



# Framework for understanding environmental antimicrobial resistance in England

Chief Scientist's Group report

August 2020

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Professor Doug Wilson  
**Chief Scientist**

# Executive summary

Antimicrobial resistance (AMR) has developed into a global public health crisis from successive decades of increased dependence on antimicrobials in humans and animals. Misuse of antimicrobials in the clinic, community, food animal production, and agriculture, and the widespread pollution of the environment from these activities, including pharmaceutical manufacturing, all contribute to the increase in AMR witnessed, globally.

The environmental dimension of AMR includes all ‘environments’ except those within or on humans and animals. The ‘environment’ can also include the indoor environment, which is inclusive of the home and hospital. The outdoor environment indirectly receives antimicrobials from upstream activities (i.e., clinical and community use of antimicrobials, wastewater, and animal meat production); these activities often also discharge antimicrobial-resistant bacteria (ARBs). There are many examples where the primary use of the antimicrobial is directly within the environment, i.e., aquaculture (antibiotics, antiparasitics), citrus (antibiotics) and cereal crops (antifungals).

Traditional endpoints used in the control of harmful chemicals in the environment, i.e., death or reduced fecundity, are not appropriate for the control of antimicrobial resistance. Antimicrobials can have toxic effects (Le Page et al., 2019), however, their effect of driving AMR occur at concentrations that can be several orders of magnitude lower in concentration than those defined as toxic to higher organisms. Moreover, antimicrobial resistance genes (ARGs) are an attribute of bacteria that allows it to survive exposure to antimicrobials. ARGs found within one bacteria can often be shared with other bacteria, facilitating the spread of the ARGs through the population, which can then spread globally. These phenomena have been increasingly witnessed in near real-time in the academic literature, e.g., mobile colistin resistance. Environments that enrich for ARGs can facilitate the transmission of these ARGs to humans and animals. Once in the gut of a human or animal, the ARG can be incorporated into the genome of pathogens, further increasing the risk of developing and spreading drug-resistant infections.

This report seeks to:

1. Provide an introduction to hazard characterisation for AMR in the environment.
2. Provide a historical perspective on the evolution of the environmental dimension of AMR as found within schematics published within the peer-reviewed literature.
3. Provide a review of the key components identified in the literature for hazard characterisation of AMR in the environment with an aim towards informing future risk assessments
4. Identify and describe existing datasets, including spatial metadata to inform future hazard characterisation and risk assessment efforts.

Seventy-three relevant datasets and reports were identified from electronically-accessible data resources. A completed list of datasets is provided electronically to determine the utility of these datasets for a hazard or risk

assessment of AMR in the environment. The spatial and temporal limitations need to be considered on a case-by-case basis. There is a substantial lack of transmission data of AMR from the environment to humans (or animals). It will be essential to use existing data to inform strategies aimed at limiting AMR selection, dissemination and transmission. However, it remains unclear the extent to which this can be done without additional data collection. It is expected that the water industry, farming, NGOs, and the government itself, will have data that is either not publically accessible or poorly accessible, which can help to strengthen efforts to examine hazard and risk from AMR in the environment.

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# 1 Introduction

## 1.1 Background to AMR

The increasing number of antimicrobial-resistant (AMR) infections worldwide are largely the result of poor antibiotic stewardship in humans and animals, widespread use in aquaculture and agriculture, poor environmental stewardship among pharmaceutical manufacturers, and the resulting environmental contamination (Fukuda et al., 2018; International Environmental AMR Forum, 2018; Singer et al., 2016). The rapid innovation and application of different classes of antimicrobials into the clinic, farm and agriculture (Kirchhelle, 2018) is not a recent phenomenon but has continued unchecked since the 1940s (Graham et al., 2016; Knapp et al., 2010).

Antimicrobials are environmentally-relevant pollutants as they inhibit or kill susceptible bacteria. Bacteria can naturally harbour the capacity for resistance to some antibiotics (Davies and Davies, 2010), a phenomenon called intrinsic resistance. Resistance can also be acquired. The latter can be achieved through a variety of mechanisms including: de novo mutation, horizontal gene transfer (HGT) and transduction from bacteriophage (Singer et al., 2016). The genome of all microorganisms, including pathogens, contain a mixture of intrinsic and acquired antibiotic resistance genes. The capacity of bacteria to survive antibiotic exposure through HGT is perhaps the most critical phenomenon that bacteria perform to maintain and spread antimicrobial resistance, globally (Marshall and Levy, 2011). Were it not for the mobilisation of resistance genes from one unrelated bacterium to another nested within an interconnected world, AMR would be a considerably more tractable challenge (Frost et al., 2019; Tarabai et al., 2019; Wang et al., 2018a; Wu et al., 2018).

Visual representations of the interconnectedness of different sources of AMR in the environment (i.e., humans, wastewater treatment plants (WWTPs), animals) or sinks for AMR (i.e., water, soil, air), and the chemicals that drive it (i.e., antimicrobials), have been characterised within England since the 1970s. One of the best described of these sources of AMR and the AMR-driving chemicals are WWTPs.

WWTPs are often central to schematics detailing locations where AMR selection, dissemination and transmission occur. WWTPs are unique in that they receive both antibiotic-resistant bacteria from people's faeces, as well as a significant fraction of the antibiotics that are consumed by the population. The co-location of antibiotics, bacteria and antibiotic resistance genes (ARGs) make WWTPs the ideal location for both selection and dissemination of AMR. The UK water industry initiated the Chemicals Investigation Programme (CIP), which assessed final effluent concentrations of chemicals, including antibiotics, metals and biocides, from 162 WWTPs in England, Scotland and Wales (Comber et al., 2017; Gardner et al., 2012, 2013) and their sludge (Comber et al., 2015; Jones et al., 2014). The CIP3 programme, which is commencing in 2020, will include a systematic assessment of AMR and antibiotics within selected WWTPs.



One of the few clear examples of AMR transmission from the environment to humans, within England, is from sewage-impacted bathing waters. A recent study of high-frequency users of Southwest England coastal waters (i.e., surfers) was shown to have significantly elevated carriage of antibiotic-resistant (putative) pathogens as compared to the control, non-bathing beachgoers (Leonard et al., 2018a). Elevated exposure to sewage-impacted coastal waters was the likely aetiology of the pathogen and resistance genes. Still, these factors cannot be easily disentangled from other potential sources of human pathogens also present in coastal waters, such as wild bird faeces and dog faeces (Leonard et al., 2018a, 2020).

