as 'indirect effect' when interventions addressed drivers of AMU/AMR related to disease management and aquaculture practices; and as 'distant effect' when the objective was to generate data, influence decision-making, mobilise resources, or create commercial gains due to export markets access or sale of alternatives to antimicrobials. Finally, the *stakeholder to influence* refers to the target of the intervention.

For all interventions described by interviewees, categories and patterns were identified across interventions and the types generated. Information on mechanisms of delivery of implementation

Table 1
Variables and corresponding categories to characterise interventions and to create types.

Variable	Categories
Function	Restricting: limit or restrain a particular behaviour; Enabling: promote a desired behaviour directly or offer favourable conditions (e.g. structural changes, such as more capacity, more resources)
Scope	International; national; sub-national; local
Implementer	Authorities; industry; R&D institutions; academia; NGOs
Compulsion	Compulsory; voluntary
Strength	Restriction or elimination of choice (high); use of incentives or disincentives to guide choice (medium); guide choice through change of the default policy (low); enable the uptake of a product or technology (low); provide information (low)
AMU/AMR effect path	Direct: reduce and control use of antimicrobials or promote adequate use of antimicrobials; Distant: generate evidence or information to decision-makers; agenda-setting and influence decision-makers; Indirect: prevent, control disease, improve health; promote improved management
Stakeholder to influence	Producers; service providers; input providers; agrifood industry; policy-makers; consumers; others

R&D, research and development; NGO, non-governmental organisation; AMU, antimicrobial use; AMR, antimicrobial resistance.

Table 2
Characteristics of the participants.

Characteristic	*n*
Country	
Uganda	1
Kenya	2
Zambia	2
Egypt	3
India	1
Bangladesh	1
Vietnam	1
Various (includes more than one of the above countries)	6
Organisation–stakeholder	
Authorities–policy-maker	1
Research in public laboratories	3
Academia	5
International R&D organisation	5
International organisation	1
Industry	2
Role in interventions	
Participation in design of AMU or AMR interventions	6
Implementation of AMU or AMR interventions or policies	8
Participation in design of general aquaculture interventions to improve aquatic health	9
Implementation of general aquaculture interventions to improve aquatic health	7
Knowledge of AMU or AMR interventions	10
Knowledge of aquaculture health interventions	17

R&D, research and development; AMU, antimicrobial use; AMR, antimicrobial resistance.

was considered for description of interventions but not for categorisation, grouping and elaboration of groups.

3 Results

3.1. Respondents

Seventeen interviews were conducted with professionals from academia, international organisations, government and the private sector, providing information about Egypt, Uganda, Kenya, Zambia, Bangladesh, India and Vietnam (Table 2). Through these interviews, information about 50 interventions with potential effect on AMU and AMR were described. Respondents provided information about similar interventions in different countries, such as national and international policies. However, some interventions were specific for a country, a species or a region, particularly in the case of research projects and programmes.

3.2. Proposed typology and its application to existing antimicrobial use/antimicrobial resistance (AMU/AMR) interventions from Asian and African countries

The proposed typology comprises seven intervention types characterised by seven variables (Table 3).

Table 4 provides the results of the application of the typology to a range of AMU and AMR interventions reported by interviewees. Key findings are summarised by type below.

3.2.1. Type 1: legislation and regulation

Interviewees from all countries mentioned the existence of legislative and regulatory frameworks implemented by authorities (extension services and inspectors) that refer to aquaculture medicinal products within the Animal Health or Fisheries Acts and regulate use. Common aspects reported were the existence of a list of banned antimicrobial products as well as inspection of input providers, pharmacies and production plants. Problems with enforcing the regulations were common, sometimes due to a lack of human resources or lack of stringent consequences when inspection is applied. Other regulations referred to the control of dis-

Table 3
Typology of interventions based on the variables identified.

Type	Function	Scope	Implementer	Compulsion	Strength	AMU/AMR effect path	Stakeholder to influence
1. Legislation and regulation	Restricting	National; international	Authorities	Compulsory	Ban or restrict choice	Direct; indirect	Agrifood industry Service providers Input providers Producers
2. Industry rules and standards	Restricting/ enabling	National; international	Industry; authorities	Voluntary/ compulsory [a]	Disincentives, incentives	Distant; direct	Agrifood industry
3. Voluntary instruments for development	Enabling	National	Authorities	Voluntary	Voluntary instruments (e.g. guidelines)	Distant	Policy-makers Authorities Producers
4. Commercial technology and alternatives to antimicrobials	Enabling	Local	R&D institutions; academia; Industry	Voluntary	Enable or facilitate the uptake of a product or technology; Provision of information	Indirect; distant	Producers
5. On-farm management interventions	Enabling	Local	R&D institutions; academia	Voluntary	Non-fiscal incentives; Voluntary activities; Enable uptake; Provision of information	Indirect	Producers
6. Learning and awareness-raising	Enabling	Local	R&D institutions; academia	Voluntary	Provision of information	Direct; indirect	Producers; Service providers; Consumers; General public
7. Activities with co-benefits for AMU and AMR and aquatic health	Enabling	Local	R&D institutions, academia	Voluntary	Voluntary activities Provision of information	Distant	Various – aquatic health decision- and policy-makers

AMU, antimicrobial use; AMR, antimicrobial resistance; R&D, research and development.
[a] Industry rules and standards can be voluntary, but not participating might result in loss of or a barrier to market access.

eases, such as the import of seed, and enforcing residues plans for export markets. Furthermore, regulations were described to outline plans for residues testing for export products as a result of international trade agreements.

