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WASH and biosecurity interventions for reducing burdens of infection, antibiotic use and antimicrobial resistance: a One Health mixed methods systematic review

Protocol

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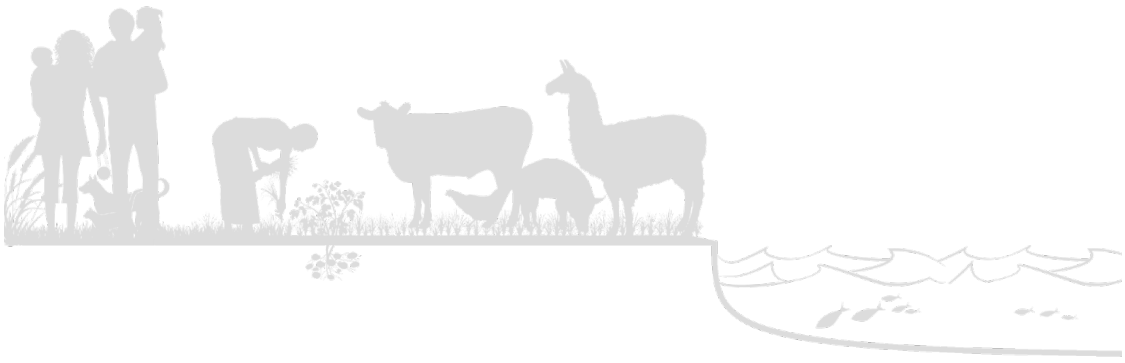

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ACRONYMS

ABR	Antibiotic resistance
ABU	Antibiotic use
AMR	Antimicrobial resistance
AMU	Antimicrobial use
BRICS	Brazil, Russia, India, China and South Africa - emerging economies.
CIs	Complex interventions
DNA	Deoxyribonucleic acid
EC	European countries
FAO	Food and Agriculture Organization of the United Nations
GAP	Global Action Plan
GBD	Global Burden of Disease
HACCP	Hazard Analysis and Critical Control Points
HCPs	Health care professionals
ICARS	International Centre for Antimicrobial Resistance Solutions
ILRI	International Livestock Research Institute
JOLIS	World Bank and IMF library catalogue
LILACs	Latin American and Caribbean Literature on Health Sciences
LMICs	Low-and-middle income countries
LSHTM	London School of Hygiene and Tropical Medicine
McREBEL	Management changes to Reduce Exposure to Bacteria to Eliminate Loses
NAP	National Action Plan
OECD	Organisation for Economic Co-operation and Development
OIE	World Organization for Animal health
PICOS	Participants, Interventions, Comparators, Outcomes, Study designs
PRISMA-P	Preferred Reporting Items for Systematic review and Meta-analysis Protocols
PROSPERO	International Prospective Register of Ongoing Systematic Reviews
QCA	Qualitative Comparative Analysis
RCTs	Randomized Control Trials
RG	Resistance-genes
RNA	Ribonucleic acid
SDGs	Sustainable Development Goals
SIs	Structural interventions
ToC	Theory of Change
WASH	Water, sanitation and hygiene
WB	World Bank
WHO	World Health Organization

GLOSSARY

Animal facilities: a building or a separate zone inside a building consisting of rooms or installations for the housing and production of animals.

Animal dwelling: a shelter where an animal lives.

AMR-sensitive interventions[1]: interventions that indirectly address AMR, but which can contribute to reduce risk or create conducive conditions for AMR-specific interventions. They can be designed and delivered in such a way that they contribute indirectly to combating AMR. Their primary purpose is not AMR control, e.g., improving access to clean water and sanitation, thereby reducing the spread of infections.

AMR-specific interventions[1]: have as their main purpose to reduce AMR; for example, establishing and enforcing regulations to ensure people can only obtain antimicrobial medicines with a valid prescription.

Biosecurity[2]: combination of practices to reduce the risk of introduction and/or spread of diseases. It can be grouped in three categories:

1. Bio-exclusion: to prevent the introduction of a new pathogen.
2. Bio-containment: to prevent escape of pathogens to neighbouring farms/animal facilities.
3. Bio-management: to control and manage pathogens already present in farms/animal facilities.

Complex interventions[3]: interventions with several interactive components. There are several dimensions of complexity: a range of possible outcomes, variability of target population, number or groups or organisational levels targeted by the intervention, degree of flexibility of the intervention.

Structural interventions[4]: interventions that seek to alter the context within which health and illness are produced and reproduced. They focus on structural factors – social, cultural, political, economic, and environmental – that shape and constrain individual, community and societal health outcomes.

Water, sanitation and hygiene interventions (WASH)[5]: interventions to improve access to these services. It can be grouped in four categories:

1. Water quantity or supply improvement: to provide or improve a water distribution system.
2. Water quality: to remove or inactivate pathogens "at source" and "at point of use".
3. Sanitation: to provide or improve sanitation and waste disposal.
4. Hygiene: to promote or implement changes in hygiene practices.

Terminology use in Theory of Change

Impact[6] (ultimate outcome, goal): The real-world change you are trying to affect. The program may contribute towards achieving this impact, and not achieve it solely on its own. E.g., reduced antimicrobial use in animals by smallholders.

Long-term outcome[6]: The final outcome the program is able to change on its own. This will be the primary outcome of the evaluation. E.g., reduced burden of bacterial infections in animals owned by smallholder/subsistence farmers.

Precondition[6] (short-term, intermediate and long-term outcomes, milestones): The intended results of the interventions. Things that don't exist now, but need to exist in order for the logical causal pathway not to be broken and the impact achieved. The logical and sequential connections between shorter-term preconditions and longer-term outcomes will be illustrated on the ToC diagram as arrows. E.g., increase access to WASH by smallholder farmers, changes in knowledge of smallholder farmers regarding biosecurity in animal production.

Ceiling of accountability[6]: Level at which you stop using indicators to measure whether the outcomes have been achieved and therefore stop accepting responsibility for achieving those outcomes. The ceiling of accountability is often drawn between the impact and the long-term outcome. E.g., project aims to improve animal health/production in smallholders, but does not accept responsibility for changing levels of disease (related to food security) in the wider population (goal), as it cannot achieve on its own (though it may contribute to it).

Indicator[6]**:** Things you can measure and document to determine whether you are making progress towards, or have achieved, each outcome. E.g., number of infections in animals, number of smallholders getting access to WASH, knowledge of smallholders about biosecurity in animal production, percentage of people receiving the interventions, amount of antibiotics used.

Interventions[6] (strategies): The different components of the complex intervention. E.g. implementation of water tanks, access to sanitation services, implementation of biosecurity measures.

Rationale[6]**:** key beliefs that underlie why one outcome is an outcome for the next, and why you must do certain activities to produce the desired outcome. Can be based on evidence or experience.

Assumptions[6]**:** an external condition beyond the control of the project that must exist for the outcome to be achieved. E.g., political willingness, funding, acceptance of the intervention by population target.

PLAIN LANGUAGE SUMMARY

1. Topic

Antimicrobial resistance (AMR) is a growing global problem. Like many other public health issues, research points to the important role of structural factors in shaping the emergence, transmission and burden of AMR. However, mirroring other areas of public health, the evidence-base of interventions that address these structural issues is slim and infrequently synthesised. Structural interventions (SIs) seek to alter the context that produces or co-produces ill-health[4]. AMR has been configured as a One Health problem to be understood in terms of human-animal-environment interconnections. Infection control and prevention is recognised as essential to addressing AMR, but how best to achieve this through a One Health perspective remains a challenge. This review addresses this gap by identifying and synthesising evidence of interventions that operate on a structural level to Improve water, hygiene, sanitation and biosecurity in communities that live and/or work with animals In Low- and Middle-Income Countries (LMICs).

2. The review in brief

The premise of this review is that interventions to improve water, sanitation, hygiene (WASH), and biosecurity intend to reduce burdens of infection and have the potential to reduce reliance on antibiotics for humans and animals. Therefore, such interventions have the ability to reduce both transmission and emergence of AMR. Two further observations inform the focus of this review: growing evidence of the insufficiency of purely technical or behavioural WASH/biosecurity Interventions to reduce disease burdens across LMICs, accompanied by calls for structural Interventions; and that most reviews retain classificatory silos of either human WASH or animal biosecurity which belies the realities of many rural and urban populations whose lives are interconnected with animals across LMIC settings. This review, therefore, addresses the potential for structural interventions on WASH/biosecurity to have an impact on Infections, antibiotic use and AMR in LMICs.

Methodologically, this review is influenced by impact assessments in development studies, where interventions are often complex in design and implementation and their effects multifaceted. The kinds of intervention that operate at a structural level are similarly challenging to identify and to characterise neatly, and are unlikely to be restricted to a randomised controlled trial design. Therefore, our search criteria and strategy are wide and our methods mixed, in order to capture potential interventions that could have an impact on our set of outcomes. In addition, in this review we recognise that interventions have impacts beyond a particular pre-defined outcome, and to be able to recommend a particular intervention strategy requires consideration of not only what that intervention comprised and required, but also what unintended consequences or co-benefits the intervention may have produced. Finally, a key consideration for this review is that many studies undertaken in Spanish, Portuguese and French speaking countries, where different interventions may have been developed and piloted, can be excluded due to language criteria, and in this case, we deliberately include studies in these languages in addition to English in the search and review.

3. What is the review about?

This systematic review will summarise evidence on how WASH and biosecurity interventions could have the potential to reduce the burden of infections, antimicrobial use and/or AMR in animal agriculture and in people in contact with animals in different country settings, with a focus on LMICs.

4. What studies are included?

Included studies have to examine the impact of WASH and biosecurity interventions on reducing burden of infections and therefore promote healthier production systems where the use of antibiotics is reduced or limited. Our review will categorise these interventions according to the context where they were performed (e.g., LMICs country, region, urban or rural, type of productions systems, livelihoods systems, agroecological situation, beneficiaries, climate conditions).

5. What is the aim of this review?

The aim of this study is to identify points for WASH and biosecurity interventions at structural and system levels that will enable reduction in reliance on antibiotics in the everyday lives of people living with animals in urbanised and rural landscapes.

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BACKGROUND

Antimicrobial resistance (AMR) is a term that comprises the existence of small portions of DNA (sometimes RNA[7]) in microbes - obtained through evolutionary mechanisms or by genetic-exchange[8] - with the potential to confer them resistance to the biocide effect of antimicrobials. It includes mechanisms of resistance to a wide class of antimicrobials, including antibacterial, antiparasitics, antivirals, and antifungals. However, this term has been widely used to describe a specific type of resistance, that is antibiotic resistance (ABR)[9]. In this review we will just focus on ABR, as global efforts are concentrated in tackling this specific resistance-mechanism in bacterial populations.

Antimicrobial Resistance is currently at the centre of a worldwide crusade to eliminate the perceived threat of returning to the pre-antibiotic era[10] where infectious diseases were decimating human populations. Although ABR is a natural phenomenon observed in bacteria, the widespread use of antibiotics in human medicine[11,12], agriculture (livestock, aquaculture and crops)[13], and consequently, the contamination of the environment[8], is being signalled as the main driver of ABR[14]. Moreover, there is already evidence of the links between ABR in animals and humans, as several studies have found resistance-genes (RG) transfer between bacteria affecting humans and animals[15-19], though without certainty of the directionality of these interactions. Hence, efforts to reduce the emergence and spread of these genes in the human-animal-environmental interface are focussed on minimizing the selective pressure put over bacteria, through strategies oriented to reduce the amount of antibiotics[20] that is used every day in health care and animal production[21].

Despite the critical importance given to AMR currently, the ***true global burden*** of AMR **is still unknown** as differences in surveillance systems, lack of reliable information in LMICs, and deficiencies of estimates of the social effects of AMR make difficult the task of assessing estimates of morbidity, mortality and economic indicators[22]. However, current initiatives to obtain a reliable measurement of the global burden of AMR are in place through the "Global Burden of Disease GBD-AMR project" (2018) which attempts to provide rigorous evidence to develop real estimates, potentially enabling a trustworthy evaluation of this burden[23]. Nonetheless, estimates of the AMR burden for humans have been recently calculated for European countries (EC), indicating that Italy (10,762 attributable deaths) and Greece (1,627 attributable deaths) bear the highest burden of AMR (>400 DALYs/100,000 population) in this area, whereas the European overall burden is estimated in 170 DALYs/100,000 population and an attributable mortality of 6.4 per 100,000 population[24]. Yet, even with reliable information, the true estimate of the AMR burden is still challenging, as Tacconelli and Pezzani (2019) remarked there is still heterogeneity in the time when infections occur; the

organization of health care systems, and factors such as demography, epidemiological settings and methods of measurements limit the possibilities of more accurate estimates[25].

The lack of information is even worse in the veterinary sector, where differences in production systems, animal species, lack of surveillance, poorly documented trends of AMR, and absence of intersectoral collaborations between health systems (human and animal), make the task of calculating the burden of **AMR in animals** even more challenging. Nonetheless, attempts to measure the burden of AMR in animal food products[26] and animals[27] with information available from some low-and-middle income countries (LMICs), indicate that north-eastern India, north-eastern China, northern Pakistan, Iran, eastern Turkey, the southern coast of Brazil, Egypt, the red river delta in Vietnam, and the surroundings of Mexico city, and Johannesburg, are hotspots of AMR resistance in animals[27]. In addition, it has been projected that between 2010 and 2030, antimicrobial consumption in production animals will increase by 99% for BRICS emerging economies (Brazil, Russia, India, China and South Africa), especially due to shifting production systems from extensive to large-scale intensive farming[26].

Furthermore, the impact of **AMR in the environment** has not been quantified and the role of the environment as a source of dissemination and transmission of AMR and antibiotic residues is not yet well documented[28]. Currently, growing evidence suggests that environmental sources of contamination with resistant-bacteria such as those found in human and animal waste (wastewater, sludges, agricultural runoffs, and manure), and use of antibiotics in plant agriculture[29] might play an important role in ABR[30,31]. For example, resistant-bacteria have been identified in wildlife animals[32,33], and for that reason these animals have been proposed as sentinels of environmental contamination with antibiotics[34]. However, studies have found that drivers of ABR in wildlife are not exclusively linked to anthropogenic causes[35], as resistant-bacteria can also be found in wildlife living in isolated locations and in remote environments[36,37]. Although some evidence suggests that the prevalence of clinically important bacteria (for humans) is higher in wild animals (such as birds and some small mammals) living in closer contact to human settlements[38] or sewage treatment plants[35], some authors question the utility of wildlife as sentinels of ABR environmental transmission as these bacteria can also be found in *untouched* environments. All these factors need to be analysed and addressed to enable the assessment of the impact of ABR in the environment and the potential consequences of maintaining a continuous transmission cycle of resistant bacteria.