Further evidence from the literature demonstrates WWTPs as a significant mechanism for AMR selection and dissemination within English rivers (Amos et al., 2014, 2015). Gouliouris et al. (2019) conducted a survey of *vancomycin-resistant Enterococcus faecium* (VREfm) in wastewater across the East of England, demonstrating that WWTP treatment of hospital and municipal wastewater did not prevent downstream dissemination of VREfm as well as genetic intermixing between wastewater and bloodstream infection strains (Gouliouris et al., 2019).

Animal husbandry represents an activity long recognised as having the potential for AMR selection, dissemination and transmission (Swann et al., 1969). Ludden et al. (2019) recently surveyed extended-spectrum-lactamases (ESBL) producing *Escherichia coli* (*E. coli*) and non-ESBL-producing *E. coli* from livestock at 29 farms in the East of England (10 cattle [5 beef cattle and 5 dairy cattle], 10 pig, and 9 poultry [4 chickens and 5 turkeys]) (Ludden et al., 2019). A comparison of mobile resistance elements across the study revealed that approximately 5% of the human ESBL *E. coli* isolates shared closely related antimicrobial resistance-associated mobile elements with those found in livestock. Notwithstanding the evidence of animal to human cross-over, the authors concluded that the predominance of *E. coli* from livestock was not closely related to isolates causing human disease in the East of England, suggesting that ESBL *E. coli* associated with serious human infection was unlikely to have originated from livestock in the study region (Ludden et al., 2019).

## 1.2 Policy drivers

The World Health Organization (WHO) Global Action Plan (GAP) on antimicrobial resistance outlines the need to strengthen the knowledge and evidence base through surveillance and research, as well as to reduce the incidence of infection through adequate sanitation, hygiene and infection prevention measures. The GAP states that there “*are still major risks associated with the occurrence of emerging pollutants, pathogens and antimicrobial-resistant bacteria in our water bodies and oceans that may impact all of society*” (World Health Organisation, 2015). The European Commission (European Commission, 2017) and United Nations Environment Assembly (United Nations, 2017), both call for scientific evidence concerning the development and spread of AMR in the environment and the risks it poses to human health and the environment. The UK government’s five- and twenty-year action plan and vision to tackle AMR acknowledge the role that the environment might play in the

selection, dissemination and transmission of AMR to humans and call for research that would help quantify and assess these hazards to inform policy and mitigation (Department of Health, 2019; HM Government, 2019).

## 2 Rationale for report

This report has identified and compiled existing datasets considered potentially useful in qualifying and quantifying AMR hazard within an environmental setting in England. In this context, a hazard is defined as a location where the agent or agents (e.g., chemicals, bacteria and resistance genes) are enriched from anthropogenic sources over background (natural) levels at that location. Hazard characterisation can be used to inform a risk assessment, which semi-quantitatively reflects the probability that the ‘hazardous agent’ impacts a particular receptor. Here, we assume the receptors to include humans, animals, wildlife, and microorganisms. Given that animals and microorganisms reside with soil and water, these can also be considered receptors—though the metric of ‘impact’ on a non-biological system will require a different metric of ‘impact’ from biological endpoints. The datasets reported here are inherently temporally and spatially limited and as such, might offer limited value for informing a hazard or future risk assessment.

The metadata associated with each dataset, found in associated data table, can be used to help determine the suitability of each dataset for hazard characterisation and/or risk assessment. All datasets have the spatial constraint of having some coverage of England. Determination of the ‘hazardous agents’ and the locations from which they are emitted into the environment were derived from a literature review, reported in Section 3. The literature review focused on capturing models of AMR in the environment since the earliest record. Datasets included in Section 5 were informed by the schematics reported in Section 3. Some datasets might best serve as a proxy measure for sources of AMR or AMR-driving chemicals (i.e., ‘hazardous agents’).

## 3 Theoretical models of AMR in the environment

### 3.1 Selection for antimicrobial resistance

Antimicrobial resistance might be a natural feature of, or indeed a natural response by, microorganisms to antagonistic chemicals (e.g., antivirals, antibiotics, antifungals), many of which are made by bacteria, fungi and plants (Kashuba et al., 2017; Magi et al., 2015; Palmer-Young et al., 2017; Perron et al., 2015; Rascovan et al., 2016). Given the opportunity afforded by evolution, horizontal gene transfer and time, all microorganisms can enhance existing resistance mechanisms and/or acquire antibiotic resistance (Holmes et al., 2016). A qualitative determination of areas within the English landscape that present an elevated hazard for AMR selection can be made by assessing where 1) bacterial abundance; 2) chemical exposure; and 3) time is maximised. How these three factors can be understood to impact AMR selection are discussed below:

**A high abundance of bacteria** – This is a quantitative parameter that is difficult to define a cut-off between low, medium and high. The metric of low, medium and high is best understood in relation to the hazard it poses to a receptor (i.e., human). A high abundance/load of bacteria in sewage that will be discharged to a river cannot be easily compared to a high load of bacteria in drinking water. The abundance of bacteria will differ by many orders of magnitude and the hazard posed to humans will vary considerably as well. The quantity of bacteria does not inherently inform one's ability to assess hazard to AMR. However, it is logical to conclude that high bacterial loads with high chemical exposures will rapidly result in AMR selection. Here, selection is defined as a combination of the following: bacterial death, horizontal gene transfer, mutation rate increase, gene up-regulation, changes in epistasis, and community compositional changes (Durão et al., 2018; Wong, 2017).

**A high abundance of AMR-driving chemicals** this includes antimicrobials (antiviral, antibiotics, antifungals, antiparasitics, anthelmintics), biocides (Kurenbach et al., 2015), metals (Zhang et al., 2019; Zhao et al., 2019), and many other non-antibiotic pharmaceuticals (Maier et al., 2018; Wang et al., 2019). This is a quantitative parameter that also has poorly defined thresholds for low, medium and high hazard. Threshold concentrations have been proposed by the pharmaceutical industry as a tool to control the AMR hazard posed by antimicrobial manufacturing facility discharge into the receiving rivers (Bengtsson-Palme et al., 2016; Tell et al., 2019). These thresholds attempt to predict the antibiotic concentrations that will inhibit or kill members of the bacterial communities in the receiving river. Only a few empirical tests of these thresholds have been examined, showing good correlations between these modelled thresholds and changes in bacterial community. However, evidence of biological effect (e.g., selection, community compositional changes) does not necessarily correlate well with clinically-relevant resistance genes (Gullberg et al., 2014; Liu et al., 2011; Murray et al., 2018, 2019; Wistrand-Yuen et al., 2018). The larger the reservoir of resistance genes in the environment, the more likely it will be that these resistance genes have an opportunity to

influence what is clinically-relevant into the future. In short, all resistance genes in the environment have the potential to become clinically relevant. Considerably more research needs to be conducted to determine the clinical relevance of AMR selection at low environmental concentrations in the environment.