3.2.2. Type 2: industry rules and standards

Certification standards were described to have contributed to AMU reduction in Asian countries for some commercial producers. Developed to establish a benchmark for sustainable production, these also included the use of chemical products and good management practices. Different transnational and national labels (e.g. VIETGAP in Vietnam) were mentioned, mainly with involvement of industry. Accordingly, different stakeholders in the agrifood business, such as importing retailers or exporting stakeholders in the value chain, demand standards for producers to comply with, set up by third-party companies. These interventions were compulsory for some segments of producers; failure to comply can limit market access to producers.

3.2.3. Type 3: voluntary instruments for development

These were voluntary and complex interventions, composed by different interventions and characterised by addressing AMU/AMR or aquatic health from a distant point, with multiple potential targets in the system. Interviewees from Egypt, Zambia, Vietnam and Bangladesh referred to a series of instruments, guidelines and plans aiming to inform other interventions, such as National Action Plans (NAPs) or strategies. Vietnam presented the most advanced plan for targeted interventions that included surveillance activities, awareness-raising and enhancement of One Health governance. Egypt and Zambia were undergoing the first stages towards interventions to mitigate AMR with the assistance of the Food and Agriculture Organization of the United Nations (FAO), who provided training and planning for the competent authorities in the country to take responsibility and assure sustainable implementation. These activities with stakeholders were described to be oriented primarily towards aquatic health following a holistic and systems approach tackling the root of the problem of AMU and AMR. Bangladesh reported to be developing a 'national fish health management strategy' including interventions regarding the use of aquatic medicinal products. Other instruments described were development projects providing funds or loans for infrastructure for improved aquatic health, capacity building or development of policy tools (e.g. regulations or guidelines).

3.2.4. Type 4: commercial technologies and alternatives to antimicrobials

Different products were mentioned as being used as prophylactics in aquaculture systems. The most common products listed were probiotics and vaccines. Probiotics were described as widely commercialised by private companies and used extensively in commercial systems with distribution through pharmacies, drug sellers or private companies distributors at the farm level. However, the effectiveness of these products is unknown. Many products lacked credibility regarding their mode of action and efficacy claims. Use of vaccines was mentioned in several interviews as 'the best method proven to decrease use of antimicrobials to very low levels'. On the other hand, some respondents expressed scepticism, arguing that mortality in these systems can be the result of a complex combination of different microbial agents. Moreover, they observed that vaccines increase production costs substantially and that it was unknown whether farmers would be willing to make such investment, or could afford it. Finally, they expressed concerns on the regulation of vaccination in LMICs that are characterised by a wide variety of systems in terms of species, sizes and levels of commercialisation, and often face problems of enforcement (as described above). Nevertheless, some interviewees

Table 4
List of interventions discussed by respondents.

	Intervention description	Country[a]	Species[b]	AMU AMR[c]	Function	Scope	Implementer	Compulsion	Strength	AMU/AMR effect path	Stakeholder to influence	Described barriers/ constraints	Effects reported; evaluation information
Type 1	**Legislation and regulatory frameworks**												
Domestic legislation and regulation	Different instruments to regulate the sale and use of antimicrobials. Lists of allowed products, dose, withdrawal time (e.g. no less than 3 weeks), role of the veterinarian as only professionals allowed to prescribe antibiotics and need to keep records. E.g. in Vietnam: Decree 39/2017/ND-CP dated 4/4/2017 on animal feeds without addition of antibiotics from 2020	EG, VT, BG, UG	General	yes	Restricting	National	Authorities	C	Ban or restrict choice	Direct	Agri-food industry; Service providers; Input providers; Producers	- Lack of enforcement, in inspection, problems with chemical shops licensing, poor quality of drugs. - Producers rarely respect dose and withdrawal times in species for domestic consumption	- - In practice, anybody can take products over the counter without prescription, and products are sold by professionals without license, sale of poor quality of AM. - No evaluation reported
	Decision No. 2625/QĐ-BNN-TY dated 21/6/2017 on '*National Action Plan for AMU management and AMR prevention in animal husbandry and aquaculture* (2017-2020)' by the Minister of Ministry of Agriculture and Rural Development. Objective: 'Mitigate the risk of antibiotic resistance in public health through controlling the antibiotic usage in livestock production and aquaculture in Vietnam'	VT	General	yes	Restricting	National	Competent authorities	C	Ban or restrict choice	Direct	Service providers Input providers	No information	No evaluation system reported
	The Fisheries and Aquaculture Bill *('A person or establishment shall not obtain veterinary therapeutic products and medicinal premixes for inclusion in fish feeds unless they are approved for use by the Chief Fisheries Officer in consultation with the Chief Veterinary Officer'*.The previous Fish Act did not regulate aquaculture activities.	UG	General	yes	Restricting	National	Authorities	C	Ban or restrict choice	Direct	Service providers Input providers Producers	Unknown stage of implementation	No evaluation system reported
	Ban of seed import to prevent Epizootic ulcerative syndrome (EUS) and Tilapia lake virus (TiLV) Control and prevention of diseases	ZA	Tilapia	no	Restricting	National	Authorities	C	Ban or restrict choice	Indirect	Agri-food industry; Input providers	No information	No evaluation system reported

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Table 4 (*continued*)