Despite the absence of **reliable AMR global burden estimates[22]**, some authors have projected a burden of 10 million attributable human deaths by 2050[39], although the source of this estimate has not been published in peer-reviewed literature[22]. This figure has motivated a global race as international and national organizations, governments and institutions around the world develop strategies to minimise the effect of this threat in the near future. In 2015, the World Health Organization (WHO) endorsed a **Global Action Plan (GAP) on AMR** based on five strategic objectives: "*1) to improve awareness; 2) to strengthen knowledge through surveillance and research; 3) to reduce the incidence of infection; 4) to optimize the use of antimicrobials; and 5) to develop the economic case for sustainable investment*"[40]. Based on these objectives, many countries around the world are developing their own National Action Plans (NAPs) for the containment of AMR.

Currently, the WHO, the World Organization for Animal Health (OIE) and the Food and Agriculture Organization of the United Nations (FAO) have joint efforts to develop a tripartite workplan embracing a "One Health" approach that will be delivered *soon* and aims to support governments in the implementation of their NAPs. According to the WHO-FAO-OIE Global Database for AMR (survey 2018-2019), from a list of 159 countries, just 6 (Guinea, Tuvalu, Nauru, San Marino, Angola and Yemen) have not yet developed a NAP, 36 have their plans under development, and just 26 countries have plans implemented with resources identified and evaluation processes in place[41].

In this context, raising awareness and educating people and health care professionals (HCPs) in ABR to encourage them to change their behaviours towards a more '*rational'* use of antibiotics are amongst the main strategies of many governments and international organizations to fight AMR[40,42,43]. However, social scientists have pinpointed the paradox of endorsing the '*One Health*' concept (which is about integration, transdisciplinarity and holistic solutions) to tackle AMR issues but mainly focusing on strategies that rely on *individuals* changing their behaviours[44]. They have highlighted the importance of **pushing the boundaries of the AMR problem beyond technical solutions**, addressing the contextual factors that play a role in AMR, especially in LMIC's settings[44-46].

These arguments, plus evidence from other public health issues (such as HIV[47] and chronic health problems[48]), suggest that **AMR interventions that just put the burden of the solution on individuals** (expecting them to change their behaviour) **are less likely to succeed** if the social context where AMR is occurring does not provide an appropriate environment for people to follow recommendations and develop good practices, especially in LMICs, where lack of sanitation and clean water, poor hygiene, no access to basic health care, high disease burden, inadequate health systems, poor nutrition, poverty (people's inability to afford a course of antibiotics), presence of counterfeit medicines, and lack of regulated drug providers, could act as barriers to maintaining healthy environments and promoting a rational use of antimicrobials in these settings[14,49,50]. These problems need to be addressed with integrated solutions, otherwise the underlying weaknesses in public health systems and challenging contexts could overthrow global efforts to combat AMR.

AMR has been described as a **challenge with important social dimensions**. The way that antibiotics are used are shaped by the ways people live, work, farm, and care for ill-health[44]. Antibiotics have been described as infrastructures[44], or as quick fix medicines[51] that compensate for deficiencies in health systems; and in the animal health field, they may also be a substitute for disinformation, poor husbandry practices, poor or no access to veterinary services, poor or inexistent animal disease prevention programmes, and lack of biosecurity and management systems. Antibiotics to date, have camouflaged deficiencies in socio-economic development plans, for both humans and animals[44]. Recognising AMR as fundamentally a development problem, the World Bank (2019) has described **'AMR-sensitive' interventions** as those that have an indirect but potentially important impact on AMR and with the potential of addressing multiple diseases at the same time, and that can create favourable conditions for '**AMR-specific' interventions** (interventions with direct effect on AMR)[1].

Examples of interventions described as AMR-sensitive are those with the potential of reducing the spread of infections such as improving access to clean water and sanitation[1]. Interventions addressing the relationship between lack of access to clean water and sanitation (WASH) and burden of infections are usually focused on improving/eliminating the *structural drivers* of the health issue. Similarly, structural interventions in social sciences are those with the potential of improving/changing the '*structures'* where the health problem is occurring.

Structural interventions (SIs) are defined by Blankenship *et al.*, (2000) as interventions directed *"to change the social context where health is produced or reproduced…they locate the source of public health problems in factors in the social, economic and political environments that shape and constrain individuals, communities, and societal health outcomes."* They focus on the three types of contextual factors that determine health: availability, acceptability and accessibility[4], and three levels of action: society, social and physical environment and population groups[52]. Several studies have highlighted the importance of SIs in addressing public health issues[4] such as: HIV/AIDS[47], chronic diseases[48], and health disparities[53].

Although **structural interventions frameworks in AMR have not yet been conceptualised**, we define structural interventions in AMR as *interventions that are about rethinking systems design, institutions and infrastructures aiming to implement new strategies that change or alter the context where AMR is occurring and replicating, to facilitate or promote safer behaviours and/or reduce risks without relying on individual behaviours, as such they target AMR at their social, political, economic and environmental roots*. Due to the complexity of AMR, it might be recommended to address this problem with a set of interventions that encompasses different types of SIs, acknowledging their potential of producing co-benefits. As stated by Blankenship *et al.*, (2000) the multidimensionality quality of SIs signifies a potential strength of these types of interventions[4]. Moreover, the implementation of interventions that tackle the AMR problem at various levels (including the socio-economic context) will contribute to the attainment of the Sustainable Development goals (SDGs), especially those associated with reduced inequalities, access to water and sanitation, and health coverage.

Structural interventions aiming to change the social conditions in which people live, reducing inequalities, such as improving or granting access to water and sanitation for poor or marginalised populations, were amongst the first strategies to be implemented in public health[54]. Currently, most research and development projects carried out, focus on improving water, hygiene and sanitation for humans and reduce diarrhoea morbidity mainly affecting children in LMICs[5,55]. Less is known about the potential of WASH interventions to reduce disease burden in animals and prevent the spread of zoonotic infections. As the population grows, raising animals at small-scale or at a domestic level becomes a more common practice in LMICs, where they are raised as a source of income and/or subsistence. Currently, meat production trends indicate that this industry has grown by 68%, 64% and 40% in Africa, Asia and South America, respectively[27]. When raised at a domestic level, animals are raised freely and with poor biosecurity measures and husbandry practices[56]. For example, free poultry scavenging is popular in these contexts, increasing the chances of children's

and adult's exposure to animal faeces[57] which may serve as a source of zoonotic infections and contamination of water sources[58,59].

Similarly, aquaculture is one of the fastest growing sectors in Asia. In Cambodia, Myanmar and Vietnam, fisheries and aquaculture are one of the most important industries for their local economies, providing opportunities for vulnerable populations living in poverty[60]. In Bangladesh, this industry provides employment to many poor people which contributes to a large share of the agricultural GDP[61]. Moreover, small-scale fisheries account for two-thirds of the total fish farms in Asia [62]. As the world demand for fish and seafood grows, aquaculture becomes an important system to meet this demand, highlighting the implications for animal health, freshwater resource management, and livelihoods of poor people.

How **WASH interventions** are conceptualised **for animal health and production is still an unexplored area**. Many recommendations to reduce burden of diseases in animals are based on creating or promoting clean environments within farms and animal facilities. Most of these measures are oriented to ensure animal food product safety for human consumption, and to reduce the spread of animal diseases that are categorised as notifiable by the OIE[63] because of their influence in the international trade of goods. The underlying power of these types of interventions of promoting and ensuring animal welfare is commonly underestimated. In some animal production systems animals are just considered as *inputs* or *commodities* in the manufacturing system neglecting their living nature. In contrast, improving animals' access to clean water is crucial to ensure their health and productivity and therefore critical for promoting global health and animal welfare. Furthermore, animal production systems can generate large amounts of waste, which when not treated become a source of environmental contamination. Lack of access to water, hygiene and sanitation measures in animal production systems is understood to create optimal conditions for the emergence and spread of dangerous pathogens (including resistance bacteria) to surrounding farms, facilitating the transmission of emergent zoonotic diseases.

In this systematic review, a range of WASH and biosecurity interventions implemented to address animal health or production issues contributing to high diseases burden in humans and animals and therefore to antibiotics use and antimicrobial resistance **will be reviewed.** We will develop a framework to conceptualize how WASH interventions influence AMR. We will identify points of intervention at the structure and systems levels that can be addressed to reduce antibiotic use (ABU), assessing the potential impact of WASH and biosecurity interventions in animal production on reducing reliance on antibiotics and consequently ABR, exposing their potential co-benefits positively impacting other infectious diseases or public health issues.

RESEARCH QUESTIONS

1. *Main research questions*

Q1. What type of WASH and biosecurity interventions that play a role in reducing the burden of infections have the potential to reduce reliance on antibiotics and therefore ABR in animals and humans?

Q2. Under which enabling or limiting conditions are these interventions effective for reducing burden of infections and ABU in animals and humans?

2. *Specific questions*

Related to question 1:

Q1.1 What are the effects of these interventions on reducing burden of infections in animals and reducing risk of infections in humans?

Q1.2 What are the effects of these interventions in animal production? How might they affect farmers/producers?

Q1.3 Have these interventions the potential of contributing to reduce ABU or create conditions for AMR-specific interventions?

Q1.4 Which are potential points of intervention at the structure and systems levels in animal production that can be addressed to reduce reliance on antibiotics?

Q1.5 How effective were these interventions? Are they sufficient or can be adapted to similar contexts?

Related to question 2:

Q.2.1 What is the impact of WASH and biosecurity interventions on reducing diseases burden and therefore ABU? Are there any critical features of successful WASH and biosecurity interventions?

Q2.2 What are the potential barriers and/or unexpected consequences that need to be addressed to implement these solutions properly? Are there enabling or limiting conditions that may enable success or failure of these structural interventions?

Q2.3 What are the characteristics of the context where these interventions were applied? How might the context have influenced the success of these interventions?

Q2.4 What are the potential co-benefits of these types of interventions?

Q2.5 Are there any research gaps in this area that need to be addressed?

Q2.6 Have any of these SIs proven to be economically and politically feasible?

AIMS

The aim of this study is to identify points for intervention at the systems and structures levels in animal production systems that will enable reduction in reliance on antibiotics in the everyday lives of people living/working with animals in urbanised and rural landscapes. The interventions identified

will be used to develop multi-species frameworks with a One Health focus that decentre the human, building on critical development frameworks with a focus on political economy in their approach. The review will outline the evidence and gaps, contributing towards the development of a research agenda on AMR-sensitive interventions.

METHODS

A comprehensive electronic search of literature in relevant databases will be performed from September 2019 to September 2020. The scope of the literature will be limited to WASH and biosecurity interventions oriented to reduce the burden of bacterial infections and reliance on antibiotics for animals and humans. To ensure we cover a wide range of interventions developed in different parts of the world we will not restrict our search by language, and we will also develop a search query in Spanish, French and Portuguese for relevant regional databases. We will include all relevant articles published from inception to 2019. This systematic review will be conducted using mixed methodologies and a combination of four different approaches: a structural approach (considering the structures and contexts where the interventions were applied, moving from individualistic behavioural solutions), a systems thinking approach (considering all the factors involved in different systems and how they influence them), a theory-driven approach (developing a theory of change (ToC) process to understand the mechanisms underlying the interventions and how and why these may have worked) and a one health approach (considering the potential benefits or consequences for humans, animals and the environment).

6. Scope of the review (PICOS statement)

6.1. Type of Participants

The review will focus on the effect of WASH and biosecurity interventions to reduce the burden of infections and reliance on antibiotics in animal production for populations living with animals and/or involved in agriculture/aquaculture with and primary focus on LMICs. These include: small-scale farmers, producers, fishermen, smallholders, community holders, pastoralists, and people/families raising animals at a domestic level. We will also look for similar interventions performed in intensive production systems to analyse how different settings could have an influence on the impact of these interventions, identify the characteristics of these interventions in different contexts and explore if interventions performed in similar species could be also applied to other settings and within which limits.

6.2. Type of Interventions

WASH and biosecurity interventions (including: programmes, policies, strategies, regulations, legislations, laws, pilots) to include will be those that can be classified as a structural intervention to reduce burden of infections and therefore reduce ABU in animal agriculture and

in people living/working with animals. Some of these types of interventions may also be classified by the World Bank as AMR-sensitive interventions[1], and include interventions such as providing/improving water and sanitation, wastewater management, and implementing biosecurity measures in animal facilities. Interventions such as vaccinations and improving animal husbandry not associated with biosecurity will be excluded from the study as they have been discussed in other reviews. In addition, interventions that solely focus on providing information or educating people without further steps will also be excluded as they do not fit the criteria to be classified as SIs. As many WASH interventions are oriented to tackle issues at structural levels, it is common that they might include a combination of activities, making the interventions more complex. In this review, we will focus on WASH and biosecurity interventions (complex or not), including those that use a mix of them. We will use the following definitions to categorise these interventions:

a. ***Water, sanitation and hygiene interventions (WASH)***[5]**:** interventions to improve access to these services. They can be grouped into four categories:
   - *Water quantity or supply improvement:* to provide or improve a water distribution system. For this review, it may include installation of water facilities (pumps, deposits, tanks) in farms, rainwater harvesting systems, access to water channels in production systems, or reduction of dry matter in animal production (increase use of silage – to reduce animals' water intake).
   - *Water quality:* to remove or inactivate pathogens "at source" and "at point of use". It may include water treatments such as filtration, sedimentation, chemical treatment, chlorination, and UV treatment.
   - *Sanitation:* to provide or improve sanitation and waste disposal. For this review, it may include: installation of waste systems, composting methods, manure treatment, septic tanks, slurry treatment, rubbish management, or disposal of biological waste.
   - *Hygiene:* to promote or implement changes in hygiene practices. For this review, it may include: equipment to facilitate farmers/producers/owners handwashing, use of disinfectants, use of hot water, cleaning of animal facilities, use of chemical products, footbaths, bedding, food storage conditions, housing, sanitizers, sterilisation, pasteurisation, pest control, maintenance of pets and birds outside animal production areas, or use of protective barriers by farm workers or animal owners.

b. ***Biosecurity***[2] interventions**:** combination of practices to reduce the risk of introduction and/or spread of diseases. It can be grouped into three categories:
   - *Bio-exclusion:* to prevent the introduction of a new pathogen (e.g. shower in and out, monitor health status previous to introduction to the farm, control of vehicles, footbath, people movement, animal movement restrictions).
   - *Bio-containment:* to prevent escape of pathogens to neighbouring farms (e.g., corralling, cleaning, disinfection, manure removal).
   - *Bio-management:* to control and manage pathogens already present in the farm (e.g., McREBEL protocols, all-in-all out systems).

c. ***Multiple interventions*:** combination of strategies including WASH and biosecurity interventions to reduce the burden of infections in animal facilities or animal dwellings.