**Time** – The longer bacteria are exposed to a chemical hazard, the more likely resistance develops and spreads within the exposed community. In practice, resistance can develop very quickly (Frimodt-Møller and Løbner-Olesen, 2019) and spread within a community on the order of hours to days (Maddamsetti and Lenski, 2018). If a chemical hazard is episodic, i.e., released into the environment as a pulse, it might be expected to have a different impact on bacterial resistance selection from a chemical, which is chronically released into the environment. The length of exposure can also be variable, such as in a river that receives untreated wastewater from storming or combined sewage overflows during high rainfall events, which can last from minutes to days. Conversely, a soil amended by biosolids containing antibiotics will, arguably, maintain continuous exposure until the antibiotic is biodegraded, biotransformed, reduced in its bioavailability, or leached away. The interaction between the concentration of antibiotic and time of exposure will be important, but there is little in the literature to leverage for understanding fundamental principles.

AMR selection is driven by factors that are under the control of industry, farmers, healthcare, and society (at a global scale). As such, source reduction of AMR-driving chemicals represents an important and likely cost effective mechanism for mitigating AMR in ‘downstream’ environments. In some cases, the drivers of selection, i.e., human antibiotic use, are driven by a series of interconnected ‘upstream’ factors that could be addressed to impact a reduction in antibiotic use. For example, increased vaccination for bacterial pathogens in a population will translate into reduced antibiotic use without imposing additional constraints on antibiotic stewardship. The implications of source reduction can be substantial for the reduced hazard of resistance selection in ‘downstream’ environments, such as rivers (Singer et al., 2011, 2019).

## 3.2 Dissemination

‘Dissemination’ refers to the release and spread of AMR-driving chemicals such as antimicrobials, metals, biocides and a growing number of other pollutants (Maier et al., 2018; Wang et al., 2018b), antimicrobial-resistance genes (ARGs) and/or antimicrobial-resistant bacteria (ARBs) across a landscape. It is theoretically possible that a source of antibiotics, ARGs and/or ARBs will not be disseminated into the wider environment; however, in practice, few sources remain contained. For example, ARBs and ARGs have been recovered in migrating birds exposed to wastewater-impacted water bodies and landfills. ARG-enriched faeces released by these birds have been found in otherwise pristine environments, often hundreds to thousands of miles away from the source (Ahlstrom et al., 2018; McCann et al., 2019; Swift et al., 2019).

Ballast water from ships has been known to be a mechanism by which invasive species are transported, again across long distances. Ballast water has been found to contain ARBs that could represent an additional AMR hazard to the

location receiving the water (Dobbs et al., 2013; Gerhard and Gunsch, 2020; Lv et al., 2018). WWTP effluent discharged into a fixed stretch of river reflects the dissemination of AMR-selecting chemicals, ARGs and ARBs not just into the immediate discharge location, but as far as 10 km downstream the length of a river (Amos et al., 2015). Conversely, grazing animals are spatially variable (e.g., graze across a wide landscape), but perform discrete episodes of urination and defecation. These faeces can remain static or be mobilised into groundwater, surface water, across the soil landscape, or carried on the shoe of a rambler traversing across a farmer's field on a designated path (Tyrrel and Quinton, 2003).

### 3.3 Transmission

Transmission of ARBs from the environment to an animal or human is achieved through direct contact with the source, as in bathing in sewage-impacted water (Leonard et al., 2018a), or through indirect contact, as in ARB-contaminated food and air. With the exclusion of food, there are relatively few papers that demonstrate the transmission of ARBs from the environment into humans (Day et al., 2019; Dorado-García et al., 2018; Gouliouris et al., 2019; Leonard et al., 2018a, 2018b, 2020; Wuthiekanun et al., 2005; Zhou et al., 2018) or animals (Arnold et al., 2016; Greig et al., 2015; Ludden et al., 2019; Smith et al., 2014; Torres et al., 2019), representing a very significant gap in our knowledge that is required to inform hazard and risk assessments. The transformation of DNA from dead bacteria into active bacteria in the environment highlights the ease by which DNA-pollution can complicate efforts to quantify exposure and transmission hazards for ARGs (Mao et al., 2014; Overballe-Petersen et al., 2013). Bacteriophage are known to inadvertently incorporate segments of the host bacterial DNA into its genome upon replication. Subsequent infection from this bacteriophage can thereby introduce ARGs into the host DNA, thereby representing a novel pathway for ARG transmission.

## 4 Schematics of AMR in the environment

Conceptual models that represent the sources of AMR-driving chemicals, ARGs and ARBs and the pathways of dissemination and transmission have existed in the literature since 1973. It can be seen that the number of sources, sinks and transmission points identified in these models have grown over the years. However, few if any of the additions to the models are recent developments, but more reflect our increasing awareness and understanding.

Shuyler (1973) details in Figure 1 the pathways by which antibiotics are transported onto feedlots. Dust, dry waste, slurry and runoff are among the principal mechanisms by which antibiotics are exported from feedlots (Shuyler, 1973).