	Intervention description	Country[a]	Species[b]	AMU AMR[c]	Function	Scope	Implementer	Compulsion	Strength	AMU/AMR effect path	Stakeholder to influence	Described barriers/ constraints	Effects reported; evaluation information
Legislation and regulation - driven by international trade	Residue monitoring plans for residues of veterinary drugs to be exported to other countries (e.g. EU, SA, US, etc.). Industry participates (exporters)	VT,EG, IN	Export	yes	Restricting	National	Authorities; (e.g. EC inspectors)	C	Ban or restrict choice	Direct	Agri-food industry;	Mainly limited to exporters	Outcomes among countries depending on the capacity and industry characteristics (feasibility to implement). No formal evaluation system, but proxy data can be obtained from systems like, the *Rapid Alert System for Food and Feed* (RASFF)*; or the US Food and Drug Administration (*FDA*)*
	Fish Inspection and Quality Assurance	KE	Export	yes	Restricting	National	Authorities	C	Ban or restrict choice	Direct	Agri-food industry;	No information	No evaluation system reported
	Regulation of establishments processing fish and fishery products for export, setting procedures for testing antibiotic residues, limits	IN	Export	yes	Restricting	National	Authorities	C	Ban or restrict choice	Direct	Agri-food industry;	IN and BG reported to face challenges to implement these systems due to the heterogeneity of industry.	No evaluation system reported
	Sanitary and Phytosanitary measures outlined by WTO/OIE	All	Export	no	Restricting	International	Authorities	C	Ban or restrict choice	Direct	Agri-food industry;	No information	No evaluation system reported
	Sanitary PS measures laid by the East African Community	UG	Export	no	Restricting	International	Authorities	C	Ban or restrict choice	Direct	Agri-food industry;	No information	No evaluation system reported
Type 2	**Industry rules and standards**												
Certification standards – market driven	National standard for Good Aquaculture Practices, such as VietGAP, which was developed based on FAO technical guidelines on aquaculture certification.	VT	General	no	Restricting	National	Authorities	V	Incentives	Indirect; Distant	Producers; Agri-food industry	Not recognised by importers, so producers of fish aiming to export were reported to not be interested – efforts for better alignment starting. Limited to exporters.	Evaluation by NGOs of compliance with control points.(2011) https: //tinyurl.com/mdhc2h56
	Transnational Certification Standards (ASC,GLOBAL G.A.P., BAP) – Main objective is the social and environmental sustainability but include good aquaculture practices related to health and restrictions in the use of antibiotics. The participation is voluntary at the start but failure to comply with the standard rules lead to the removal of certification and loss of market access.	VT, IN, BG	Export	no	Restricting use of AM; enabling access to markets	International	Industry	V/C*	Disincentives; incentives	Distant; Indirect: Direct	Producers; Agri-food industry;	Uptake driven by the export requirements and consumer and industry demands. Affect the access to markets. Irregular uptake.	Evaluation systems in place. No evaluation information obtained.

(*continued on next page*)

Table 4 (*continued*)

	Intervention description	Country[a]	Species[b]	AMU AMR[c]	Function	Scope	Implementer	Compulsion	Strength	AMU/AMR effect path	Stakeholder to influence	Described barriers/ constraints	Effects reported; evaluation information
Type 3	**Voluntary instruments for development**												
National Action Plans (NAPs) for AMR	Aim: establish and enable regulation and pro-active action towards the AMR control. More advanced stage in South-East Asian countries (e.g. VT); EG, ZA and UG in early stages, working with authorities for the implementation. Focus areas for intervention (2016-2020): (a) Improve awareness on AMR and related threats, (b) Develop capacity for surveillance and monitoring of AMR/AMU in food and agriculture, (c) Strengthen governance related to AMR/AMU in food and agriculture, (d) Promote good practices in food and agriculture systems and the prudent use of antimicrobials. Designed by FAO. Described to follow a One Health approach, common plan for agriculture, livestock and aquaculture, joint committees, enhanced communication. In Vietnam: Linked to surveillance activities (Type 7), improved legislation and regulation (Type 1), good aquaculture practices (Type 5), awareness campaigns (Type 6), improved governance (legislation and regulatory framework)	VT, EG, ZA, UG	General	yes	Enabling	National	Authorities; R+D institutions	V	Voluntary instrument (guide-lines)	Distant	Policy makers; Authorities; health providers, producers	Lack of information about how One Health principles are realised, e.g. integration, decision-making processes between agencies communication feedback, etc	No information available, in some countries only at early stages. Available evidence in (Chua et al. 2021, including human and animal systems

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Table 4 (*continued*)