6.3. Types of Comparisons

For this review, we will not use a comparator. Interventions performed in LMICs with (another intervention or no intervention) or without comparison groups will be included.

6.4. Types of Outcomes

The primary outcomes to identify in these interventions are reduction of number of infections and reduction of antimicrobial use. Reduction of number of infections may be measured by calculating the reduction on the number of bacteria isolated from animal premises, reduction of AMR-bacteria isolates, reduction of the incidence/prevalence of infections/diseases, and reduction of morbidity/mortality rates. Reduction of ABU may be measured by quantifying the reduction of antibiotic prescriptions, reduction of medicated animal feed, reduction in the number of veterinarian visits, and reduction of antibiotic residues in animal products.

Secondary outcomes to be measured are for example: productivity (average daily gain, feed conversion ratio, cost of animal production, effects on economy), income (reported household income or net-returns), food security (quality of animal products obtained, and number of infections in people consuming these products or exposed to the production environment), and environmental contamination (presence/absence of similar bacteria strains in the environment from neighbouring farms). These secondary outcomes will be included just if the selected study also includes information for primary outcomes.

6.5. Types of Study designs

To be included in this review the selected studies must have been performed by using mixed methods, qualitative and quantitative methodologies, including both experimental (randomized control trials, non-randomized control trials, community-based studies, quasi experimental studies, before-and-after studies, uncontrolled studies, interrupted time series, matched control, regression-discontinuity) and epidemiological (case series, individual case reports, cross-sectional studies and longitudinal studies) study designs. Qualitative studies, including ethnographic research, action research, surveys and in-depth interviews will be used to explore to document factors influencing the implementation of interventions. To define the type of study design we will use the algorithm in appendix II[64]. Additionally, studies providing an economic evaluation for cost-effectiveness, cost-analysis and cost-benefit will be included. For this review, numerical data analysis will be based on the results of studies that included a quantitative assessment of the effectiveness of the intervention and were identified as low risk of bias by the methodological assessment tool described below.

7. Search strategy and literature sources

7.1. Search terms

Search terms used to identify relevant literature are summarised in the following table. The search strategy included terms related to animal farming, types of production systems, location of the production system, antibiotic use, burden of infections and interventions/strategies focusing on water, hygiene and sanitation, and biosecurity measures. The search will be performed in seven steps as follows:

Set	aiTerms	Keywords
1	farmer$ OR pastoralist$ OR "small-hold*" OR smallhold* OR "small hold*" OR "small-scale" OR "small scale" OR "small farmer" OR "small grower" OR "rural farm$" OR "indigenous farmer$" OR agribusiness OR agricultur* OR aquacultur* OR "agricultural worker$" OR "animal breeder$" OR producer OR villager$ OR "farm worker$" OR farmworker$ OR farmhand OR "household farm*" OR "farming household$" OR "household farm$" OR (animal$ NEAR/3 household?) OR "family farming" OR "family-based farm?" OR farming OR shepherd$ OR farmland OR cooperative OR (animal$ NEAR/3 backyard) OR "free-range" OR "organic farming" OR "sub-sistence farm*" OR "subsistence farm*" OR "family farm*" OR "artisanal farm*" OR (artisanal NEAR/5 farm*) OR fisherman$ OR fisher$ OR "fishing communit*" OR "artisanal fisherman" OR "artisanal fish*" OR "artisanal aquaculture" OR (nomad$ NEAR/3 production system) OR "semicommercial farm$" OR "semi-commercial farm$" OR "noncommercial farm$" OR "non-commercial farm$" OR "animal owner" OR "animal health worker$" OR "commercial farm$" OR "intensive farming" OR "intensive system" OR "commercial-scale production"	Humans Participants
2	farm$ OR farming OR livestock OR "animal agriculture" OR "food animal$" OR "farm animal$" OR "animal production" OR "food production" OR "food producing animal$" OR "food-producing animal$" OR "farm-level" OR "backyard poultry" OR flock$ OR herd OR "market animal$" OR "dairy farming" OR ruminant$ OR bovine OR cow$ OR cattle OR calf OR calves OR heifer OR "beef animal$" OR beef OR "dairy animal$" OR goat$ OR caprine OR porcine OR pig$ OR swine OR pork OR sow$ OR piglet$ OR ovine OR sheep OR ewe OR mutton OR lamb$ OR camelids OR alpaca OR cria OR llama OR tui OR rabbit OR aquaculture OR aquafarming OR pisciculture OR fish OR seafood OR crustacean$ OR mollusc$ OR shellfish OR "fish farm*" OR "fish hatcher*" OR fisheries OR polyculture OR "marine aquaculture" OR "freshwater aquaculture" OR mariculture OR finfish OR "aquatic organism$" OR "aquatic animal$" OR pond$ OR chicken$ OR chick$ OR poultry OR aviculture OR broiler$ OR chook OR hen$ OR "laying hen$" OR "egg laying" OR cock OR pullet$ OR rooster OR roaster$ OR duck$ OR duckling$ OR turkey OR geese OR equine OR horse$	Animals
3	WASH OR WATSAN OR "water access" OR "water quality" OR "clean water" OR "water-sharing" OR watering OR freshwater OR groundwater OR "ground water" OR borehole OR "water conditioner" OR rainwater OR "pipe water" OR pipewater OR "water source" OR "household well$" OR "water treatment" OR "water bodies" OR "waterways" OR "tubewell$" OR "water supply" OR "water safety" OR filtration OR "safe water" OR pond$ OR "river$ diversion" OR "hydraulic structure$" OR chlorination OR "irrigation channels" OR "irrigation canals" OR "canal water" OR "water mills" OR pump OR (water NEAR/5 dam$) OR (water NEAR/3 pit) OR "irrigation system$" OR swamp$ OR "flood recession" OR "water harvest*" OR "water system$" OR "water storage" OR "potable water" OR "electroly?ed water"	Interventions *a. Water* *b. Sanitation* *c. Hygiene* *d. Biosecurity*

	OR "catch* rainwater" OR "harvest* rainwater" OR "water salinity" OR "drinking water" OR "wastewater management" OR sanitation OR slurry OR "dirty water" OR manure OR "waste management" OR "waste disposal" OR compost* OR "septic tank" OR excre* OR faeces OR feces OR fecal OR def$ecation OR sewage OR sewerage OR "litter treatment$" OR (litter NEAR/2 treatment) OR sanitizer$ OR hygiene OR cleaning OR washing OR disinfect* OR "hygienic measures" OR antibiocides OR chemicals OR "water rinse" OR autoclaving OR sterilisation OR decontaminat* OR "boot? scrubbing" OR biosecurity OR biosafety OR "bio-exclusion" OR "bio-containment" OR "bio-management" OR bioexclusion OR biocontainment OR biomanagement OR "protective barriers" OR "protective equipment" OR "protective clothing" OR "McREBEL protocol$" OR crossfostering OR "safe handling" OR "ASEAN GAHP" OR "good animal husbandry practices" OR isolation OR fencing OR corralling OR "building fence$" OR thinning OR bedding OR depopulation OR "empty days" OR "all-in-all-out production" OR "stocking density" OR ventilation OR "dry bedding" OR "feed storage" OR "tank cleaning" OR fumigation OR "pest control" OR "fly screen$" OR cull* OR "litter* system" OR (housing NEAR/5 animal$) OR corral* OR cage$ OR "on-farm carnivorous pets" OR "second-hand equipment" OR foothbath OR footwear OR quarantine OR "animal movement" OR "pasteuri?ation"	
4	(reduc* NEAR/5 "burden of infections") OR (decrease* NEAR/5 "burden of infections") OR "low* burden of infections" OR (reduc* NEAR/5 "burden of disease$") OR (decrease* NEAR/5 "burden of disease$") OR "low* burden of disease$" OR (reduc* NEAR/5 "disease$ burden") OR (decrease* NEAR/5 "disease$ burden") OR "low* disease$ burden" OR (reduc* NEAR/5 "infection$ burden") OR (decrease* NEAR/5 "infection$ burden") OR "low* infection$ burden" OR (reduc* NEAR/5 "resistant bacteri*") OR (decrease* NEAR/5 "resistant bacteri*") OR "low* resistant bacteri*" OR (reduc* NEAR/5 "microb* infection") OR (decrease* NEAR/5 "microb* infection") OR "low* microb* infection$" OR (reduc* NEAR/5 "microb* coloni?ation") OR (decrease* NEAR/5 "microb* coloni?ation") OR "low* microb* coloni?ation" OR (reduc* NEAR/5 "bacteri* coloni?ation") OR (decrease* NEAR/5 "bacteri* coloni?ation") OR "low* bacteri* coloni?ation" OR (reduc* NEAR/5 "bacteri* contamination") OR (decrease* NEAR/5 "bacteri* contamination") OR "low* bacteri* contamination" OR (reduc* NEAR/5 "bacteri* concentration") OR (decrease* NEAR/5 "bacteri* concentration") OR "low* bacteri* concentration" OR (reduc* NEAR/5 "bacteri* count$") OR (decrease* NEAR/5 "bacteri* count$") OR "low* bacteri* count$" OR (reduc* NEAR/5 "bacteri* load$") OR (decrease* NEAR/5 "bacteri* load$") OR "low* bacteri* load$" OR (reduc* NEAR/5 infection$) OR (decrease* NEAR/5 infection$) OR "low* NEAR/5 infection$" OR (reduc* NEAR/5 incidence) OR (decrease* NEAR/5 incidence) OR "incidence reduction" OR "low* incidence" OR (reduc* NEAR/5 prevalence) OR (decrease* NEAR/5 prevalence) OR "low* prevalence" OR "prevalence reduction" OR (reduc* NEAR/5 seroprevalence) OR (decrease* NEAR/5 seroprevalence) OR "low* seroprevalence" OR "seroprevalence reduction" OR (decrease* NEAR/5 mortality) OR (reduc* NEAR/5 mortality) OR "low* mortality" OR "mortality reduction" OR (reduc* NEAR/5 morbidity) OR (decrease* NEAR/5 morbidity) OR "morbidity reduction" OR "low* morbidity" OR (reduc* NEAR/3 "antibiotic prescription$") OR (decrease* NEAR/3 "antibiotic prescription$") OR (low* NEAR/3 "antibiotic prescription$") OR (reduc* NEAR/3 "antimicrobial prescription$") OR (decrease* NEAR/3 "antimicrobial prescription$") OR (low* NEAR/3 "antimicrobial prescription$") OR (reduc* NEAR/3 "antimicrobial prescribing") OR (decrease* NEAR/3 "antimicrobial prescribing") OR (low* NEAR/3 "antimicrobial prescribing") OR (reduc* NEAR/3 "antibiotic	Outcomes

	prescribing") OR (decrease* NEAR/3 "antibiotic prescribing") OR (low* NEAR/3 "antibiotic prescribing") OR (reduc* NEAR/5 "veterinary visit$") OR (decrease* NEAR/5 "veterinary visit$") OR (low* NEAR/3 "veterinary visit$") OR (reduc* NEAR/5 "veterinary service$") OR (decrease* NEAR/5 "veterinary service$") OR (low* NEAR/3 "veterinary service$") OR (reduc* NEAR/5 "antibiotic residues") OR (decrease* NEAR/5 "antibiotic residues") OR (low* NEAR/3 "antibiotic residues") OR (reduc* NEAR/5 "antimicrobial residues") OR (decrease* NEAR/5 "antimicrobial residues") OR (low* NEAR/3 "antimicrobial residues") OR (reduc* NEAR/5 "antimicrobial resistan*") OR (decrease* NEAR/5 "antimicrobial resistan*") OR (low* NEAR/3 "antimicrobial resistan*") OR (reduc* NEAR/5 "antibiotic resistan*") OR (decrease* NEAR/5 "antibiotic resistan*") OR (low* NEAR/3 "antibiotic resistan*") OR (reduc* NEAR/5 AMR) OR (decrease* NEAR/5 AMR) OR (low* NEAR/3 AMR) OR (reduc* NEAR/5 ABR) OR (decrease* NEAR/5 ABR) OR (low* NEAR/3 ABR) OR (reduc* NEAR/5 "drug-resistan*") OR (decrease* NEAR/5 "drug-resistan*") OR (low* NEAR/3 "drug-resistan*") OR (reduc* NEAR/5 "drug$ resistan*") OR (decrease* NEAR/5 "drug$ resistan*") OR (low* NEAR/3 "drug$ resistan*") OR (reduc* NEAR/5 "multidrug-resistan*") OR (decrease* NEAR/5 "multidrug-resistan*") OR (low* NEAR/3 "multidrug-resistan*") OR (reduc* NEAR/5 "multiple-drug resistan*") OR (decrease* NEAR/5 "multiple-drug-resistan*") OR (low* NEAR/3 "multiple-drug-resistan*") OR (reduc* NEAR/5 "multiple drug resistan*") OR (decrease* NEAR/5 "multiple drug resistan*") OR (low* NEAR/3 "multiple drug resistan*") OR (reduc* NEAR/5 "antimicrobial use") OR (decrease* NEAR/5 "antimicrobial use") OR (low* NEAR/3 "antimicrobial use") OR (reduc* NEAR/5 AMU) OR (decrease* NEAR/5 AMU) OR (low* NEAR/3 AMU) OR (reduc* NEAR/5 "antibiotic use") OR (decrease* NEAR/5 "antibiotic use") OR (low* NEAR/3 "antibiotic use") OR (reduc* NEAR/5 "antibiotic usage") OR (decrease* NEAR/5 "antibiotic usage") OR (low* NEAR/3 "antibiotic usage") OR (reduc* NEAR/5 "antimicrobial usage") OR (decrease* NEAR/5 "antimicrobial usage") OR (low* NEAR/3 "antimicrobial usage") OR (reduc* NEAR/5 ABU) OR (decrease* NEAR/5 ABU) OR (low* NEAR/3 ABU) OR (reduc* NEAR/3 "use of antimicrobials") OR (decrease* NEAR/3 "use of antimicrobials") OR (low* NEAR/3 "use of antimicrobials") OR (reduc* NEAR/3 "use of antibiotics") OR (decrease* NEAR/3 "use of antibiotics") OR (low* NEAR/3 "use of antibiotics") OR (reduc* NEAR/3 "antimicrobial drug$") OR (decrease* NEAR/3 "antimicrobial drug$") OR (low* NEAR/3 "antimicrobial drug$") OR (reduc* NEAR/3 "veterinary drug$") OR (decrease* NEAR/3 "veterinary drug$") OR (low* NEAR/3 "veterinary drug$")	
5	intervention$ OR implementation OR experiment OR monitor* OR program* OR pilot$ OR initiative$ OR strateg* OR polic* OR method$ OR measures OR technique OR legislation$ OR regulation$ OR effectiveness OR "cost-effectiveness" OR "cost-benefit" OR "cost-analysis" OR "cost-utility" OR "cost effectiveness" OR "cost benefit" OR "cost analysis" OR "cost utility" OR "economic evaluation" OR impact	Study Types
6	LMICs OR LMIC OR "low-and-middle income countries" OR "developing countries" OR "Latin America" OR Africa OR Asia OR "South America" OR "Central America" OR Afghanistan OR Albania OR Algeria OR Angola OR "Antigua and Barbuda" OR Argentina OR Armenia OR Azerbaijan OR Bangladesh OR Belarus OR Belize OR Benin OR Bhutan OR Bolivia OR "Bosnia and Herzegovina" OR Botswana OR Brazil OR "Burkina Faso" OR Burundi OR "Cabo Verde" OR Cambodia OR Cameroon OR "Central African Republic" OR Chad OR China OR Colombia OR Comoros OR "Democratic Republic of Congo" OR Congo OR "Cook Islands" OR "Costa Rica" OR "Côte d'Ivoire" OR Cuba OR Djibouti OR Dominica OR "Dominican Republic" OR Ecuador OR Egypt OR "El Salvador" OR "Equatorial Guinea" OR Eritrea OR Ethiopia	LMIC's