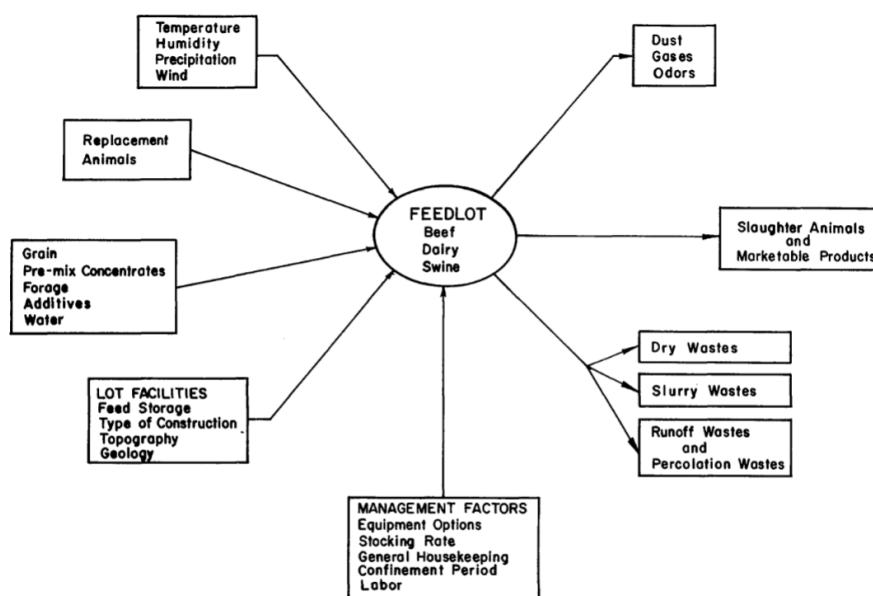
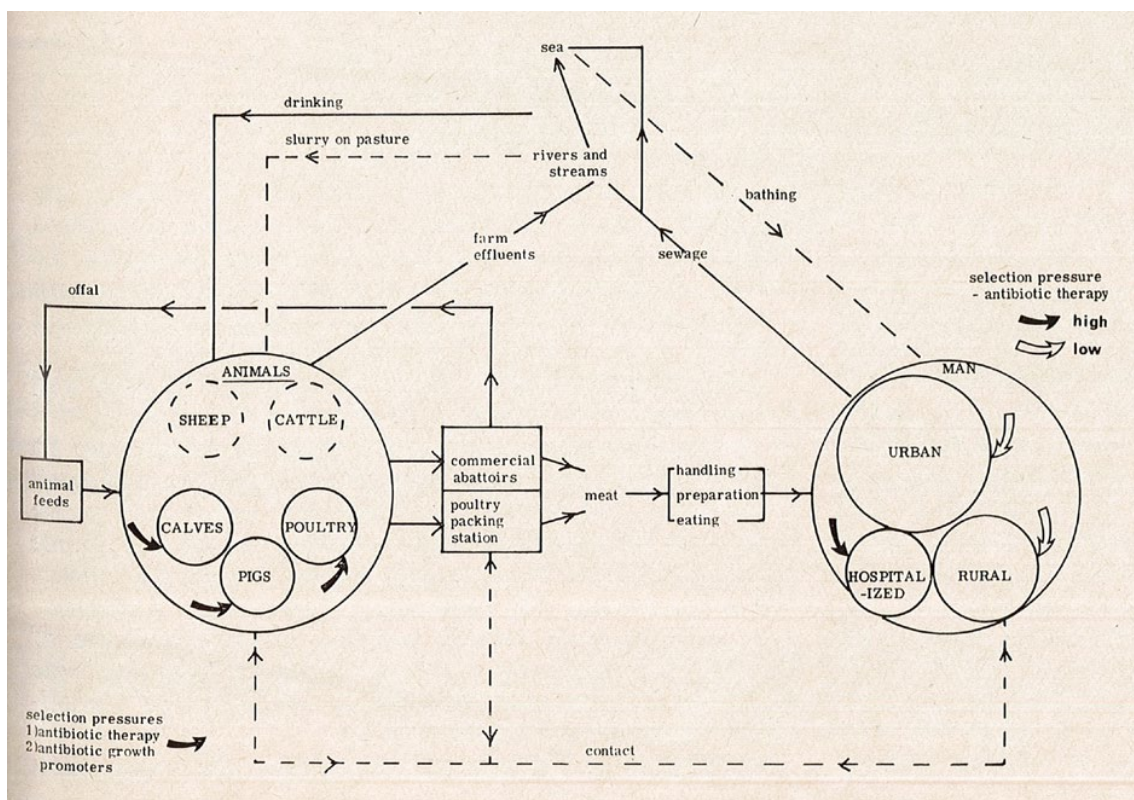


Figure 1. Schematic by Shuyler (1973) reproduced in Addison (1984) of the role of feedlots in the movement of antibiotic on and off the feedlot.

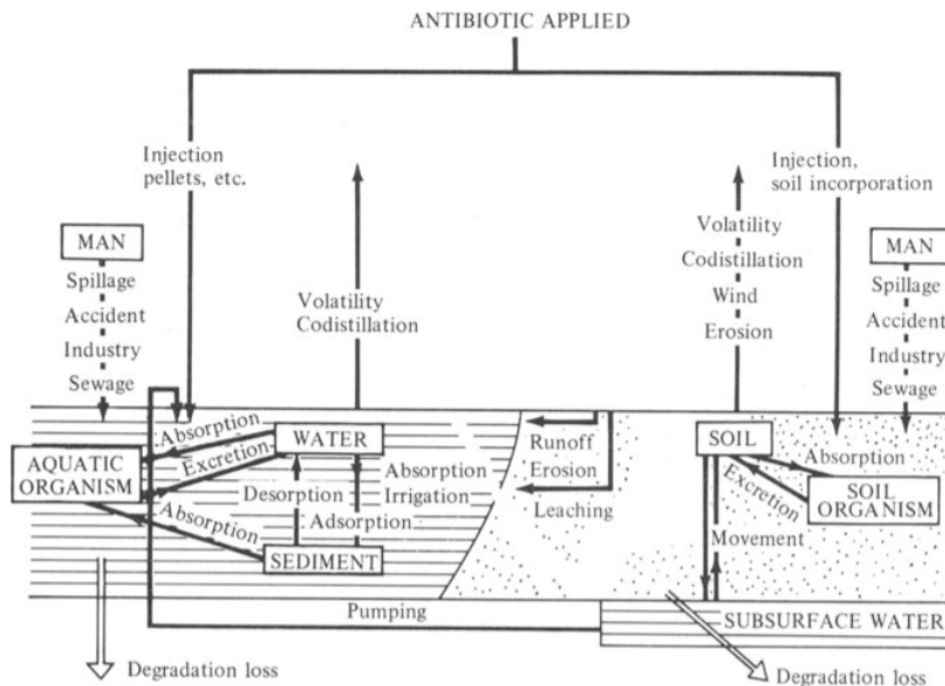
Lindon et al. (1977) highlight in Figure 2 the role that therapeutic and growth promoter antibiotic use plays in driving AMR in animal meat production. Growth promotion is banned in the EU, but antibiotic use in animal meat production remains high for some sectors (e.g., pigs) (Veterinary Medicines Directorate, 2019). Evidence of offal use in the animal feed was highlighted as a hazard for transmission of AMR, which was only eliminated in the 1990s after the spread of bovine spongiform encephalopathy. The effluent from farms was shown to be connected to rivers and streams, with further impacts on the sea, bathing, drinking water and pasture through land spreading. The authors qualitatively distinguished locations that exhibit high and low 'selection pressure'. Calve, pig and poultry production, as well as hospitals, represent areas where selection was deemed high. Low selection was seen to occur in the community setting (i.e. urban and rural setting).