	Intervention description	Country[a]	Species[b]	AMU AMR[c]	Function	Scope	Implementer	Compulsion	Strength	AMU/AMR effect path	Stakeholder to influence	Described barriers/ constraints	Effects reported; evaluation information
Progressive Management Pathway (PMP)	To assist countries, as systematic frameworks for planning and monitoring risk reduction strategies for control of major livestock and zoonotic diseases. Developed by FAO	All	General	no	Enabling	National	Authorities; R+D institutions	V	Voluntary instrument (guide-lines)	Distant	Authorities	No information	No evaluation system reported
FAO-PMP-AMR	FAO *Progressive Management Pathway for Antimicrobial Resistance* (FAO-PMP-AMR) - Guide to assist countries in the implementation of NAPs	All	General	yes	Enabling	National	Authorities; R+D institutions	V	Voluntary instrument (guide-lines)	Distant	Authorities	No information	No evaluation system reported
National Fish Health Management Strategy	The strategy address general fish health, and included aquatic medicinal products as a component of the plan.	BG	General	no	Enabling	National	Authorities; R&D institutions, industry	V	Voluntary instrument (guide-lines)	Distant	Authorities; health providers, producers	No information	No evaluation system reported. Unknown stage of implementation
Development projects: loans or large–funds for investment in infrastructure and capacitation for fish health and food safety and development of plans, as well as other activities	*Zambia Aquaculture Enterprise Development Project* (ZAEDP) – Loan includes investment in infrastructure and activities promoting animal health management, control of disease (see in Type 7)	ZA	General	no	Enabling	National	Various (depending on the component: authorities, R&D institutions, etc.)	V	Voluntary instrument	Distant	Policy makers; authorities; R&D institutions	No information	Evaluation report available (supplementary file 2) Information about detailed output indicators achieved by 2019: - no specific AMU or AMR indicators. https://projectsportal.afdb.org/dataportal/VProject/show/P-ZM-AAF-002
	Fleming Fund programme: UK funded, aims to strengthen the legal and regulatory framework, build infrastructure, providing funds to support the uptake and implementation of NAPs including fellowships training (BG), investment in infrastructure. In Bangladesh: Fish Inspection and Quality Control Laboratory – Savar; In Vietnam, a pilot project committed to collectively develop a clear implementation and operational plan to deliver the actions set out under this NAP for AMR (2015)	BG, VT	General	yes	Enabling	National	Private sector, R&D institution, Academia	V	Voluntary instrument	Distant	Policy makers; authorities; R&D institutions	No information	Outcomes of project in evaluation by independent private consultancy Itad. Evaluation Questions are focused on: generation of data at country-level, alignment and coherence of AMR investments, sustainability, use of AMR data for policy/regulation and behaviour change, sharing of data at international level, and value for money

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Table 4 (*continued*)

	Intervention description	Country[a]	Species[b]	AMU AMR[c]	Function	Scope	Implementer	Compulsion	Strength	AMU/AMR effect path	Stakeholder to influence	Described barriers/ constraints	Effects reported; evaluation information
Type 4	**Commercial technologies and alternatives to antimicrobials**												
Prophylactic health products (PHPs)	Promotion of the use of PHPs including probiotics, prebiotics, immunostimulants, bioflock, by health providers and agri-food industry. In Bangladesh, a systematic survey of shrimp grow-out farms, hatcheries, and PHPs sellers, identified up to 200 products.	KE, IN, VT, BG, EG	General		Enabling	Local	Industry	V	Enable the use of a product; Provide information	Distant	Producers	Lack of regulatory framework reported in most countries. Manufacturing quality problems similar to AM: ineffective active ingredient concentrations, contamination with bacteria pathogenic to humans, fraudulent inclusion of antibiotics. presence of antimicrobial resistance genes. (IMAQulate project)	Research projects - (Ali et al. 2021; Haque et al. 2021)
Vaccines	Different projects were described to be in current development of bacterial vaccines in Egypt and Vietnam. Characterised by the collaboration of national research centres, universities and private sector	EG, VT	Catfish; Tilapia	no	Enabling	Local	Academia; R&D institutions (National research centres); Industry	V	Enable the use of a product; provide information	Indirect	Producers	In development stage in most LMICs. Described as unfeasible due to high costs in comparison to other products and currently impractical (individual application)	Diverse projects in experimental stages.
Improved genetics	Dissemination Genetically Improved Abbassa Nile tilapia (GIANT – G9) – selected for faster growth from seed to harvest and high survival rate. Provided to 38% of the total Egyptian fish farmers. Distributed for free by WorldFish to broodstock centres, which disseminated fry to 40% hatcheries	EG	Tilapia	no	Enabling	Local	R&D institutions (WorldFish and National research centres)	V	Enable the use of a product; provide information	Indirect	Producers	Project limited to a limited number farms, not scaled up	In references, available impact assessment: higher production parameters- differences between areas, hypothesised to be due to other management factors.
	Genetically Improved Farmed Tilapia (GIFT)	BG, VT	Tilapia	no	Enabling	Local	R&D institutions (WorldFish and National research centres)	V	Enable the use of a product; provide information	Indirect	Producers	Failure in countries like VT due to lack of understanding by designers and implementers on farmer's needs, lack of adaptation to the context, insufficient genetic resources	Positive effect in other Asian countries in improving resilience of tilapia, but no evidence on disease impact and AMU.

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Table 4 (*continued*)

	Intervention description	Country[a]	Species[b]	AMU AMR[c]	Function	Scope	Implementer	Compulsion	Strength	AMU/AMR effect path	Stakeholder to influence	Described barriers/ constraints	Effects reported; evaluation information
Other	Other alternatives: biocontrol agents, plant extracts, antioxidants - At the research project stage	UG,EG	General	no	Enabling	Local	R&D institutions; Academia	V	Enable the use of a product; provide information	Indirect	Producers	No information	No information
	Bacteriophage therapy - At the research project stage	UG,EG	General	no	Enabling	Local	R&D institutions (National research centres); Academia	V	Enable the use of a product; provide information	Indirect	Producers	No information	No information
Type 5	**On-farm management interventions**												
Research projects and programmes	**Best management practices (BMPs)** Included measures to prevent a situation of poor water quality, leading to stress and mortalities. Uptake of improved genetics and training (up to 2,400 fish farmers). Part of IEIDEAS project: *Improving Employment and Incomes through the Development of Egypt's Aquaculture Sector* launched in 2011 by WorldFish. Supported by: Swiss Agency for Development and Cooperation	EG	Tilapia	no	Enabling	Local	R&D institutions (WorldFish), NGO (CARE Egypt)	V	Enable or facilitate the uptake of a technology	Indirect	Producers	Scaling up implementation on more farmers is highly dependent on donor support.	Uptake of improved genetics and training (up to 2,400 fish farmers). Good reception when yields increased. More efficient feed utilisation and higher profitability: US$16,000 in extra profit generated per farm and US$27m total value added by the project. https://tinyurl.com/5aj5m577
	Farm trial testing efficacy of probiotics in feed and in water , IMAQulate project *'Evaluating Costs and Benefits of Prophylactic Health Products (PHPs) and Novel Alternatives on Smallholder Aquaculture Farmers in Asia and Africa'":*	BG, IN, KE	General	no	Enabling	Local	R&D institutions; industry; Academia	V	Enable or facilitate the uptake of a technology	Indirect	Various	No information reported.	Available: https://tinyurl.com/3ch4pykw
	FISH, CGIAR Research Program on Fish Agri-Food Systems (from 2017 to 2022), with a cluster on fish health	ZA, BG, EG	Tilapia	no	Enabling	Local	R&D institutions (WorldFish)	V	Enable or facilitate the uptake of a technology	Indirect	Producers	No information reported.	No information reported.
	PESCA project , to guide improvement of policies to increase fish production through cage aquaculture with reduced impacts on the water environment of the African Great Lakes (AGLs) and promoting use of those practices through adaptive research	UG, ZA, KE	Tilapia	no	Enabling	Local	Academia; R&D institutions	V	Enable or facilitate the uptake of a technology	Indirect	Producers	No information	No information
	Use of close systems	EG	Tilapia	no	Enabling	Local	Academia and R&D institutions (WorldFish)	V	Enable or facilitate the uptake of a technology	Indirect	Producers	No information reported.	No information reported.