	OR Fiji OR Gabon OR Gambia OR Georgia OR Ghana OR Grenada OR Guatemala OR Guinea OR "Guinea-Bissau" OR Guyana OR Haiti OR Honduras OR India OR Indonesia OR Iran OR Iraq OR Jamaica OR Jordan OR Kazakhstan OR Kenya OR Kiribati OR "Democratic People's Republic of Korea" OR Kosovo OR Kyrgyzstan OR Lao People's Democratic Republic OR Lebanon OR Lesotho OR Liberia OR Libya OR "Former Yugoslav Republic of Macedonia" OR Madagascar OR Malawi OR Malaysia OR Maldives OR Mali OR "Marshall Islands" OR Mauritania OR Mauritius OR Mexico OR Micronesia OR Moldova OR Mongolia OR Montenegro OR Montserrat OR Morocco OR Mozambique OR Myanmar OR Namibia OR Nauru OR Nepal OR Nicaragua OR Niger OR Nigeria OR Niue OR Pakistan OR Palau OR Panama OR "Papua New Guinea" OR Paraguay OR Peru OR Philippines OR Rwanda OR "Saint Helena" OR Samoa OR "São Tomé and Príncipe" OR Senegal OR Serbia OR Sierra Leone OR "Solomon Islands" OR Somalia OR "South Africa" OR "South Sudan" OR "Sri Lanka" OR "Saint Lucia" OR "Saint Vincent and the Grenadines" OR Sudan OR Suriname OR Swaziland OR "Syrian Arab Republic" OR Tajikistan OR Tanzania OR Thailand OR "Timor-Leste" OR Togo OR Tokelau OR Tonga OR Tunisia OR Turkey OR Turkmenistan OR Tuvalu OR Uganda OR Ukraine OR Uzbekistan OR Vanuatu OR Venezuela OR Vietnam OR "Wallis and Futuna" OR "West Bank and Gaza Strip" OR Yemen OR Zambia OR Zimbabwe	
7	**((1 OR 2) AND 3 AND 4 AND 5 AND 6)**	**COMBINE**

Search terms for other language are included in appendix IX.

7.2. Search query

Our search strategy will be built using relevant Boolean operators, truncation signs and wild cards for each database included. The search query will be reviewed by the librarian of the London School of Hygiene and Tropical Medicine.

7.3. Databases

The following databases will be used to search for articles relevant to the research topic:

- ISI Web of Science
- PubMed
- EBSCO (Databases: AGRICOLA, Africa wide, CINAHL, Academic Search, FRANCIS,)
- ASSIA (Applied Social Science Index and Abstracts)
- AgEcon (Research in agricultural and applied Economics)
- AGORA (Global online research in agriculture)
- OVID (Databases: CAB Abstracts, Global Health, Embase, MEDLINE, Veterinary Science, Social Work Abstracts, PsycINFO®)
- Cochrane Library
- Global Health Library
- EMRO Library
- Epistemonikos

- Pro-Quest (Pais INDEX, Sociological Abstracts, International Bibliography of Social Science, Worldwide Political Science Abstracts).
- Trip (Turning research into practice)

Regional databases (other languages)

Latin America and The Caribbean

- Lilacs
- Scopus
- Scielo - Spanish and Portuguese
- BIREME (Virtual Health Library) - Spanish and Portuguese
- HINARI
- E-Revistas - Spanish
- Redalyc – Spanish and Portuguese

African

- AIM (African Index Medicus)
- AfricaPortal

Asia

- IMSEAR (Index Medicus for the South-East Asian Region
- WPRIM (Western Pacific Region Index Medicus)
- Chinese Science Citation database

A hand search of literature will be conducted in the following sources.

- FAO reports (Agris)
- JPIAMR platform
- JSTOR
- JOLIS (Joint Libraries of the World Bank and IMF)
- The World Bank database of documents and reports
- CGSpace – CGIAR
- International Development and Research Centre (IDRC) Digital Library

Grey Literature

- Google Scholar (Google Academico - Spanish)
- Open grey
- New York Academy of Med's grey lit report

Additional articles will also be identified by looking at the references of relevant literature and by consultation with experts or other researchers. Unavailable full-text articles will be obtained by contacting and requesting them from the authors.

7.4. Restriction terms

Our search will be restricted to articles covering WASH and biosecurity interventions other than education and training strategies that just provide information. The lists of articles retrieved from each database will be downloaded into EndNote version X9 (Thomson Reuters, New York, USA) and duplicates will be removed.

8. Study selection and data extraction

The literature review process will be illustrated using a flow chart (appendix IV). The review will be conducted in two stages. In the first stage, two researchers (S.K and P.T) will screen the titles and abstracts of all the articles extracted, and will decide if they fit the inclusion criteria. Any queries will be moderated by C.P. In the second stage, independently two researchers (S.K and P.T), will examine the full-text of potentially relevant articles selected in the first stage thoroughly to confirm they fit the eligibility criteria. Inter-rater observer agreement will be quantified by kappa[65]. Any disagreements will be resolved through discussion and consensus between the first two reviewers, or when necessary with a third reviewer (C.P or C.C). Articles will be then assessed using the risk of bias assessment tool and data will be extracted using the forms in appendixes V and VI.

8.1. Eligibility criteria

Each study selected must meet the following criteria

8.1.1. Population

8.1.1.1. Inclusion criteria

- The study includes an animal component in the intervention.
- The animal component analyses strategies to reduce burden of infections in livestock, poultry, aquaculture, and regional farm animals including (goats, alpaca, llama, camels, rabbits, turkey, ducks, and guinea pigs).
- The study covers WASH and biosecurity interventions implemented inside farms, or in animal production systems, or at community/household level aiming to reduce burden of infections.
- The study covers WASH and biosecurity interventions in animal production systems (including intensive farming, small-holders farming, subsistence farming, pastoralists, fishermen, pisciculture systems) and/or in people living/working in animals

8.1.1.2. Exclusion criteria

- Interventions that were applied outside animal production systems (such as disinfection of animal transport vehicles or carcass disinfection) will be excluded.
- Interventions testing disinfectants "in vitro" or at laboratories will be excluded.

8.1.2. Interventions

8.1.2.1. Inclusion criteria

- The study describes a structural intervention with the potential of reducing the burden of infections and therefore antimicrobial use in animal production systems or in people working/living with animals (including intensive farming, small-holders and subsistence farming).
- The study describes a WASH and biosecurity interventions (including programmes, policies, strategies, regulations, legislations, laws, pilots) to reduce burden of infections and therefore reduce ABU in animal agriculture and in people living/working with animals. Some of these types of interventions may also be classified by the World Bank as AMR-sensitive interventions (World Bank 2019.), and include interventions such as providing/improving water and sanitation, wastewater management, and implementing biosecurity measures in animal facilities.
- The study includes an intervention tested within and across a country classified as LMICs. Studies with a multi-country approach will also be included.
- The study includes a methodological assessment of the intervention and/or analyses the impact of the intervention on animal agriculture.

8.1.2.2. Exclusion criteria

- Interventions that rely on people changing their behaviour or that put the burden of the solution on the individual rather than on systems will be excluded from the study, such as interventions that solely focus on providing information or educating people without further steps, as they do not fit the criteria to be classified as SIs.
- Interventions such as vaccinations and improving animal husbandry measures not associated with biosecurity will be excluded from the study as they have been discussed in other reviews.
- Articles or reports where the intervention is limited to human health facilities.

8.1.3. Study designs

8.1.3.1. Inclusion criteria

- The study describes a primary research study (original article).
- For this review, randomized control trials, non-randomized control trials, community-based studies, quasi-experimental studies, before-and-after studies, uncontrolled studies, interrupted time series, matched control, regression-discontinuity will be included.

8.1.3.2. Exclusion criteria

- Purely descriptive studies and non-systematic reviews will be excluded.

- Unavailable articles/reports will be excluded from the study if the author, after contact, does not provide them in full-text.
- Qualitative studies, including ethnographic research, action research, surveys and in-depth interviews will be only used to document factors influencing the implementation of interventions.

8.2. Outcome measures

8.2.1.1. Inclusion criteria

- Interventions where the primary outcomes are:
    - Reduction of number of infections (measured by calculating the reduction on the number of bacteria isolated from animal premises, reduction of AMR-bacteria isolates, reduction of the incidence/prevalence of infections, and reduction of morbidity/mortality rates or reduction of the incidence or prevalence of diseases), and
    - Reduction of antimicrobial use (measured by quantifying the reduction of antibiotic prescriptions, reduction of medicated animal feed, reduction in the number of veterinarian visits, and reduction of antibiotic residues in animal products).

8.2.1.2. Exclusion criteria

- Other outcomes not mentioned above will be excluded.

Articles retrieved that do not meet the inclusion criteria after full-text examination will be listed in a supplementary file together with the reasons for their exclusion. As this study aims to evaluate interventions in multiple complex systems, no studies will be excluded based on quality assessment. Quality assessments commonly have RCTs as a '*gold standard*' design for evaluating interventions, however RCTs normally assume a linear relationship between the intervention and the outcome, which in complex interventions is not always the case as multiple pathways can generate the same outcome[66]. Instead, quality issues will be examined as a source of heterogeneity, accounting for differences in the study results.

8.3. Prioritise exclusion criteria

- Purely descriptive studies and reviews will be excluded.
- Articles or reports where the intervention is limited to human health facilities.
- Interventions testing disinfectants "in vitro" or at laboratories will be excluded.
- Interventions that were applied outside production systems (such as disinfection of animal transport vehicles or carcass disinfection) will be excluded.

- Interventions that rely on people changing their behaviour or that put the burden of the solution on the individual rather than on systems will be excluded from the study, such as interventions that solely focus on providing information or educating people without further steps as they do not fit the criteria to be classified as structural interventions
- Interventions such as vaccinations and improving animal husbandry measures not associated with biosecurity will be excluded from the study, as they have been discussed in other reviews.
- Interventions focussing on other outcomes than reduction of the number of infections (measured by calculating the reduction on the number of bacteria isolated from animal premises, reduction of the incidence/prevalence of infections, or reduction of morbidity/mortality rates or reduction of the incidence or prevalence of diseases), reduction of antimicrobial use (measured by reduction of antibiotic prescriptions, reduction of medicated animal feed, reduction in the number of veterinarian visits, and reduction of antibiotic residues in animal products) or reduction of resistant-bacteria (measured by reduction of AMR-bacteria isolates) will be excluded from the study.
- Unavailable articles/reports will be excluded from the study if the author, after contact, does not provide them in full-text.
- Studies types such as qualitative studies, including ethnographic research, action research, surveys and in-depth interviews will be only used if they document factors influencing the implementation of interventions.

9. Bias assessment

Once the first round of articles has been selected we will check the methodological validity of the articles prior to inclusion in the review using the bias assessment tool built following SYRCLE's rob tool[67] based on Cochrane Rob tool (Appendix III). For each criterion applied, scoring of low, medium or high risk will be assigned according to the number of biases detected in the study. These scores will be utilized to categorise the interventions and provide an evidence-based list of recommendations with strong potential to be effective. For this review, low quality articles will be defined based on the number of flaws in their design. Studies with problems with no control for confounders, poor definitions of control groups, selective reporting, unclear description of inclusion and exclusion criteria, poor data analysis methodologies, and unclear outcomes, will be categorised as low quality.

10. Data extraction

Data extraction will be performed using the forms in appendixes V and VI, and data extracted from each article will include information regarding: conditions of the study, characteristics of the population, characteristics of the context, characteristics of the intervention, outcomes and intervention effects. All the articles selected will be categorized by their year of publication, the initiative represented, scope covered within the work, geographic distribution of where the initiative

was conducted, methods employed, features of each intervention/system/program (intensity, duration, frequency, method of delivering, context, seasonality, population characteristics, efficacy and effectiveness), study design and performance indicators for each intervention. When missing from the study or report we will seek to obtain key unpublished information (such as context related factors or any relevant missing data) by directly contacting the authors. Statistical data will be extracted from the study to conduct a meta-analysis; however, this will depend on the quality and complexity of the studies reviewed and the number of studies found for each intervention type.

10.1. Data to be extracted: study design

Type of study, Study design, Duration of study, Sample size, Means, OR

10.2. Data to be extracted: Population

- For animals: Animal species involved, Type of production system, Type of feed utilised, Agroecological situation, Climate conditions, Specific location (Estate, Province, Capital, District, Community,), Availability of animal health support (Veterinary clinics, Veterinarians, Vet Technicians, Para-veterinarians, Community AH workers, None).
- For humans (including farm workers and people living with animals): Population type (producer, farmer, worker, shepherd, fishermen, animal keeper, a person living in the farm or raising animals in the backyard). Livelihood system. Type of setting (Urban, Peri-urban, Peri-rural, Rural, Remote/isolate). Population target - beneficiaries, Social or cultural characteristics, Source of income.