**Figure 2. Schematic by Linton (1977) detailing the selection pressures from antibiotic therapy and growth promoters across the environmental landscape**



Addison (1984) details in Figure 3 the fate and transport of antibiotics on feedlots. Antibiotics can impact and transfer into, and through soil and water as a result of spillage, accident, industry, and sewage, as well as incorporation as a component of feed added directly to or incorporated into water and soil. After administering antibiotic feed additives, losses occur through surface run-off, sediment loss, volatilization, organisms uptake, and degradation (Addison, 1984).



**Figure 3. Schematic by Addison (1984) detailing antibiotic fate and transport in the environment.**

Addison (1984) illustrates in Figure 4 the transport of antibiotics as conceptualised within an “Antibiotic Transport and Run-off (ATR) Model”. The model contains four ‘antibiotic storage zones’ within the soil profile: surface zone, upper zone, lower zone, and groundwater zone. The model assumes surface run-off, sediment loss, antibiotic adsorption-desorption, and antibiotic volatilization and degradation. Each of these fate mechanisms allows for the dissemination of antibiotics into different environmental compartments, with final dissemination into streams or groundwater. Although it is theoretically possible for antibiotics to be disseminated into the atmosphere through volatilization, it likely constitutes a small component of the total fate of antibiotics in the soil-feedlot setting. It is reasonable to expect the soil to which antibiotics, ARGs and ARBs are adsorbed could be blown into the atmosphere where they are diluted across the landscape and contribute more substantially to their dissemination.

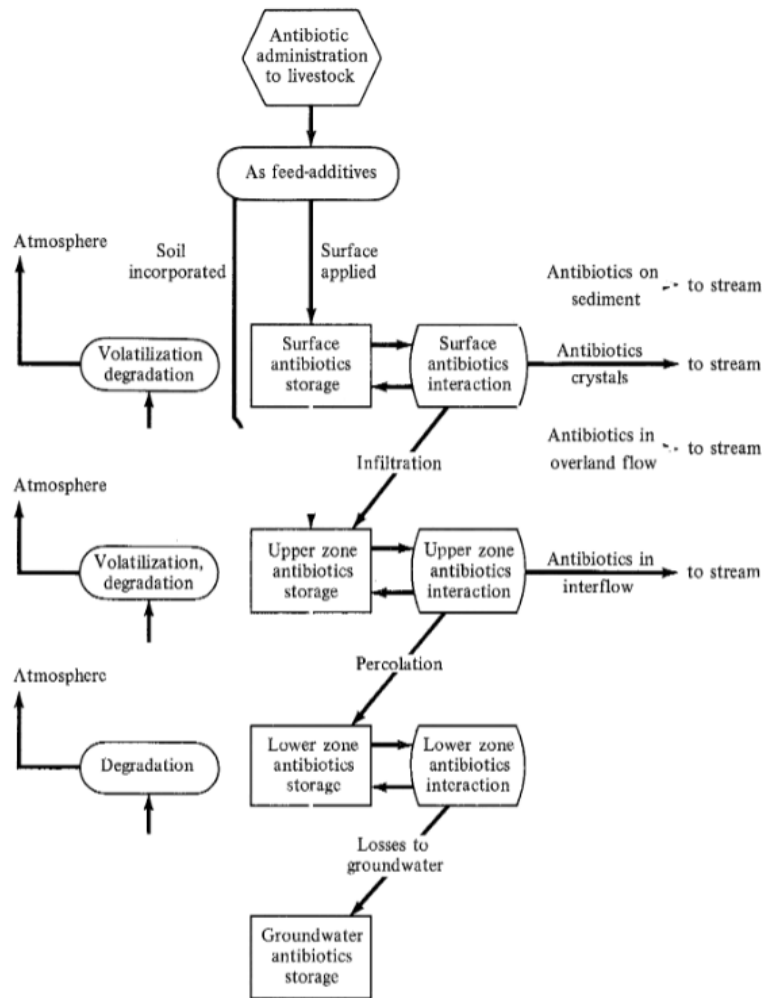



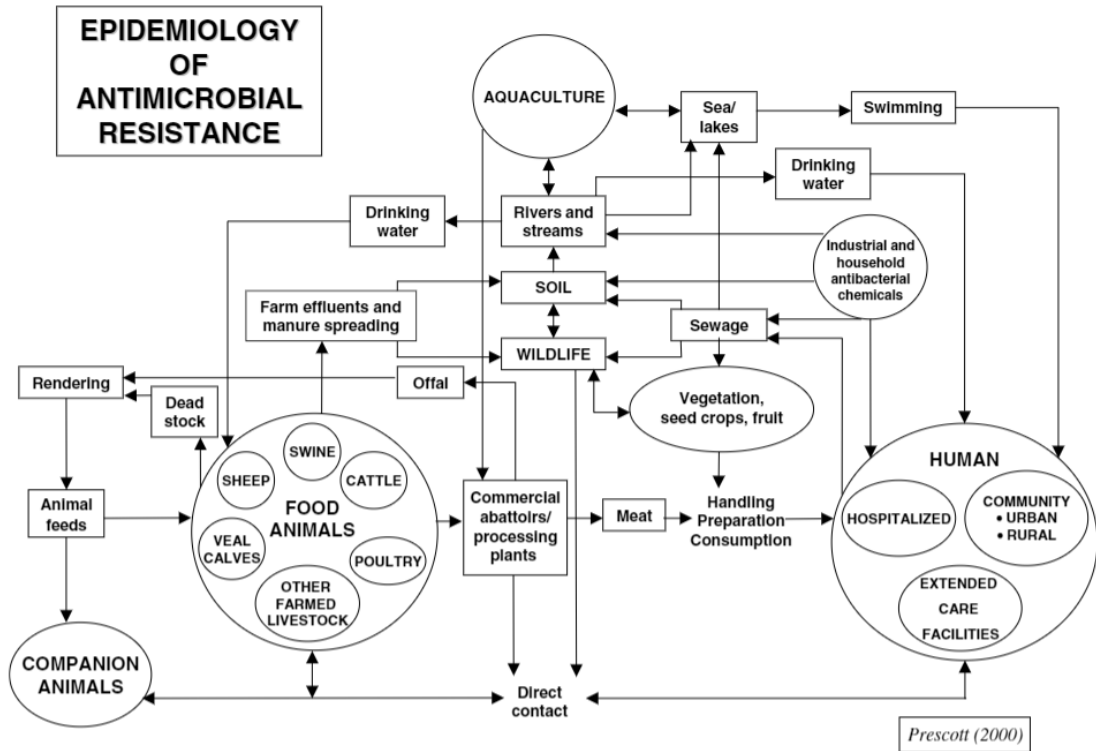


Fig. 3. Flowchart of antibiotic movement in ATR model:  = data input,  = function, and  = storage.