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Table 4 (*continued*)

	Intervention description	Country[a]	Species[b]	AMU AMR[c]	Function	Scope	Implementer	Compulsion	Strength	AMU/AMR effect path	Stakeholder to influence	Described barriers/ constraints	Effects reported; evaluation information
Type 6	**Learning and awareness-raising**												
Awareness campaign	Campaign about AMR through digital communication. The intervention was informed by a survey and investigation of effective ways of implementation; broadcasted on different media platforms	BG	General	yes	Enabling	Local	Academia and R&D institutions (WorldFish)	V		Provision of information	Direct	Producers, General public	No information	No information
	Dept. of animal health established collaborative program with media channels and newspapers, to develop mass media program on AMU and AMR (Result of NAP – linked to Type 2)	VT	General	yes	Enabling	Local	Authorities and media	V		Provision of information	Direct	Producers, General public	No information	No information
	Agricultural shows used to increase awareness on AMR, health and disease management	UG	General	yes	Enabling	Local	Authorities (extension officers)	V		Provision of information	Direct	Producers	No information	No information
	Farmers symposiums - USAID FISH program	UG	General	no	Enabling	Local	R&D institutions	V		Provision of information	Indirect	Producers	No information	No information
Training	Training programme for aquaculture farmers part of the '*aquaculture enterprise development project*'(Part of ZAEDP, in Type 3)	ZA	Tilapia	no	Enabling	Local	Authorities	V		Provision of information	Indirect	Producers	No information	No information
	Workshops with large commercial farms and small scale farmers for training in good aquaculture management practices	ZA,VT	Tilapia	no	Enabling	Local	Authorities; International R&D institutions	V		Provision of information	Indirect	Producers	No information	No information
	Using well known professionals and producers as ambassadors to give advice and information, get acceptance from farmers to participate in the programs to improve health management	EG	Tilapia	no	Enabling	Local	Authorities; R&D institutions)	V		Provision of information	Indirect	Health providers	No information	No evaluation
	Training of trainers (ToT). In BG, plan for future project, based on FAO training of trainers in poultry systems. In VT, currently used.	BG, VT	General	yes	Enabling	Local	Authorities; R&D institutions	V		Provision of information	Indirect	Health providers	No information	No evaluation
	Training courses for veterinary services in management of AM use	VT	General	yes	Enabling	Local	Authorities; R&D institutions)	V		Provision of information	Direct	Health providers	No information	No evaluation
	Training Course on Development of an Active Surveillance for EUS and TiLV using the FAO 12-point surveillance checklist	ZA	General	no	Enabling	Local	Academia; R&D institutions	V		Provision of information	Indirect	Health providers;	No information	No information

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Table 4 (*continued*)

	Intervention description	Country[a]	Species[b]	AMU AMR[c]	Function	Scope	Implementer	Compulsion	Strength	AMU/AMR effect path	Stakeholder to influence	Described barriers/ constraints	Effects reported; evaluation information
Networking	SARNISSA *Sustainable Aquaculture Research Networks in Sub Saharan Africa*. Started as a 3 year project funded by the European Commission, aiming to establish a platform to promote dialogue between aquaculture individuals. Currently it works as an online research network via Facebook (more than 6000 followers from African and international countries)	SSA	General	no	Enabling	Local	Academia; R&D institutions	V	Provision of information	Indirect	Producers	No information	Active network in social media, provides knowledge exchange platform to stakeholders, mainly from African countries. More than 6500 members. https://tinyurl.com/3nw67fhm
	WAFICOS - *Walimi Fish Farmers' Cooperative Society*	UG	General	no	Enabling	Local	Academia; R&D iinstitutions	V	Provision of information	Indirect	Producers	No information	Private sector linkages were reported to be strengthened, fostering aquaculture development in 2010, 315 members had direct access to advisory services, appropriate technologies, farm inputs, markets and credit facilities.
	PESCA project	UG,KE, ZA,	Tilapia	no	Enabling	Local	Academia; R&D institutions	V	Provision of information	Indirect	Producers	No information	No information
Type 7	**Activities with co-benefits**												
Surveillance activities	AMR and AMU. Only point prevalence surveys were described, mainly driven by NAP (Type 2), and/or previously as projects funded by international institutions. Data to be used as benchmark	VT	Catfish; shrimp; tilapia	yes	Enabling DM	Local; National	R&D institutions	V	Provision of information	Direct; Distant	Decision makers	Limited to main production species	No information
	Residues monitoring activities. Linked to Type 1 (requirements by trade agreements)	VT,EG,BG,IN	Export	yes	Enabling DM	Local; National	Industry	V	Provision of information		Decision makers	Limited to main production species	No information
	Point prevalence surveys. Investigation of infectious diseases, EUS and TiLV, in wild populations. Disease screening in specific region. Designed by FAO - Part of the *Zambia Aquaculture Enterprise Development Project* (ZAEMP)	ZA	Wild pop.	no	Enabling DM	Local	Authorities; R&D institutions (WorldFish)	V	Provision of information	Direct; Distant	Decision makers	Limited to main production species	No information