10.3. Data to be extracted: intervention of interest

- Type of intervention, Intervention aim, Method of delivering, Methods employed, Frequency, Environmental element, Microorganism involved (if relevant), Description of intervention – WASH component, Intervention groups (N° and description), Authorities/ stakeholders involved, Duration of intervention, Number of people affected by the intervention. Recruitment method, Exclusion or inclusion criteria of the intervention, Characteristics of the intervention, Data to be extracted: primary outcome(s).
- Intervention Outcomes, Method of assessing outcomes, Statistical analysis conducted, Baseline results, Post-intervention results. Beneficial outcomes. Outcomes and Intervention effects

10.4. Data to be extracted: other

- Authors, Aim, Type of publication, Language, Year, Source, Journal, Country, Region, Interdisciplinary collaborations, stakeholders involved, Characteristics of the context. Potential Co-benefits, Adverse events, unintended consequences, Barriers identified, Evaluation design, Research gaps identified.

11. Synthesis methods

Information obtained from the articles will be summarised in two steps:

1. Firstly, synthesizing evidence (to answer Q1) to provide a narrative of the potential pathways to reduce burden of infections and ABU through WASH and biosecurity interventions.

   Data extracted from the interventions in the forms mentioned above will be tabulated and summarized narratively presenting summary statistics for the interventions analysed. Articles will be categorized by intervention type and country and will be reported in tables according to their bias assessment. We will group the interventions based on their similarities and according to their region and context. In an iterative process we will create a description of a set of contexts that might share similar characteristics according to their region, type of production system, animal species represented, characteristics of the population, agroecological system, climate conditions (seasonality), political environment, level of income, and the livelihood system that they represent. We will conceptualise WASH and biosecurity interventions for animal health/production in different contexts, considering that a one-policy-for-all approach might not be possible in different country settings.

2. Secondly, evaluating this synthesis through theory of change (to answer Q2), to identify the key elements that made interventions successful in the given context.

   With data collected from the interventions, we will develop an overall ToC framework to understand the causal pathways of how WASH interventions could impact burden of infections and ABU. A graphic from this process will be included in the review indicating causal pathways, possible assumptions, indicators, outcomes and goals identified on the interventions reviewed. This will help to explain how context related factors might influence the results of the interventions. The main objective of this step will be to untangle *how* and *why* an intervention works in a specific context and whether or not it may be possible to adapt it to new settings or scale it up to a wider population.

3. Thirdly, if possible, a meta-analysis with the statistical data obtained from high-quality studies in the bias assessment, and when necessary sensitivity analysis to verify the robustness of the findings. The execution of this analysis will depend on the complexity and potential heterogeneity of the interventions paying attention to the diversity of the studies. Many WASH interventions can be classified as complex interventions (CIs)[66]. CIs include multiple interactive components that are affected by contextual factors so to capture this complexity with a metanalysis will be challenging. If we find at least five studies with the same intervention type, same study type (either RCTs or observational) and same outcomes reported we will group the studies by applying a random effect (including mean differences and SD for continuous outcomes and risk ratios for binary outcomes) and perform a meta-analysis considering the dispersion of results amongst the studies. Confidence intervals at 95% will be calculated together with two-sided P-values.

12. Data analysis

Data extracted from the interventions selected will be analysed by using mixed methods for quantitative and qualitative studies. Information from both types of studies will be analysed to identify how the interventions operated and were implemented, identify contextual factors that might be influencing either by enabling or impeding the interventions, and provide systematic explanations about how and why interventions worked or failed to work and which could be some potential unintended consequences (positive or negative) of such interventions.

To analyse quantitative data a meta-analysis will be conducted with the statistical data obtained from our analysis. As mentioned, the execution of this analysis will depend on the complexity and potential heterogeneity of the interventions to include in this review. To capture relevant information from interventions not associated with quantitative data a theoretical analysis will be performed by using a set of questions (appendix VIII) as a guide to evaluate the potential impact of the interventions to be reviewed. Questions included in this guide are based on critical points highlighted by impact evaluation literature[68,69]. Information extracted from qualitative studies will be used to contextualise the interventions, provide complementary perspectives, and provide insights regarding their implementation. A theory of change (ToC)[6] approach will also be applied, to develop a theoretical understanding of how change was or could be produced[64]. ToC will also be used to explore how different settings/context conditions could influence differences in the effectiveness of the interventions, or how these factors could be enabling multiple pathways to effectiveness. Data extraction forms will be based on and modified for this study from the Cochrane Public Health Group and EPOC Group 'Good practice data extraction form'. The results of the study will be reported using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA-P) checklist[70] (Appendix VIII). We will use the EPPI Reviewer 4 software (Thomas, Brunton, & Graziosi, 2010) - for managing the articles included in the review.

13. Strengthens and Limitations

This is the first review that will explore how WASH interventions in animal health/production could influence burden of infections and antimicrobial use. We will not restrict our search by language and we will additionally make efforts to capture literature published in other important languages relevant for some LMICs. We will also attempt to capture all relevant literature by searching in relevant regional databases. However, we acknowledge that even making these efforts the studies captured may not be representative of the whole population living in these countries, and in addition we might omit unpublished or non-evaluated strategies.

We also recognise that measuring the benefits and unintended consequences of these interventions and their relevance to the AMR agenda might be limited as even when it is logical to suggest that reducing burden of infections might reduce the need for antibiotic treatment, measuring the direct effect of these types of interventions in empirically reducing ABU is challenging in different animal production contexts. Lastly, as our search will be performed in the early months

of 2020, evidence from studies published towards the end of 2019 will be potentially missed from our searches.

14. Review team

Roles and responsibilities for each review panel member:

- Review protocol, database search, articles screening moderator: Chris Pinto (LSHTM)
- First screener and data extraction: Sarai Keestra
- Second screener and data extraction: Pranav Tandon
- Systematic review methodology advisor: Clare Chandler (LSHTM)
- Analysis, written report and publication: Chris Pinto (LSHTM)/ Sarai Keestra (LSHTM) / Clare Chandler (LSHTM)/ Pranav Tandon (McMaster University)
- Reviewer, expert in the topic area (SIs, AMR): Clare Chandler (LSHTM), Oliver Cumming (LSHTM)
- Advisory board: Jeff Waage (IHH-A4NH), Frank Berthe (WB), Claire Chase (WB), Anders Daalsgard (ICARS), Kate Medlicott (WHO), Amy Pickering (Tufts University)

15. Institutions involved

- The London School of Hygiene and Tropical Medicine (LSHTM)
- The International Livestock Research Institute (ILRI)
- The consultative Group for International Agricultural Research (CGIAR)
- The World Bank Group
- The International Centre for Antimicrobial Resistance Solutions (ICARS)
- World Health Organisation (WHO)

16. Funding

This is a project of the Improving Human Health (IHH) Programme - London School of Hygiene and Tropical Medicine (LSHTM) – UK. It is funded by the Agriculture for Nutrition and Health Program (A4NH) of the Consultative Group for International Agricultural Research (CGIAR).

17. Declaration of interest

The authors declare not to have vested interest in the outcomes of this review or describe findings in an impartial way.

18. Project Timetable

N°	Activities	S	O	N	D	J	F	M	A	M	J	J	A	S	O	N	D
1	Definition of the features of the review	X															

2	Writing the proposal – first draft	X	X												
3	Definition of search terms		X	X											
4	Correcting the proposal – final draft				X	X									
5	Publication of protocol in PROSPERO						X	X							
6	Data base search							X	X						
7	Eligibility assessment								X	X					
8	Full text screening and articles selection									X	X	X			
9	Data extraction										X	X	X		
10	Data analysis												X	X	
11	Writing the results, discussion and recommendations – article first draft													X	X
12	Review by advisors													X	X	X
13	Corrections according to reviewers' comments – final draft															X
14	Sending to publication															X

Appendix I: Relevance screening tool for articles

1. Does the title / abstract describe a primary research study (as opposed to a review)

   Yes No Unclear

2. Does the title / abstract refer to a structural intervention with the potential of reducing the burden of infections, AMU or AMR?

   Yes No Unclear

3. Does the title/abstract include information about an intervention, trial, pilot, initiative, strategy, programme, study, policy or experiment with emphasis on animal health/production systems, agricultural communities, or people working/living with animals?

   Yes No Unclear

4. Does the study include an assessment/analysis of the intervention accounting for its impact on animal agriculture systems or on people working and living with animals?

   Yes No Unclear

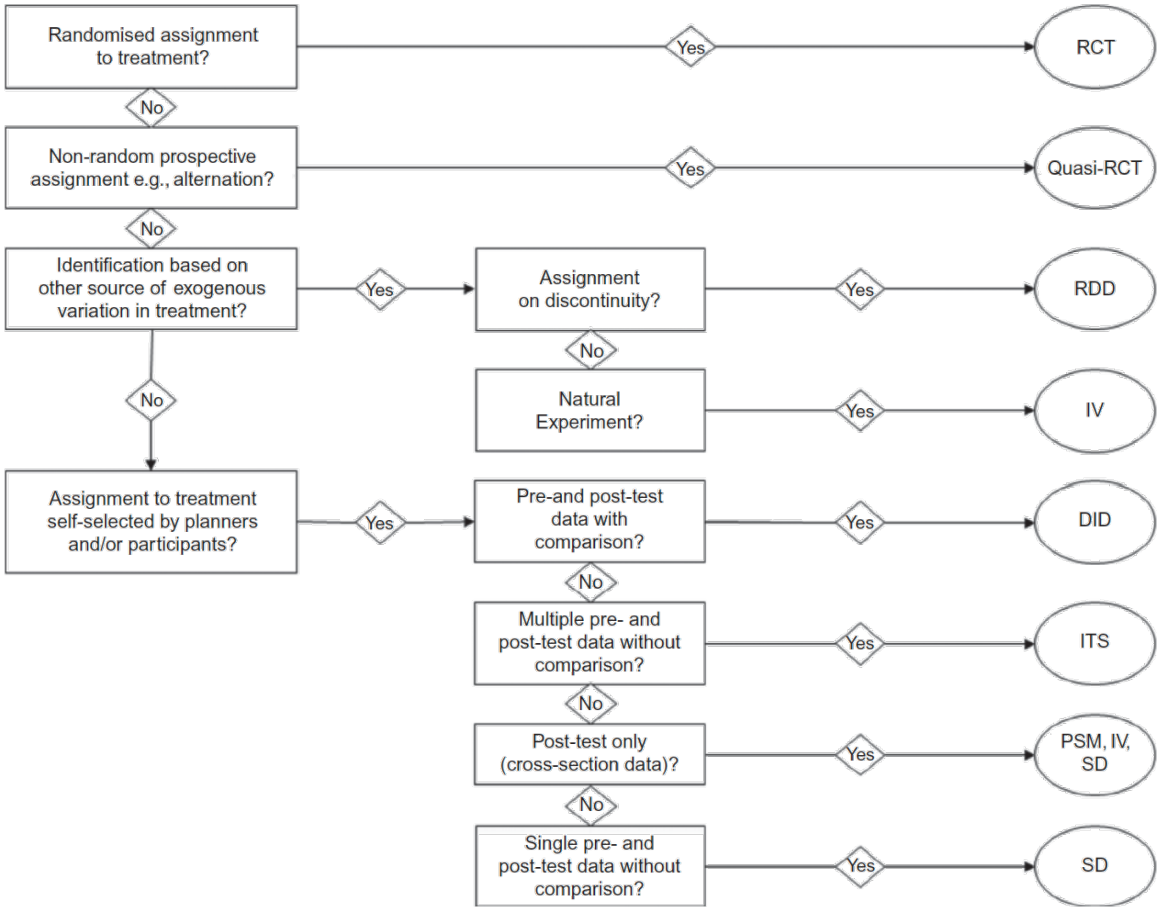
5. Does the study include an intervention with an expected outcome of reducing burden of infections/diseases, antimicrobial use or antimicrobial resistance?

   Yes No Unclear

Must answer "yes" to all questions for the reference to advance to full text assessment

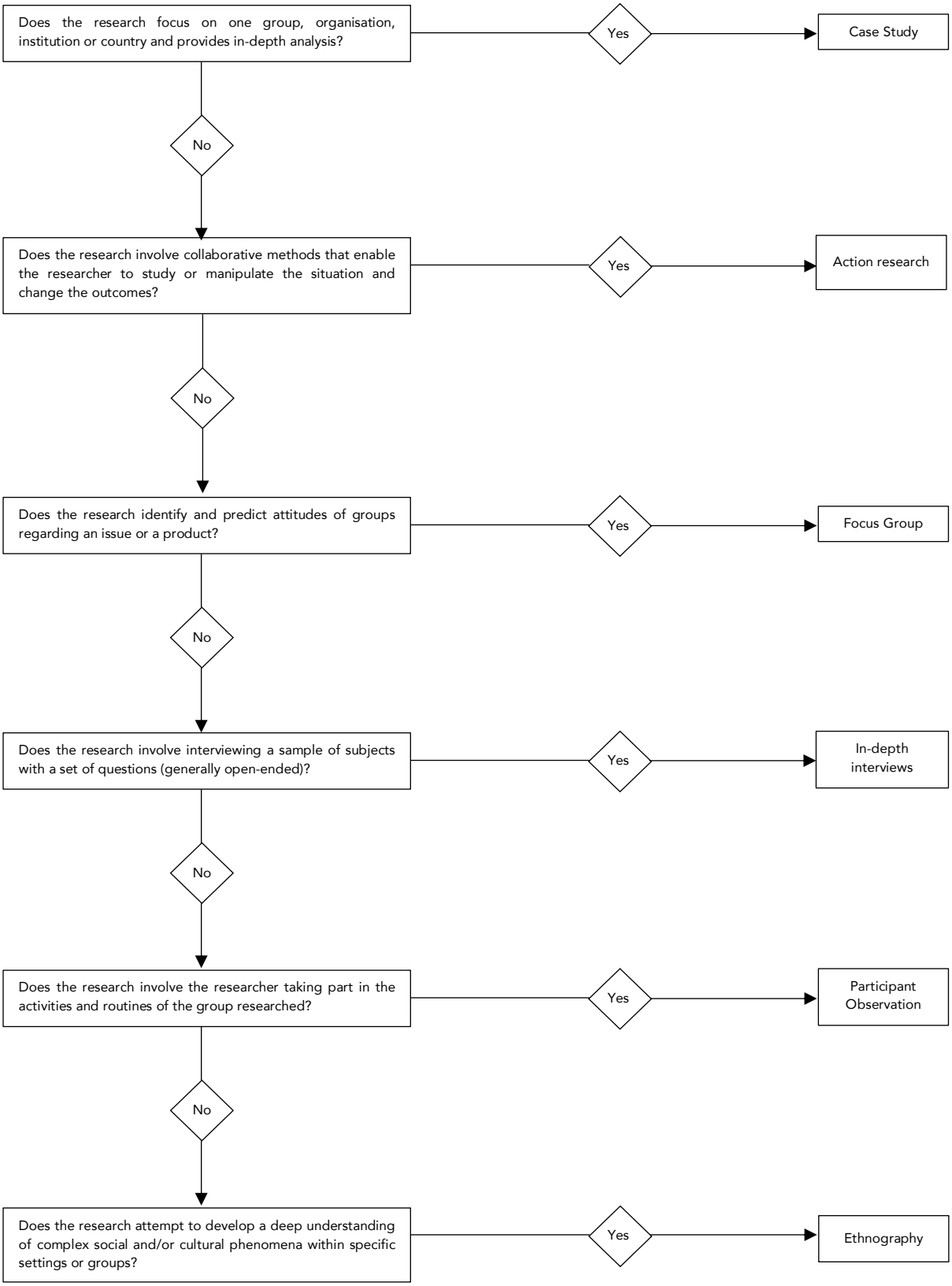
Appendix II: Study design algorithms

A. Quantitative methods



RCT: Randomised control trials, RDD: regression discontinuity design, IVs: instrumental variables, DIDs: difference-indifferences, ITS: interrupted time series, PSM: propensity score matching, SD: single differences. Source: Waddington *et al.*, 2013 [64]