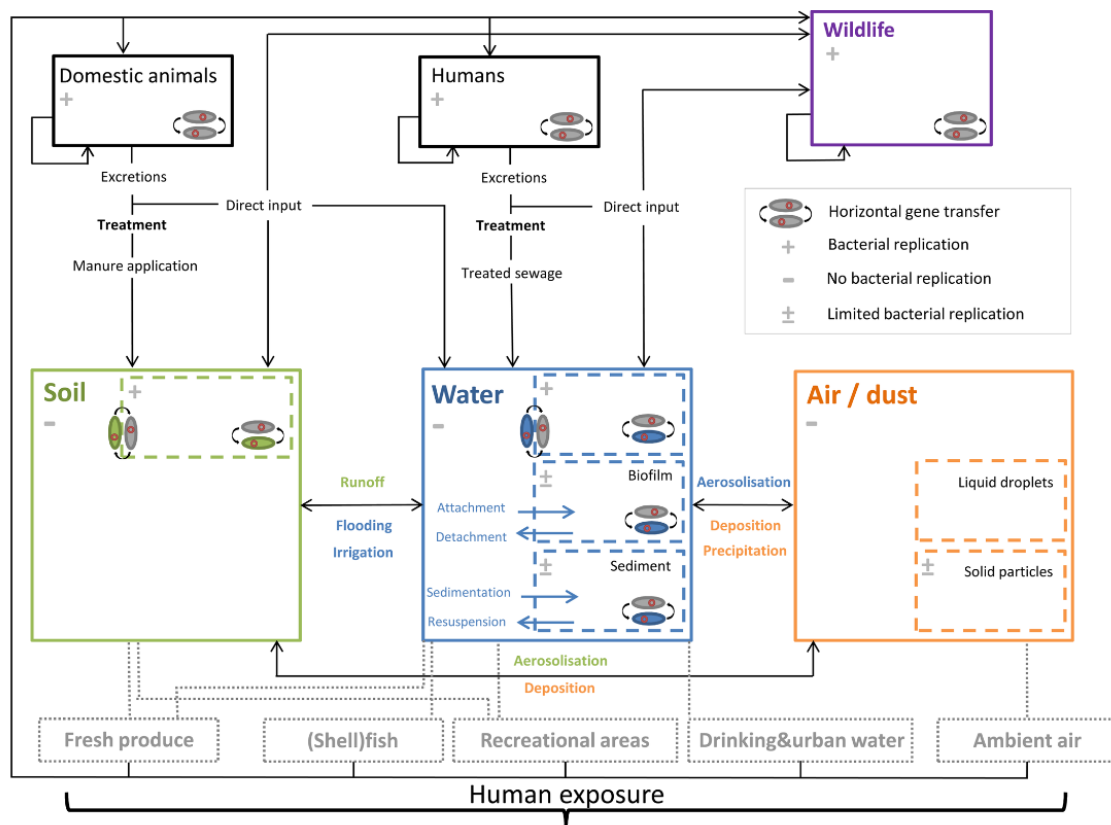
**Figure 4. Schematic in Addison (1984) of the antibiotic storage zones that can be used to model the fate of antibiotics in feed lots.**

Boerlin and Reid-Smith, 2008, reproduced and modified a figure from "Antimicrobial Therapy in Veterinary Medicine" by Prescott and Baggott, 1988, which details the interconnectedness of the elements held within the One Health Perspective on how antimicrobial resistance flows between different sources within the environment (Boerlin and Reid-Smith, 2008; Boerlin and White, 2013). This schematic includes a combination of sources (e.g., aquaculture, animal feed), pathways (e.g., soil, rivers, effluent), and exposure routes (e.g., swimming, drinking water, meat). Notably, it also includes wildlife, which demonstrates recognition of the ubiquitous nature and global spread of AMR, at the time.



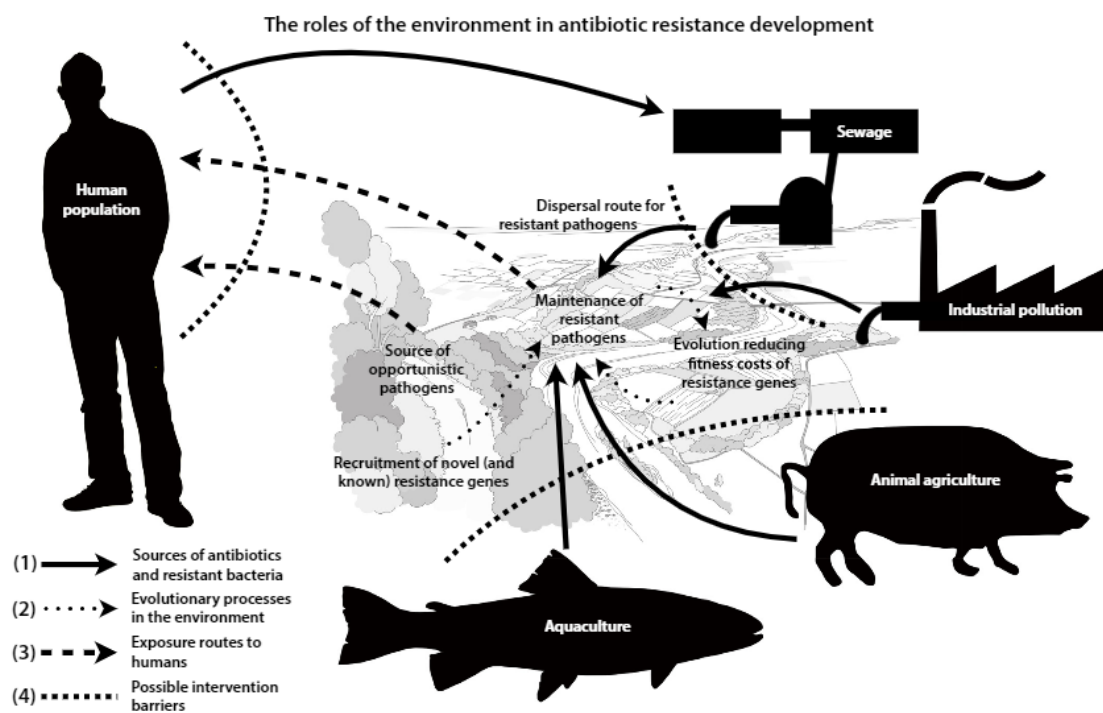
**Figure 5. The pathways of resistance transmission. This diagram depicts the epidemiology of antimicrobial resistance and plausible pathways of spread between various environments.**