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Table 4 (*continued*)

	Intervention description	Country[a]	Species[b]	AMU AMR[c]	Function	Scope	Implementer	Compulsion	Strength	AMU/AMR effect path	Stakeholder to influence	Described barriers/ constraints	Effects reported; evaluation information
Decision tool support	PEDIGREE analysis tool: *Risk-based pedigree-analysis for regulation of prophylactic aquaculture health products and improved smallholder health management in Bangladesh.* Project to develop **risk analysis tool** to assist users in identifying high risk products based on different indicators. raise awareness among stakeholders and support uptake of effective regulatory frameworks at the national level that can lead to more effective health management in aquatic small-holder systems. Based on evidence from IMAQulate project	BG	General	no	Enabling DM	Local	Authorities; Academia;R&D institutions (National research institutes); NGOs; industry	V	Provision of information	Distant	Producers	https://tinyurl.com/u7y3ynwr	No information
	PESCA – project to develop a decision support tool to guide improvement of policies to increase fish production with negligible impact on the environment. It includes fish health elements	UG, KE, ZA,	Tilapia species	no	Enabling decision making	Local	R&D institutions (National research institutes); Authorities	V	Provision of information; voluntary guidelines	Distant	Producers	No information	No information
	Mobile app with all information on diseases – teamed up with a private service to unsure sustainability	UG	All	no	Enabling decision making	Local	Authorities; industry	V	Provision of information	Distant	Producers	No information	No information
Reporting platforms with potential benchmark effect	FAO AMR surveillance reporting platform. In development and implementation. Tools to generate evidence of AMU/AMR	-	General	yes	Enabling decision making	National	FAO	V	Provision of information	Direct; Distant	Various	No information	In development
	OIE AMU surveillance reporting platform. In development and implementation. Tools to generate evidence of AMU/AMR	-	General	yes	Enabling decision making	National	OIE	V	Provision of information	Direct; Distant	Various	No information	In development

EG, Egypt; UG, Uganda; KE, Kenya; ZA, Zambia; BG, Bangladesh; IN, India; VT, Vietnam; SSA, sub-Sahara Africa DM, decision-making.
NOTE: Available resources provided by interviewees can be found in Supplementary File 2.
[a] *Country* refers to the location where the intervention was described to take place.
[b] *Species*: 'general' = the intervention was applied to all aquaculture species or irrespective of the species.
[c] In AMU/AMR: 'yes'= if intervention is designed to address AMU/AMR; 'no'= the main purpose is to address other objectives but could have an effect on AMU/AMR.

believed that vaccination might be feasible in more homogeneous production systems with support from the private sector, if it is affordable for the producer.

3.2.5. Type 5: on-farm management interventions

These were described as critical to prevent disease, to maintain aquatic health and for the profitability of activities. These types of interventions were aligned with the introduction of certification standards (Type 2) and were driven by development projects (Type 3). A positive effect on practices was described but it was bounded to the duration of the programme. In Vietnam, despite the high adoption of certification standards by commercial exporters, interviewees described that best management practices are considered a burden among some producers and 'not worth the effort', which was also described by interviewees in other countries. General training activities were found in all countries, mainly to address aquatic management and in sub-Saharan African countries also to engage farmers in aquaculture activities. In addition, behavioural influences were described. Across all countries, respondents highlighted the effect of who delivers the information to engage producers in practices, programmes and technologies. Producers with good production performance in Egypt were described to be role models and were used as ambassadors for other peers, while service and input providers acted as distributors of information between different producers. Furthermore, the use of group messaging networks via mobile devices was described among participants to exchange information such as market prices of fish with the potential of norm setting.

3.2.6. Type 6: learning and awareness-raising

One example from Bangladesh illustrated an awareness campaign on AMU and AMR. The intervention, informed by a survey and investigation of effective ways of implementation, was designed and implemented through a collaboration of academia and research and development organisations, and broadcasted on different media platforms. Engagement and responses on social media were monitored, using analytical parameters including views, likes and comments. While such interventions were thought to have potential, some interviewees in other countries raised concerns about the potential negative repercussions from the media involvement in topics that can create food scares. One such example described was the negative impact of European Union (EU) media on Asian seafood markets.

3.2.7. Type 7: activities with co-benefits for antimicrobial use (AMU) and antimicrobial resistance (AMR) and aquaculture health

Interviewees mentioned surveillance systems, the development of decision tools, and tools with potential benchmarking effect as a group of voluntary activities that provide evidence on AMU and AMR or aspects related to aquatic health, and guide the design of interventions and decision-making. Among the interviewed LMICs countries, Vietnam was found to be the most advanced in the implementation of surveillance activities, strengthened because of the NAP. However, the system was said to have been implemented on an ad hoc basis in commercial commodities using point prevalence studies, otherwise relying on samples sent to the authorities by farmers in situation of disease, as passive surveillance. One of the critical points described was the need for integrated surveillance protocols for AMU and AMR across animal, human and environment systems. In addition, different projects were described to develop and apply tools for decision-makers and different levels of the system.