B. Qualitative methods



Appendix III: SYRCLE's Rob bias assessment tool[67]

Part 1: Aspects of the intervention to be evaluated

Item	Type of bias	Domain	Description of domain	Review authors judgment
1	Selection bias	Sequence generation	Describe the methods used, if any, to generate the allocation sequence in sufficient detail to allow an assessment whether it should produce comparable groups.	Was the allocation sequence adequately generated and applied? (*)
2	Selection bias	Baseline characteristics	Describe all the possible prognostic factors or animal characteristics, if any, that are compared in order to judge whether or not intervention and control groups were similar at the start of the experiment.	Were the groups similar at baseline or were they adjusted for confounders in the analysis?
3	Selection bias	Allocation concealment	Describe the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen before or during enrolment.	Was the allocation adequately concealed? (*)
4	Performance bias	Random housing	Describe all measures used, if any, to house the animals randomly within the animal room.	Were the animals randomly housed during the experiment?
5	Performance bias	Blinding	Describe all measures used, if any, to blind trial caregivers and researchers from knowing which intervention each animal received. Provide any information relating to whether the intended blinding was effective.	Were the caregivers and/or investigators blinded from knowledge which intervention each animal received during the experiment?
6	Detection bias	Random outcome assessment	Describe whether or not animals were selected at random for outcome assessment, and which methods to select the animals, if any, were used.	Were animals selected at random for outcome assessment?
7	Detection bias	Blinding	Describe all measures used, if any, to blind outcome assessors from knowing which intervention each animal received. Provide any information relating to whether the intended blinding was effective.	Was the outcome assessor blinded?
8	Attrition bias	Incomplete outcome data	Describe the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. State whether attrition and exclusions were reported, the numbers in each intervention group (compared with total randomized animals), reasons for attrition or exclusions, and any re-inclusions in analyses for the review.	Were incomplete outcome data adequately addressed? (*)
9	Reporting bias	Selective outcome reporting	State how selective outcome reporting was examined and what was found.	Are reports of the study free of selective outcome reporting? (*)
10	Other	Other sources of bias	State any important concerns about bias not covered by other domains in the tool.	Was the study apparently free of other problems that could result in high risk of bias? (*)

Part 2: Additional signalling questions are included to assist judgment. "Yes" indicates low risk of bias; "no" indicates high risk of bias; and "unclear" indicates an unclear risk of bias. If one of the relevant signalling questions is answered with "no," this indicates high risk of bias for that specific entry.

1) Was the allocation sequence adequately generated and applied?	
*Did the investigators describe a random component in the sequence generation process such as: ■ Referring to a random number table; ■ Using a computer random number generator. Additional info: Examples of a non-random approach:	Yes/No/Unclear

- Allocation by judgment or by investigator's preference;
- Allocation based on the results of a laboratory test or a series of tests;
- Allocation by availability of the intervention;
- Sequence generated by odd or even date of birth;
- Sequence generated by some rule based on animal number or cage number.

2) Were the groups similar at baseline or were they adjusted for confounders in the analysis?

*Was the distribution of relevant baseline characteristics balanced for the intervention and control groups? Yes/No/Unclear

*If relevant, did the investigators adequately adjust for unequal distribution of some relevant baseline characteristics in the analysis? Yes/No/Unclear

*Was the timing of disease induction adequate? Yes/No/Unclear

Additional info:

The number and type of baseline characteristics are dependent on the review question. Before starting their risk of bias assessment, therefore, reviewers need to discuss which baseline characteristics need to be comparable between the groups. In an SR investigating the effects of hypothermia on infarct size, for example, gender distribution, left ventricular weight and heart rate and blood pressure should be similar between the groups at the start of the study.

A description of baseline characteristics and/or confounders usually contains:

- The sex, age and weight of the animals
- Baseline values of the outcomes which are of interest in the study

Timing of disease induction:

In some prevention studies, the disease is induced after allocation of the intervention. For example, in an experiment on preventive probiotic supplementation in acute pancreatitis, pancreatitis is induced after allocation of the animals to the probiotic or control group. To reduce baseline imbalance, the timing of disease induction should be equal for both treatment groups.

Examples of adequate timing of disease induction:

- The disease was induced before randomization of the intervention.
- The disease was induced after randomization of the intervention, but the timing of disease induction was at random, and the individual inducing the disease was adequately blinded from knowing which intervention each animal received.

3) Was the allocation to the different groups adequately concealed during?

*Could the investigator allocating the animals to intervention or control group not foresee assignment due to one of the following or equivalent methods? Yes/No/Unclear

- Third-party coding of experimental and control group allocation Central randomization by a third party

Sequentially numbered opaque, sealed envelopes

Additional info:

Examples of investigators allocating the animals being possibly able to foresee assignments:

- Open randomization schedule
- Envelopes without appropriate safeguard

- Alternation or rotation
- Allocation based on date of birth
- Allocation based on animal number
- Any other explicitly unconcealed procedure of a non-random approach

4) Were the animals randomly housed during the experiment?

*Did the authors randomly place the cages or animals within the animal room/facility? Yes/No/Unclear

- Animals were selected at random during outcome assessment (use signaling questions of entry 6).

*Is it unlikely that the outcome or the outcome measurement was influenced by not randomly housing the animals? Yes/No/Unclear

The animals from the various experimental groups live together in one cage/pasture (e.g., housing conditions are identical).

Additional info:

Examples of investigators using a non-random approach when placing the cages:

- Experimental groups were studied on various locations (e.g., group A in lab A or on shelf A; Group B in Lab B or on shelf B).

5) Were the caregivers and/or investigators blinded from knowledge which intervention each animal received during the experiment?

*Was blinding of caregivers and investigators ensured, and was it unlikely that their blinding could have been broken? Yes/No/Unclear

- ID cards of individual animals, or cage/animal labels are coded and identical in appearance.
- Sequentially numbered drug containers are identical in appearance.
- The circumstances during the intervention are specified and similar in both groups (#).
- Housing conditions of the animals during the experiment are randomized within the room (use criteria of entry 4).

Additional info:

Examples of inappropriate blinding:

- Colored cage labels (red for group A, yellow group B)
- Expected differences in visible effects between control and experimental groups
- Housing conditions of the animals are not randomized within the room during the experiment; use criteria of entry 4
- The individual who prepares the experiment is the same as the one who conducts and analyses the experiment
- Circumstances during the intervention are not similar in both groups (#)

Examples where circumstances during the intervention were not similar:

- Timing of administration of the placebo and exp drug was different.
- Instruments used to conduct experiment differ between experimental and control group (e.g., experiment about effects abdominal pressure; exp group receives operation and needle to increase pressure, while control group only has the operation).

***The relevance of the above-mentioned items depends on the experiment. Authors of the review need to judge for themselves which of the above-mentioned items could cause bias in the results when not similar. These should be assessed.*

6) Were animals selected at random for outcome assessment?	
*Did the investigators randomly pick an animal during outcome assessment, or did they use a random component in the sequence generation for outcome assessment?	Yes/No/Unclear
■ Referring to a random number table;	
■ Using a computer random number generator;	
■ Etc.	
7) Was the outcome assessor blinded?	
*Was blinding of the outcome assessor ensured, and was it unlikely that blinding could have been broken?	Yes/No/Unclear
■ Outcome assessment methods were the same in both groups.	
■ Animals were selected at random during outcome assessment (use signalling questions of entry 6).	
*Was the outcome assessor not blinded, but do review authors judge that the outcome is not likely to be influenced by lack of blinding?	Yes/No/Unclear
(e.g., mortality)	
Additional info:	
This item needs to be assessed for each main outcome.	
8) Were incomplete outcome data adequately addressed? (*)	
*Were all animals included in the analysis?	Yes/No/Unclear
*Were the reasons for missing outcome data unlikely to be related to true outcome? (e.g., technical failure)	Yes/No/Unclear
*Are missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups?	Yes/No/Unclear
*Are missing outcome data imputed using appropriate methods?	Yes/No/Unclear
9) Are reports of the study free of selective outcome reporting? (*)	
*Was the study protocol available and were all of the study's pre-specified primary and secondary outcomes reported in the current manuscript?	Yes/No/Unclear
*Was the study protocol not available, but was it clear that the published report included all expected outcomes (i.e. comparing methods and results section)?	Yes/No/Unclear
Additional info:	
Selective outcome reporting:	
- Not all of the study's pre-specified primary outcomes have been reported;	
- One or more primary outcomes have been reported using measurements, analysis methods or data subsets (e.g., subscales) that were not pre-specified in the protocol;	
- One or more reported primary outcomes were not pre-specified (unless clear justification for their reporting has been provided, such as an unexpected adverse effect);	
- The study report fails to include results for a key outcome that would be expected to have been reported for such a study.	
10) Was the study apparently free of other problems that could result in high risk of bias? (*)	
*Was the study free of contamination (pooling drugs)?	Yes/No/Unclear
*Was the study free of inappropriate influence of funders?	Yes/No/Unclear
*Was the study free of unit of analysis errors?	Yes/No/Unclear

*Were design-specific risks of bias absent?	Yes/No/Unclear
*Were new animals added to the control and experimental groups to replace drop-outs from the original population?	Yes/No/Unclear

Additional info:

The relevance of the signalling questions (Table 3) depends on the experiment. Review authors need to judge for themselves which of the items could cause bias in their results and should be assessed.

Contamination/pooling drugs:

Experiments in which animals receive – besides the intervention drug – additional treatment or drugs which might influence or bias the result.

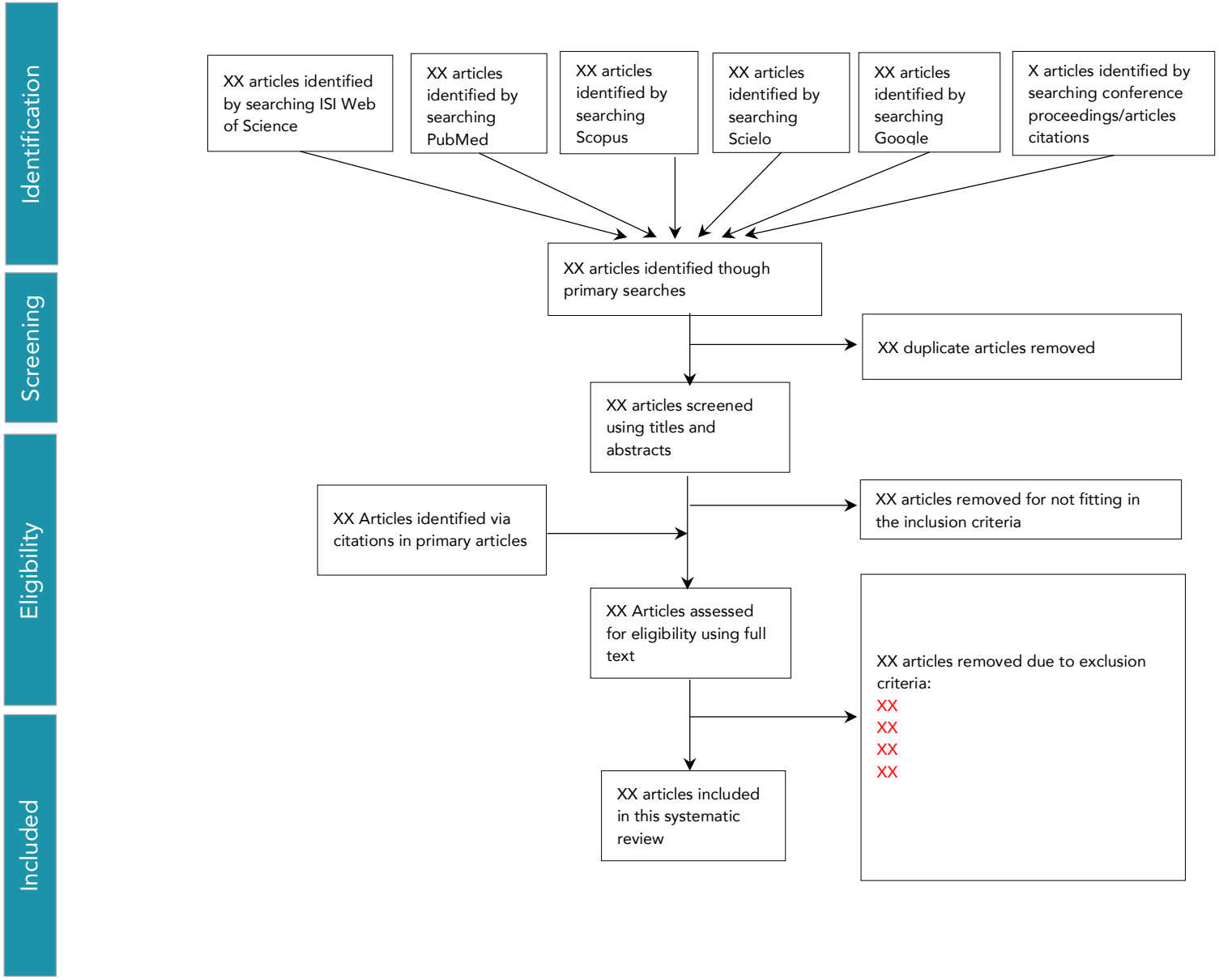
Unit of analysis errors:

- Interventions to parts of the body within one participant (i. e., one eye exp; one eye control).
- All animals receiving the same intervention are caged together, but analysis was conducted as if every single animal was one experimental unit.