Huijbers et al. (2015) published a schematic, shown in Figure 6, of environmental compartments, contamination sources, exposure-relevant sites, and processes affecting survival and spread of bacteria (Huijbers et al., 2015). Figure 6 is among the first schematics to specifically detail the role of horizontal gene transfer in the spread of AMR. The compartments identified by the authors are less diverse than those noted in Figure 5. Here the authors focus on the dissemination and transmission of AMR in the environment and how it can relate to human exposure. The authors identify five areas where transmission of AMR from the environment to humans is most likely: 1) fresh produce; 2) shellfish, 3) recreational areas; 4) drinking and urban water and 5) ambient air. Although dust was mentioned as early as 1973 as a source of antibiotics from feedlots to the atmosphere; it was not until very recently that air was recognised as a potentially important pathway for ARGs and ARBs dissemination.



**Figure 6. Schematic environmental AMR: environmental compartments, contamination sources, exposure-relevant sites, and processes affecting survival and spread of bacteria.**

Larsson et al. (2018) present a schematic in Figure 7, which speaks to the factors that contribute to the maintenance of resistant pathogens in the environment (Larsson et al., 2018). Here the authors the main sources of antibiotics and ARBs into the environment: 1) humans; 2) sewage; 3) industrial pollution; 4) animal agriculture; and 5) aquaculture. The authors distinguish between these sources and the evolutionary processes that they drive in the environment, which reduce the fitness cost associated with the acquisition of any new ARGs. The survival of ARBs and the evolution of ARGs in an environment devoid of antimicrobial pressure has been witnessed and remains a complex phenomenon to understand with few guiding principles to use at present (Knöppel et al., 2017; Rodríguez-Verdugo et al., 2013). Nevertheless, it remains an important phenomenon to understand within the larger challenge of AMR. The chronic nature of these drivers of AMR reinforces the importance of ‘time’ as a defining factor—with enough ‘time’, the evolution and recruitment of novel resistance genes into environmental bacteria and pathogens is inevitable.



**Figure 7. Schematic produced by Larsson et al. (2018) of environmental AMR**

Singer et al. (2016) show in Figure 8, a schematic of the drivers of AMR in the environment and how these chemicals and ARGs move across areas of regulatory interest for the Environment Agency of England (Singer et al., 2016). This schematic is not as extensive in the many pathways of antibiotic and ARG/ARB dissemination as previous schematics have been, but it is unique in that it attributes importance to the non-antibiotic drivers of AMR (e.g., biocides and metals). Notably, the authors highlight the direct relevance of each source of antibiotics/pollutants and/or ARGs to the work of environmental regulators.

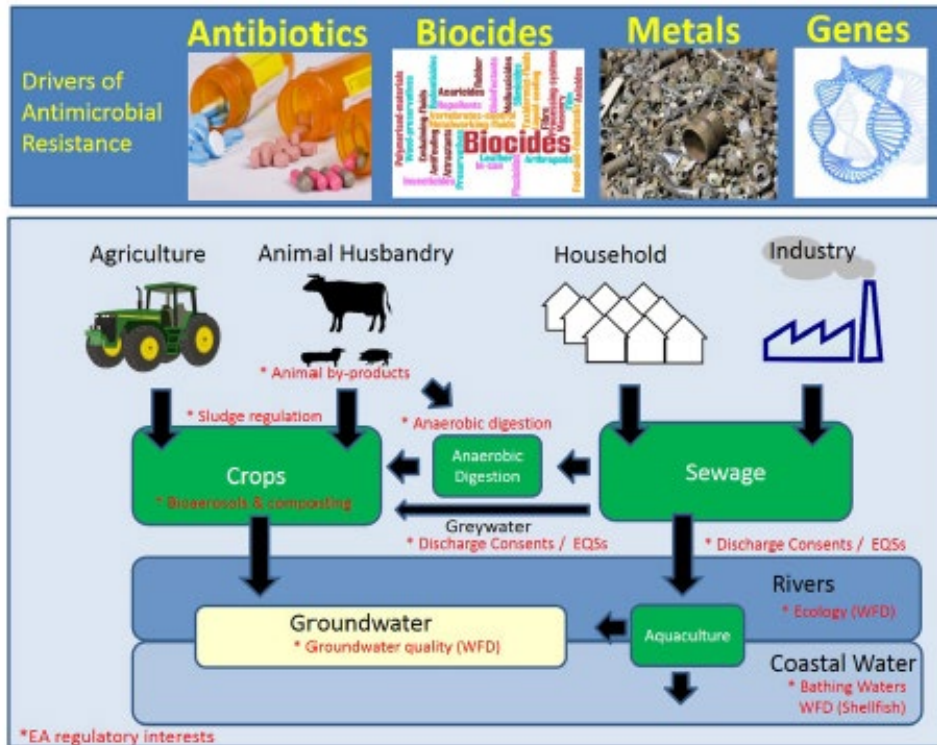


Figure 8. Schematic detailing the movement of chemical and genetic drivers of AMR through the environment.

The United Nations Environment Programme provides a schematic of the interconnectedness of different stakeholders that contribute to selection, dissemination and transmission of AMR in the environment (UN Environment Programme, 2017). This schematic is important as it is one of the first to embrace the principles of One Health and the relevance of the environment to humans and animal health.