Fig. 3 shows the effect paths of interventions types. Most of the types (1 to 6) included interventions with a potential indirect effect on AMU and AMR, focusing on control of diseases and prevention as well as improved management. Interventions designed to specifically tackle AMU and AMR predominantly acted directly or distantly.

4. Discussion

In this work, we developed a typology for interventions to address AMU and AMR in aquaculture in LMICs. A total of seven distinct types of interventions were proposed based on seven variables. This typology is useful to understand how the problem of AMU and AMR is and can be tackled in aquaculture, to identify similarities and differences across selected countries, and to support the design, implementation and future evaluation of interventions to address AMU and AMR. The typology developed is multidimensional, as types are the result of the combination of different variables (or dimensions). It is a conceptual typology that 'explicates the meaning of a concept (the interventions) by mapping out its dimensions (the variables)' [29]. Application of the typology (Table 4; Fig. 3) allowed the classification and characterisation of interventions in aquaculture with a potential effect to reduce the risk of AMR. This showed that the most frequent interventions specifically designed to address AMR in the sector were legislation and regulation (Type 1) and NAPs for AMR (Type 3). These were mentioned in all of the countries considered but were at different stages of implementation. All respondents described different barriers to the enforcement of legislation and regulation, except regulations for products intended for export. Other interventions only implemented in specific countries were the use of point prevalence surveys for AMU and AMR surveillance, only mentioned in Vietnam (Type 7), enhanced by the NAP implementation, and AMR/AMU awareness-raising media campaigns in Bangladesh and Vietnam (Type 6). Nearly all types included interventions with indirect effects, such as promoting good aquaculture practices or prevention of disease, and all countries presented interventions acting at distant points, generating evidence for decision-making and strengthening the system, through financing support or capacity building. These were expected to lead to a reduction of AMR risk in the system.

While the typology developed here focused on AMU and AMR, other important topics emerged; in particular, the misuse of other chemicals such as malachite green or potassium permanganate ($KMnO_4$) as well as the quality of prophylactic medicinal products and antimicrobials. It became evident that factors driving their use were similar to those described for antimicrobials and that solutions may need to focus on underlying causes and structures. In any case, a combination of interventions, or interventions combining different activities in the system, will be necessary given the complexity of the problem and the multitude of drivers and pathways to AMR. Hence, a package of interventions may combine technical aspects (e.g. use of vaccines) with structural interventions, e.g. legislative and regulatory frameworks, effective enforcement systems, industry or other stakeholders' investments in equipment and infrastructure to improve management practices, and behavioural interventions to increase awareness, uptake, disease reporting and improve management.

Given the limited number of professionals interviewed in this study, the findings may not be fully representative, but no new information was offered with further interviewees and arguments became repetitive among the target population, i.e. data saturation was achieved. Also, the typology can be applied, tested, expanded and refined in the AMU/AMR community as and when more data or information become available. In the intervention conceptualisation, the main focus was on behavioural change, which can be more appropriate to understand individualised solutions and places the responsibility on the individual [30]. However, multiple interventions reported addressed indirect and distant parts of the system and were of a structural nature . AMR in aquaculture is a

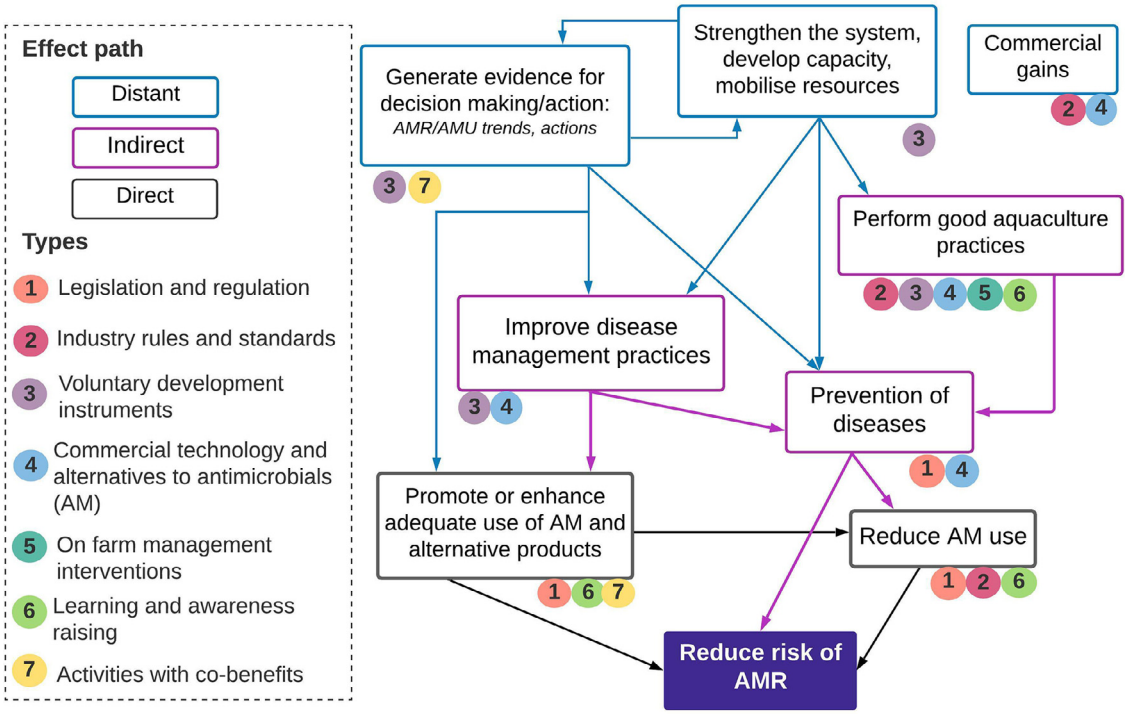

Fig. 3. Types of intervention in aquaculture in relation to the AMU/AMR effect in the system to achieve a reduction of AMR. AMU, antimicrobial use; AMR, antimicrobial resistance.