Design-specific risks of bias:

- Crossover design that was not suitable (intervention with no temporary effect, or the disease is not stable over time)
- Crossover design with risk of carry-over effect
- Crossover design with only first period data being available
- Crossover design with many animals not receiving 2nd or following treatment due to large number of drop-outs probably due to longer duration of study
- Crossover design in which all animals received same order of interventions
- Multi-arm study in which the same comparisons of groups are not reported for all outcomes (selective outcome reporting)
- Multi-arm study in which results of different arms are combined (all data should be presented per group)
- Cluster randomized trial not taking clustering into account during statistical analysis (unit of analysis error)
- Crossover design in which paired analysis of the results is not taken into account

Appendix IV: Literature review process – flow chart



Appendix V: Data extraction tool for selected articles part 1.

STUDY ID	GENERAL INFORMATION									STUDY CHARACTERISTICS				POPULATION CHARACTERISTICS				CONTEXT CHARACTERISTICS						
	Article name	Authors	Aim	Type of publication	Language	Year	Source/ Journal	Country	Region	Interdisciplinary collaborations	Type of study	Study design	Duration of study	Sample size	Population target - beneficiaries	Recruitment method	Exclusion or inclusion criteria	Social or cultural characteristics	Type of setting (Urban, Peri-urban, Peri-rural, Rural, Remote/isolate)	Type of production system	Type of feed utilised	Livelihood system	Agroecological situation	Climate conditions	Specific location (Estate, Province, Capital, District, Community)	Availability of animal health support (Veterinary clinics, Veterinarians, Vet technicians, Para-veterinarians, Community AH workers, None)

Appendix VI: Data extraction tool for selected articles part 2.

GENERAL		INTERVENTION CHARACTERISTICS												OUTCOMES					INTERVENTION EFFECTS							
Study ID	Article name	Type of intervention	Intervention aim	Method of delivering	Methods employed	Sample size	Frequency	Animal involved	Environmental element	Microorganism involved (if relevant)	Description of intervention – WASH component	Intervention groups (N° and description)	Authorities/ stakeholders involved	Duration of intervention	Intervention Outcomes	Method of assessing outcomes	Statistical analysis conducted	Baseline results	Post intervention results	Estimation of effects	Beneficial outcomes	Potential Co-benefits	Adverse events, unintended consequences	Barriers identified	Evaluation design	Research gaps identified

Appendix VII: Questionnaire to guide theoretical analysis of the impact of interventions to review.

QUESTIONS	CRITERIA
1. Was a baseline assessment performed at the beginning of the study?	In prospective studies, baseline assessments are common as they allow the generation of valid counterfactuals. In contrast, retrospective studies a baseline assessment is not performed and evidence could be more debatable.
2. How many intervention components were incorporated?	If more than one component was incorporated, check if there were relevant outcomes/indicators specified for each component.
3. Was there a comparison group?	If comparison groups were used, it is important to know if there were possibilities of interactions between components of the experimental and control group.
4. Was the WASH intervention aimed to be implemented at a public source or at farm/household levels (point-of-use)?	Where the intervention was applied might have an effect in the results and sustainability of the intervention.
5. Was the delivery method use the most appropriate for the intervention?	Delivery methods affect the results of the interventions and are key for their success. If delivery methods are not monitored, fails in the interventions could be misunderstood.
6. Who was in charge of the delivery of these services? If services were provided, did they come from private or public companies?	It is important to consider if services were provided by private entities, as sometimes private companies have little incentive to improve services of marginalised populations.
7. Where the methods to evaluate the effect of the intervention appropriate?	Interventions with limited sample sizes, or little effect than expected could be mistakenly categorised as ineffective.
8. Were the more relevant stakeholders identified?	It is desirable that all the stakeholders are identified (both those involved in the implementation and those affected by the intervention). This is commonly done through workshops or mapping exercises.
9. Was the intervention followed up for enough time (to ensure changes persist)?	Consider that sustainability of interventions is commonly an underestimated feature.
10. Were the main and secondary outcome clearly stated?	If outcomes are not clearly stated, difficult to evaluate the results of the intervention.
11. Were the indicators to measure the outcomes clearly identified? If yes, were these indicators quantitative or qualitative?	Indicators allow the assessment of the performance of the intervention, and to identify if assumptions made were correct. Quantitative can be measured in numbers, qualitative is descriptive in nature and open ended (the responses are hard to anticipate).
12. Was a process evaluation carried out?	Process evaluation involves to know how and why intervention works, understand failure or unintended consequences, assess fidelity and quality of implementation. It helps to determine if failure of the intervention was due to implementation rather than ineffectiveness of the intervention.
13. How fidelity was assessed in the intervention? Was a strict standardise methodology applied or did they allow adaptation to local circumstances? If so were the limits specified and the variations recorded?	Fidelity of the intervention indicates what was implemented compare with the original intention or design of the intervention.
14. Were the attributed changes directly related to the intervention?	Important to check if there are grounds to believe that outcomes could be credibly attributed to the intervention, and if there is a causal relationship.
15. Has the intervention been developed by using a ToC approach? If yes, did the article described in detail how ToC informed the development and evaluation of the intervention?	ToC approaches enable critical appraisal of the results of the interventions. They provide information about how change can be produced, and allow the identification of the assumptions that explain the steps that lead to the aim of the intervention.
16. When interventions involved peoples' activities, were the incentives for the change proposed clearly identified?	If people are unaware of the incentives for change, the sustainability of the intervention could be threatened, as people could stop using/applying the activity/hardware proposed by the intervention.
17. Was the evaluation of the impact of the interventions complemented with information on costs?	The assessment of intervention costs is a critical step in the evaluation of interventions. Interventions might be successful but if expensive it would be difficult to implement at a large scale. Analysis can be done through cost-benefit, cost-effectiveness or cost-analysis.
18. If costs of the intervention were assessed, did they include depreciation of any hardware physical maintenance or attrition on time?	Commonly, costs evaluations do not include these elements as part of the intervention costs, however they could critically impact the total cost of the strategy proposed.
19. If high-technology was involved, was this developed internally (endogenous capacity) or externally (imported from other contexts)?	Consider that if technology is developed externally and export to another context no endogenous capacity will be built within the system for the development of locally appropriate solution.
20. Was the political-economic environment (where the intervention was operated) considered in the evaluation process?	Contextual factors can determine sometimes if the intervention proposed

Appendix VIII: PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol[70]

Section and topic	Item No	Checklist item	P#
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	
Support:			
Sources	5a	Indicate sources of financial or other support for the review	
Sponsor	5b	Provide name for the review funder and/or sponsor	
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	

Appendix IX: Search terms for different languages

1. Spanish:

Set	Terms	Keywords
1	Granjero OR pastor OR pastoralismo OR "pequeño productor" OR campesino OR ganadero OR agricultor OR "criador de animales" OR porcicultor OR avicultor OR "trabajador de granja" OR "pequeño criador" OR "crianza artesanal" OR "granja familiar" OR "asociación de productores" OR cooperativa OR "granja comercial" OR "crianza intensiva" OR "crianza extensiva" OR "productor de leche" OR "crianza trashumante" OR trashumancia OR "animales en el patio" OR "criador informal" OR ganadería OR "crianza semiextensiva" OR "crianza estabulada" OR "ganadería extensiva" OR "ganadería intensiva" OR "ganadería nómada" OR "ganadería trashumante" OR "ganadería de autoconsumo" OR "ganadería de subsistencia" OR "pequeña y mediana ganadería" OR "crianza de traspatio" OR " ganadería de doble propósito" OR "ganadería rural" OR "ganadería de traspatio" OR pescador OR acuicultor OR piscicultor	Humans Participants
2	Granja OR ganado OR "animal de producción" OR "ganado de carne" OR "ganado de leche" OR "ganado de doble propósito" OR "ganado criollo" OR bovino OR vacuno OR ovino OR porcino OR caprino OR equino OR aviar OR "pequeños rumiantes" OR vacas OR vaquillonas OR terneros OR terneras OR ovejas OR cerdos OR marranas OR puercos OR chanchos OR alpacas OR tuis OR cabras OR cabrito OR caballos OR yeguas OR cuyes OR aves OR gallinas OR pollos OR patos OR pavos OR conejos OR "animal de granja" OR hato OR "sector pecuario" OR avicultura OR porcicultura OR acuicultura OR mariscos OR pescado OR langostinos OR cangrejos OR tilapia OR salmón OR trucha OR	Animals
3	ASH OR SIASAR OR agua OR higiene OR saneamiento OR limpieza OR lavado OR pozos OR bombas OR manantiales OR estanques OR "lagunas de oxidación" OR letrinas OR heces OR desechos OR excretas OR compost OR "lavado de manos" OR desinfección OR desinfectante OR esterilización OR autoclavado OR tratamiento OR pediluvios OR botas OR bioseguridad OR aislamiento OR molino OR estiércol OR "medidas de protección" OR descontaminación OR bioexclusión OR biocontención OR biogestión OR Bioexclusión OR biocontención OR biomanejo OR "barreras protectoras" OR "equipo de protección" OR "ropa protectora" OR indumentaria OR guantes OR "protocolo McREBEL" OR ventilación OR "cama seca" OR "almacenamiento de alimento" OR "limpieza del tanque" OR fumigación OR "control de plagas" OR "mosquitero" OR jaula OR galpón OR instalaciones OR corrales OR "cerco perimetral" OR maples OR cuarentena OR "movimiento de animales" OR "pasteurización" OR "todo dentro-todo fuera" OR "malla antipájaros" OR "control biológico" OR incineración OR filtración	Interventions *a. Water* *b. Sanitation* *c. Hygiene* *d. Biosecurity*
4	Infección OR enfermedad OR incidencia OR prevalencia OR seroprevalencia OR mortalidad OR morbilidad OR "recuento de colonias" OR "carga bacteriana" OR "colonización bacteriana" OR "concentración bacteriana" OR "recuento bacteriano" OR "aislamiento bacteriano" OR "bacteria resistente" OR "uso de antimicrobianos OR "uso de antibióticos" OR "resistencia antimicrobiana" OR "Resistencia antibiótica" OR "prescripción de antibióticos" OR "prescripción de antimicrobianos" OR "visita veterinaria" OR "servicio veterinario" OR "experto veterinario" OR "residuos de antibióticos" OR "residuos de antimicrobianos" OR RAM OR multidrogo-resistente OR multiresistente OR multiresistencia OR "uso de antimicrobianos" OR "uso de antibióticos"	Outcomes
5	Intervención OR implementación OR experimento OR monitoreo OR programa OR piloto OR iniciativa OR estrategia OR "política publica" OR método OR medidas OR	Study Types

	técnica OR legislación OR regulación OR "ensayo de control aleatorio " OR cohorte OR "casos-controles" OR "ensayo de control no aleatorio" OR "basado en la comunidad" OR "antes y después" OR "control emparejado" OR "regresión-discontinuidad" OR "serie de casos" OR "informe de caso " OR "estudio de caso" OR "estudio transversal" OR "estudio longitudinal" OR "discontinuidad de regresión" OR "variables instrumentales" OR " diferencias de indiferencia" OR "coincidencia de puntaje de propensión" OR "diferencias únicas" OR "investigación etnográfica" OR "investigación de acción" OR encuestas OR "entrevista en profundidad" OR efectividad OR "costo-efectividad" OR "costo-beneficio" OR "análisis de costos" OR "costo-utilidad" OR "rentabilidad" OR "costo beneficio" OR "análisis de costos" OR "costo utilidad" OR "evaluación económica" OR impacto	
6	"países de ingresos bajos y medios" OR "países en desarrollo" OR "países sub-desarrollados" OR "América Latina" OR Latinoamérica OR Sudamérica OR Asia OR África OR "Centro América" OR "América Central" OR Afganistán OR Albania OR Argelia OR Angola OR "Antigua y Barbuda" OR Argentina OR Armenia o Azerbaiyán OR Bangladesh o Bielorrusia OR Belice OR Benín OR Bután OR Bolivia OR "Bosnia y Herzegovina" OR Botsuana OR Brasil OR "Burkina Faso" OR Burundi OR "Cabo Verde" OR Camboya OR Camerún OR "República Centroafricana" OR Chad OR China OR Colombia OR Comoras OR "República Democrática del Congo" OR Congo OR "Islas Cook" OR "Costa Rica" OR "Costa de Marfil" OR Cuba OR Djibouti OR Dominica OR "República Dominicana" OR Ecuador OR Egipto OR "El Salvador" OR "Guinea Ecuatorial" OR Eritrea OR Etiopía OR Fiji OR Gabón OR Gambia OR Georgia OR Ghana OR Granada OR Guatemala OR Guinea OR "Guinea-Bissau" OR Guyana OR Haití OR Honduras OR India OR Indonesia OR Irán OR Iraq OR Jamaica OR Jordania OR Kazajstán OR Kenia OR Kiribati OR "República Popular Democrática de Corea" OR Kosovo OR Kirguistán OR Laos OR Líbano OR Lesoto OR Liberia OR Libia OR "Antigua República Yugoslava de Macedonia" OR Madagascar OR Malawi OR Malasia o Maldivas OR Mali OR "Islas Marshall" OR Mauritania OR Mauricio OR México OR Micronesia OR Moldavia OR Mongolia OR Montenegro OR Montserrat OR Marruecos OR Mozambique OR Myanmar OR Namibia OR Nauru OR Nepal OR Nicaragua OR Níger OR Nigeria OR Niue OR Pakistán OR Palao OR Panamá OR "Papua Nueva Guinea" OR Paraguay OR Perú OR Filipinas OR Ruanda OR "Santa Elena" OR Samoa OR "São Tomé y Príncipe" OR Senegal OR Serbia OR Sierra Leona OR "Islas Salomón" OR Somalia OR "Sudáfrica" OR "Sudán del Sur" OR "Sri Lanka" OR "Santa Lucía" OR "San Vicente y las Granadinas" OR Sudán OR Surinam OR Suazilandia OR Siria OR Tayikistán OR Tanzania OR Tailandia OR "Timor-Leste" OR Togo OR Tokelau OR Tonga OR Túnez OR Turquía OR Turkmenistán OR Tuvalu OR Uganda OR Ucrania OR Uzbekistán OR Vanuatu OR Venezuela OR Vietnam OR "Wallis y Futuna" OR "Cisjordania y la Franja de Gaza" OR Yemen OR Zambia OR Zimbabue	LMIC's
7	**((1 OR 2) AND 3 AND 4 AND 5 AND 6)**	**COMBINE**

2. Portuguese:

Set	Terms	Keywords
1	Agricultor OR pastor OR pastoral OR "pequeno produtor" OR camponês OR "criador de animais" OR "criador de porcos" OR "criador de aves de capoeira" OR "trabalhador agrícola" OR "criador pequeno" OR "criação artesanal" OR "associação familiar" OR "dos produtores" OR cooperativa OR "fazenda comercial" OR "criação intensiva" OR "criação extensiva" OR "produtor de leite" OR "criação transumana" OR transumanidade OR "animais no pátio" OR "criador informal" OR	Humans Participants