One Health problem that needs to be addressed using integrated systems approaches to health that also account for other determinants different from the characteristics of the individual, that influence the risk behaviour and risk of AMR. In the next stages, it will be important to account for these aspects and to investigate operational issues related to feasibility, implementation barriers and delivery mechanisms, when applying it in a specific context; these are often neglected and undervalued in the literature and may need to be investigated qualitatively in collaboration with designers and implementers. When applying the typology proposed, users can expect that each country shows a different profile of interventions based on the development of the sector and its characteristics, e.g. whether there are export and/or domestic activities, the proportion and development of intensive commercial systems, and the diversity of species produced. Also, differences can be expected dependent on a country's AMU goals and its commitment to NAPs.

An important use of the typology will be to characterise interventions to address AMU and AMR in aquaculture in LMICs as part of an evaluation strategy. Evidence on the intervention outcomes in aquaculture was found to be fragmented. The development of regulatory frameworks and alert systems by the EU in the early 2000s, in particular as a response to antibiotic use violations, has been described to drive the development of residues monitoring in Asian countries [31], which consequently might have driven a decrease of AMU to respect withdrawal times. However, this is restricted to products destined for export. Furthermore, these requirements and activities can also appear in conjunction with third-party certification standards (Type 2). In Egypt, the impact of best management practices (Type 5) was assessed, whereby the performance, production and profitability of farms receiving best management practices training was compared with a control group. The study showed how variable costs (e.g. feed) in adopters of best management practices were considerably lower and profitability was significantly higher [32]. However, these also relied on the use of nudges to increase uptake, such as the use of ambassadors, and the effect was observed to be bound to the duration of the programme. In Bangladesh, an awareness campaign to provide information on the risks of AMU and AMR and adequate practices was formally designed and the effects evaluated. Linked to an awareness-raising campaign on AMR using multimedia material, a project assessed the potential of digital communication for effective information provision on AMR, showing high acceptability of the system of information provision [33]. The use of these interventions and their potential are under-researched in animal health. A number of barriers have been cited in other fields such as the difficulty to convey complex scientific messages [34]. However, with the current availability of technology, these types of intervention are argued to have a potential for effective provision of information. There is also some evidence being generated on the impact of small-scale interventions, such as the randomised controlled trial probiotics project conducted in Bangladesh [35].

The scarce evidence on interventions in aquaculture to address AMU and AMR stands in stark contrast to the wide range of interventions proposed for public health and their respective evaluation plans. In aquaculture, positive effects of interventions are currently documented mainly for commercial systems that are driven by export activities. To conduct meaningful evaluations, it will be important to establish effective surveillance and monitoring systems both for AMU and AMR. In the context of AMU in aquaculture, surveillance information on AMR, AMU and/or residues can inform the design of interventions to reduce AMU and AMR. Activities to obtain these data have been enhanced by NAPs in countries where such plans have been implemented. This typology can be applied to inform the design of future evaluations of interventions, by identifying key variables to be assessed and monitored as well as barriers and constraints to be addressed to improve design. The evidence generated could be used to develop a scoring system for decision-making on interventions, such as prioritisation of actions or benchmarking, and to address design and implementation needs based on the context.

A lack of evaluation does not mean that there is no change or impact. However, only with an evaluation, i.e. a systematic process to examine critically a project, programme or activity, is it possible to judge the effectiveness and value of an intervention. The interviews showed that many countries with important aquaculture production are in different stages of activities to tackle AMR in aquaculture influenced by the scale of production, awareness and the perceived scale of the problem in a country, among other factors. In the future, countries may also wish to consider AMR-sensitive strategies in line with recommendations made by the World Bank [36]. In addition, the AMResilience Project [37] recently developed a comprehensive theoretical framework for the design, implementation, assessment and evaluation of effective AMR interventions in socioecological systems [38], and further proposed a One Health platform to systematically gather evidence of interventions [39]. Our typology complements this body of work as it will help to characterise existing and future interventions in a systematic and practical way. This is particularly important for aquaculture systems, as they often receive less attention compared with human and terrestrial animal systems, and they present higher complexity due to the diversity of farming systems, species, socioeconomic contexts and stakeholders involved. This typology can provide a foundation for benchmarking and contribute to efforts that aim to study and promote solutions for the AMR challenge in aquaculture systems.

In conclusion, the present study identifies seven types of interventions to address AMU/AMR in aquaculture using information from systems in African and Asian countries. This approach allows the classification and description of interventions and represents the basis to build evidence and to inform future work to design, implement and evaluate interventions to reduce AMU and AMR.

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Ethical approval

Ethical approval for the interviews was granted by the Royal Veterinary College's Ethics Committee [approval no. URN SR2019-0325].

Competing interests

None declared.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijantimicag.2021.106495.

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