	"criação de animais" OR "criação estável semi-extensiva" OR "gado extensivo" OR "gado intensivo" OR "gado nômade" OR "gado transumante" OR "gado autoconsumo" OR "gado de subsistência" OR "gado pequeno e médio" OR "criação de animais quintal" OR "gado de dupla finalidade" OR "gado rural" OR "gado de quintal" OR pescador OR aquicultura OR piscicultor	
2	"Exploração agrícola" OR gado OR "dupla finalidade" OR "gado crioulo" OR vacina OR ovelha OR porcos OR cabras OR cavalos OR vacas OR novilhas OR bezerros OR cordeiros OR ovelhas OR porcos OR alpacas OR tuis OR cabras OR éguas OR pássaros OR galinhas OR patos OR coelhos OR "animal de fazenda" OR rebanho OR "setor pecuário" OR aves OR porcos reprodução OR mariscos OR peixes OR camarões OR caranguejos OR tilápia OR salmão OR truta	Animals
3	água OR higiene OR saneamento OR limpeza OR lavagem OR poços OR bombas OR nascentes OR lagoas OR "tanques de oxidação" OR latrinas OR fezes OR resíduos OR excrementos OR composto OR "lavagem das mãos" OR desinfecção OR desinfetante OR esterilização OR esterilização OR autoclavagem OR tratamento OR calçado OR botas OR biossegurança OR isolamento OR moinho OR estrume OR "medidas de proteção" OR descontaminação OR bioexclusão OR biocontenção OR biogestão OR Bioexclusão OR biocontenção OR biomanejo OR "barreiras protetoras" OR "equipamentos de proteção" OR "roupas de proteção" OR roupas OR luvas OR "protocolo McREBEL" OR ventilação OR "cama seca" OR "armazenamento de alimentos" OR "limpeza de tanques" OR fumigação OR "controle de pragas" OR "mosquiteiro" OR gaiola OR galpão OR instalações OR canetas OR "perímetro" OR bordos OR quarentena OR "movimento dos animais" OR "pasteurização" OR "tudo em geral" OR "malha de pássaro" OR "controle biológico" OR incineração OR filtração	Interventions *a. Water* *b. Sanitation* *c. Hygiene* *d. Biosecurity*
4	Infecção OR doença OR incidência OR prevalência OR soroprevalência OR mortalidade OR morbidez OR "contagem de colônias" OR "carga bacteriana" OR "colonização bacteriana" OR "concentração bacteriana" OR "contagem bacteriana" OR "isolamento bacteriano" OR "bactéria resistente" OR "uso de antimicrobianos OR "uso de antibióticos" OR "resistência antimicrobiana" OR "Resistência a antibióticos" OR "prescrição de antibióticos" OR "prescrição de antimicrobianos" OR "visita veterinária" OR "serviço veterinário" OR "resíduos veterinários" OR "resíduos de antibióticos" OR "resíduos antimicrobianos" OR RAM OR multirresistente OR multirresistência	Outcomes
5	Intervenção OR implementação OR experimento OR monitoramento OR programa OR piloto OR iniciativa OR estratégia OR "política pública" OR método OR medidas OR técnica OR legislação OR regulamentação OR "estudo randomizado de controle" OR coorte OR "caso-controle" OR "teste de controle não aleatório "OR" comunitário "OR" antes e depois" OR "controle correspondente" OR "regressão-descontinuidade" OR "série de casos" OR "relato de caso" OR "estudo de caso" OR "estudo transversal" OR "estudo longitudinal" OR "descontinuidade de regressão" OR "variáveis instrumentais" OR "diferenças de indiferença" OR "coincidência do escore de propensão" OR "diferenças únicas" OR "pesquisa etnográfica" OR "pesquisa-ação" OR pesquisas OR "entrevista aprofundada" OR eficácia OR "custo-benefício" OR "análise de custo" OR "custo-utilidade" OR "rentabilidade" OR "análise de custo" OR "custo-utilidade" OR "avaliação econômico" OR impacto	Study Types
6	"países de baixa e média renda" OR "países em desenvolvimento" OR "América Latina" OR "América do Sul" OR Ásia OR África OR "América Central" OR Afeganistão OR Albânia OR Argélia OR Angola OR "Antígua e Barbuda" OR Argentina OR Armênia ou Azerbaijão OR Bangladesh ou Bielorrússia OR Belarus OR	LMIC's

	Belize OR Benin OR Butão OR Bolívia OR "Bósnia e Herzegovina" OR Botsuana OR Brasil OR "Burkina Faso" OR Burundi OR "Cabo Verde" OR Camboja OR Camarões OR "República Centro-Africana" OR Chade OR China OR Colômbia OR Comores OR "República Democrática do Congo" OR Congo OR "Ilhas Cook" OR "Costa Rica" OR "Costa do Marfim" OR Cuba OR Djibuti OR Dominica OR "República Dominicana" OR Equador OR Egito OR "El Salvador" OR "Guiné Equatorial" OR Eritreia OR Etiópia OR Fiji OR Gabão OR Gâmbia OR Geórgia OR Gana OR Granada OR Guatemala OR Guiné OR "Guiné-Bissau" OR Guiana OR Haiti OR Honduras OR Índia OR Indonésia OR Irã OR Iraque OR Jamaica OR Jordânia OR Cazaquistão OR Quênia OR Kiribati OR "República Popular Democrática Da Coreia" OR Kosovo OR Quirguistão OR Laos OR Líbano OR Lesoto OR Libéria OR Líbia OR "Antiga República Jugoslava da Macedônia" OR Madagáscar OR Malawi OR Malásia ou Maldivas OR Mali OR "Ilhas Marshall" OR Mauritânia OR Maurício OR México OR Micronésia OR Moldávia OR Mongólia OR Montenegro OR Montserrat OR Marrocos OR Moçambique OR Mianmar OR Namíbia OR Nauru OR Nepal OR Nicarágua OR Níger OR Nigéria OR Niue OR Paquistão OR Palau OR Panamá OR "Papua Nova Guiné" OR Paraguai OR Peru OR Filipinas OR Ruanda OR "Santa Helena" OR Samoa OR "São Tomé e Príncipe "OR Senegal OR Sérvia OR Serra Leoa OR "Ilhas Salomão "OR Somália OR "África do Sul" OR "Sudão do Sul" OR "Sri Lanka" OR "Santa Lúcia" OR "São Vicente e Granadinas" OR Sudão OR Suriname OR Suazilândia OR Síria OR Tadjiquistão OR Tanzânia OR Tailândia OR "Timor-Leste" OR Togo OR Tokelau OR Tonga OR Tunísia OR Turquia OR Turquemenistão OR Tuvalu OR Uganda OR Ucrânia OR Uzbequistão OR Vanuatu OR Vanuatu OR Venezuela OR Vietnã OR "Wallis e Futuna" OR " Cisjordânia e Faixa de Gaza "OR Iêmen OR Zâmbia OR Zimbábue	
7	**((1 OR 2) AND 3 AND 4 AND 5 AND 6)**	**COMBINE**

3. French:

Set	Terms	Keywords
1	Agriculteur OR berger OR pastoralisme OR "petit producteur" OR paysan OR éleveur OR "éleveur de porc" OR "éleveur de volaille" OR "ouvrier agricole" OR "petit éleveur" OR "élevage artisanal" OR "association de ferme familiale" OR "association des producteurs" OR coopérative OR "ferme commerciale" OR "élevage intensif" OR "élevage extensif" OR "éleveur laitier" OR "élevage transhumant" OR transhumance OR "animaux dans la cour" OR "éleveur informel" OR bétail OR "élevage semi-extensif" OR "élevage stable" OR "bétail extensif" OR "bétail intensif" OR "bétail nomade" OR "bétail transhumant" OR "bétail autoconsommé" OR "bétail de subsistance" OR "petit et moyen bétail" OR "élevage arrière-cour" OR "bétail à double usage" OR "bétail rural" OR "bétail arrière-cour" OR pêcheur OR aquaculture OR pisciculteur	Humans Participants
2	Ferme OR bovins OR "animal de production" OR "bovins de boucherie" OR "bovins laitiers" OR "bovins à double usage" OR "bovins créoles" OR bovins OR ovins OR porcins OR caprins OR équins OR aviaires OR "petits ruminants "OR vaches OR génisses OR veaux OR veaux OR moutons OR porcs OR alpagas OR tuis OR chèvres OR chevaux OR juments OR cobayes OR oiseaux OR poulets OR canards OR dindes OR lapins OR "animal de ferme" OR hato OR élevage OR aviculture OR "élevage de porc" OR aquaculture OR "fruits de mer" OR poisson OR crevettes OR crabes OR tilapia OR saumon OR truite	Animals
3	WASH OR eau OR hygiène OR assainissement OR nettoyage OR lavage OR puits OR pompes OR ressorts OR bassins OR "bassins d'oxydation" OR latrines OR excréments OR déchets OR compost OR "lavage des mains" OR désinfection OR	Interventions *a. Water* *b. Sanitation*

	désinfectant OR stérilisation OR autoclavage OR traitement OR pédiluvium OR bottes OR "bio sûreté" OR isolation OR moulin OR fumier OR "mesures de protection" OR décontamination OR "bio confinement" OR "bio gestion" OR "bio exclusion" OR "bio confinement" OR "barrières de protection" OR "équipement de protection" OR "vêtements de protection "OR vêtements OR gants OR "protocole McREBEL "OR ventilation OR "lit sec" OR "stockage de nourriture" OR "nettoyage de réservoir" OR fumigation OR "lutte antiparasitaire" OR "moustiquaire" OR cage OR hangar OR installations OR enclos OR "clôture périmétrique" OR érables OR quarantaine OR "mouvement animalier" OR "pasteurisation" OR "tout-en-un" OR "filet d'oiseau" OR "control biologique" OR incinération OR filtration	*c. Hygiene* *d. Biosecurity*
4	Infection OR maladie OR incidence OR prévalence OR séroprévalence OR mortalité OR morbidité OR "dénombrement des colonies" OR "charge bactérienne" OR "colonisation bactérienne" OR "concentration bactérienne" OR "dénombrement bactérien" OR "isolement bactérien" OR "bactérie résistante" OR "utilisation d'antimicrobiens OR "utilisation d'antibiotiques" OR "résistance aux antimicrobiens" OR "résistance aux antibiotiques" OR "prescription d'antibiotiques" OR "prescription d'antibiotiques" OR "visite vétérinaire" OR "service vétérinaire" OR "expert vétérinaire" OR "déchets d'antibiotiques" OR "résidus antimicrobiens" OR RAM OR "multi résistants" OR "utilisation d'antimicrobiens"	Outcomes
5	Intervention OR "mise en œuvre" OR expérience OR suivi OR programme OR pilote OR initiative OR stratégie OR "politique publique" OR méthode OR mesures OR technique OR législation OR réglementation OR "essai de contrôle randomisé" OR cohorte OR "cas-témoins" OR "test de contrôle non-aléatoire" OR "communautaire" OR "avant et après" OR "contrôle apparié" OR "régression-discontinuité" OR "série de cas" OR "rapport de cas" OR "étude de cas" OR "étude transversale" OR "étude longitudinale" OR "discontinuité de régression" OR "variables instrumentales" OR "différences d'indifférence" OR "coïncidence du score de propension" OR "différences uniques" OR "recherche ethnographique" OR "recherche-action" OR enquêtes OR "entretien approfondi" OR efficacité OR "rapport coût-efficacité" OR "coût-avantage" OR "analyse de coût" OR "coût-utilité" OR "rentabilité" OR "avantage-coût" OR "utilité de coût" OR "évaluation économique" OR impact	Study Types
6	"pays à revenu faible et intermédiaire" OR "pays en développement" OR "Amérique latine" OR "Amérique du Sud" OR "Amérique centrale" OR Afrique OR Asie OR Afghanistan OR Albanie OR Algérie OR Angola OR "Antigua-et-Barbuda" OR Argentine OR Arménie OR Azerbaïdjan OR Bangladesh OR Bélarus OR Belize OR Bénin OR Bhoutan OR Bolivie OR "Bosnie-Herzégovine" OR Botswana OR Brésil OR "Burkina Faso" OR Burundi OR "Cap-Vert" OR Cambodge OR Cameroun OR "République centrafricaine" OR Tchad OR Chine OR Colombie OR Comores OR "République démocratique du Congo" OR Congo OR "Îles Cook" OR "Costa Rica" OR "Côte d'Ivoire" OR Cuba OR Djibouti OR Dominique OR "République dominicaine" OR Équateur OR Égypte OR "El Salvador" OR "Guinée équatoriale" OR Érythrée OR Éthiopie OR Fidji OR Gabon OR Gambie OR Géorgie OR Ghana OR Grenade OR Guatemala OR Guinée OR "Guinée-Bissau" OR Guyane OR Haïti OR Honduras OR Inde OR Indonésie OR Iran OR Irak OR Jamaïque OR Jordanie OR Kazakhstan OR Kenya OR Kiribati OR "République Populaire Démocratique de Corée" OR Kosovo OR Kirghizistan OR Laos OR Liban OR Lesotho OR Libéria OR Libye OR "Ancienne République yougoslave de Macédoine" OR Madagascar OR Malawi OR Malaisie ou Maldives OR Mali OR "Îles Marshall" OR Mauritanie OR Maurice OR Mexique OR Micronésie OR Moldavie OR Mongolie OR Monténégro OR Montserrat OR Maroc OR Mozambique OR Myanmar OR Namibie OR Nauru OR Népal OR Nicaragua OR Niger OR Nigéria OR Nioué OR Pakistan OR Palaos OR	LMIC's

	Panama OR "Papouasie-Nouvelle-Guinée" OR Paraguay OR Pérou OR Philippines OR Rwanda OR "Sainte-Hélène" OR Samoa OR "São Tome et Principe" OR Sénégal OR Serbie OR Sierra Leone OR "Îles Salomon" OR Somalie OR "Afrique du Sud" OR "Soudan du Sud" OR "Sri Lanka" OR "Sainte-Lucie" OR "Saint-Vincent-et-les Grenadines" OR Soudan OR Suriname OR Swaziland OR Syrie OR Tadjikistan OR Tanzanie OR Thaïlande OR "Timor-Leste" OR Togo OR Tokelau OR Tonga OR Tunisie OR Turquie OR Turkménistan OR Tuvalu OR Ouganda OR Ukraine OR Ouzbékistan OR Vanuatu OR Venezuela OR Vietnam OR "Wallis et Futuna" OR " Cisjo rdania et la bande de Gaza "OR Yémen OR Zambie OR Zimbabwe	
7	**((1 OR 2) AND 3 AND 4 AND 5 AND 6)**	**COMBINE**

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