**Figure 9. UN Environment Programme schematic of the interconnectedness of the One Health paradigm and the central role that rivers play throughout.**

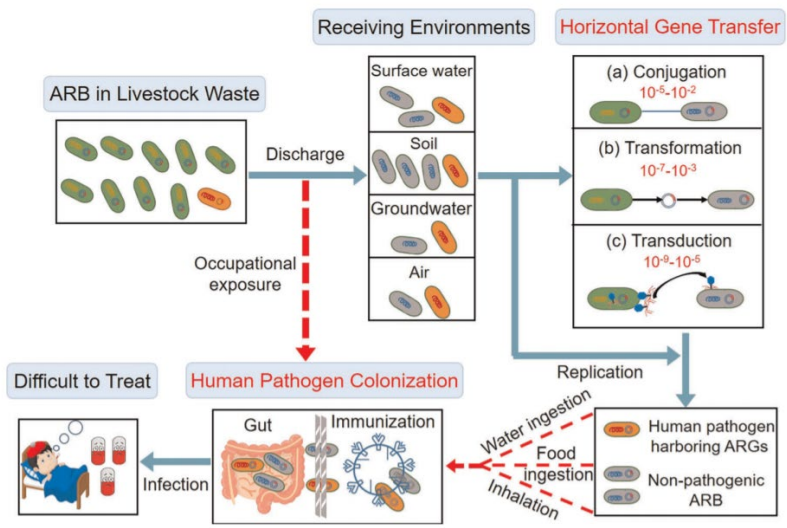
The CDC Antibiotic Resistance Threat Report 2019 (Centre for Disease Control, 2019) focuses on the interconnectedness of the One Health approach. This schematic provides a richer understanding of the dissemination and transmission risk which other schematics do not often combine. This schematic includes many transmission risks that are not necessarily unique to AMR, but also apply to infectious diseases. It is, however, important to note that this schematic is one of the few produced by the US government to embrace a One Health perspective on AMR. The inclusion of air travel highlights that AMR risks traverse both state and national boundaries



**Figure 10. A Complex Web: Everything is Connected.**

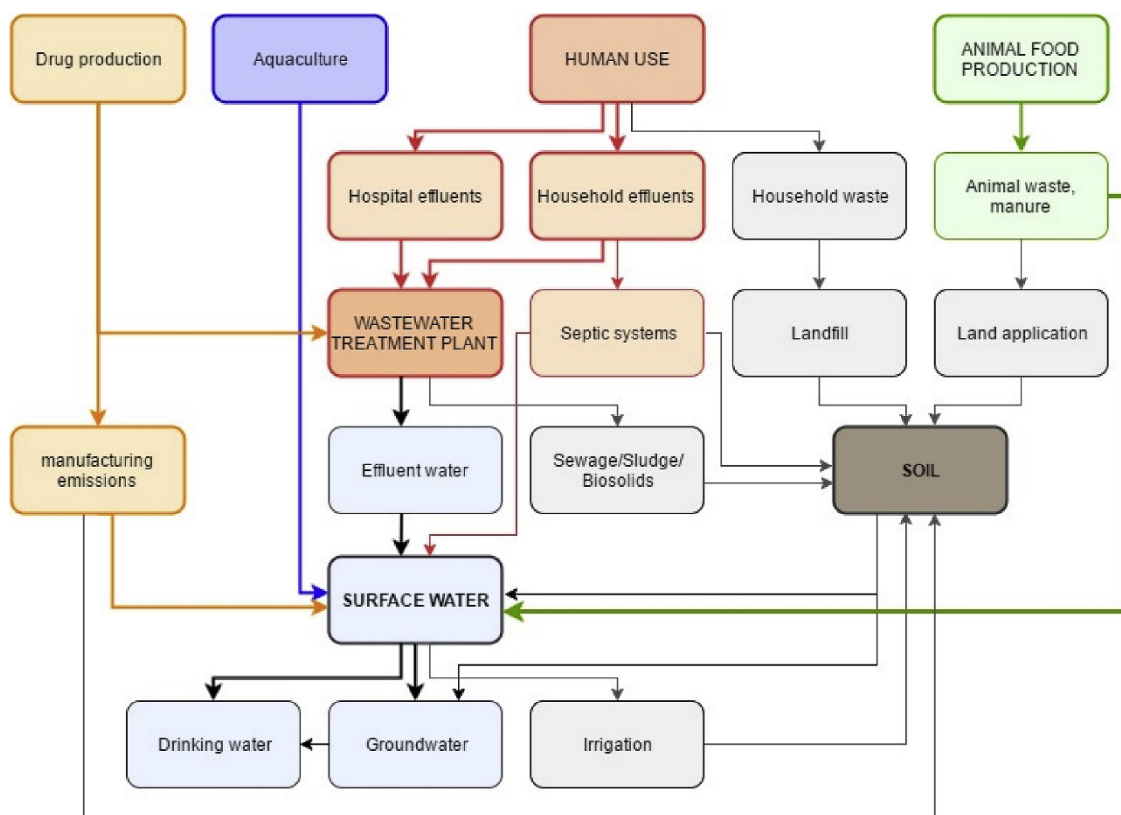


He et al. (2020) published a schematic detailing the dissemination and transmission risk that livestock waste poses to the environment and human health. The authors characterise four environments that receive livestock waste: surface water, soil, groundwater and air (He et al., 2020). Estimates for the dissemination risk for ARGs from HGT by means of conjugation are proposed, arguably the most likely mechanism by transformation, at a rate of  $10^{-5}$  to  $10^{-2}$  per cell, which is to mean that on average between 100 and 10,000 cells are needed to undergo the transformation of ARGs. A similar but slight lower rate of HGT is projected to occur by transformation, i.e., acquisition of naked DNA from the environment, at a rate of  $10^{-7}$  to  $10^{-3}$  per cell. A projected even lower rate of ARG transfer is projected to occur via transduction, i.e. by bacteriophage, at a rate of  $10^{-9}$  to  $10^{-5}$  per plaque forming unit. Given that there are  $>10^7$  cells in a gram of soil, it is expected that these processes are capable of occurring in all environments but limited by other factors such as bacterial density, nutrient availability, pollutant/chemical exposure, temperature, and time.



**Figure 11. Schematic produced by He et al. (2020) of the ARG dissemination pathways from livestock waste to humans.**

Kovalakova et al. (2020) provide in Figure 11 a schematic that, uniquely, includes landfills and septic systems, which are routinely omitted on previous schematics of the interconnectedness of antibiotics and ARG pathways into and within the environment (Kovalakova et al., 2020). The author used the colour of the arrows to designate the transport of antibiotics for different applications: human consumption (red), animal food industry (green), aquaculture (blue), and manufacturing (orange) to the surface waters.



**Figure 12. Transport of antibiotics to the surface waters from human consumption, aquaculture, drug production and animal food production.**

## 4.1 Gaps in the schematics

Schematics presented in this section contain a large number of areas within the environment from which chemicals, such as antibiotics, are released, as a product of manufacturing, disposal and use (e.g., human, animal, aquaculture, and farming). A thorough risk assessment of the hazards posed by dissemination and transmission of ARG-driving chemicals will need to be conducted to help inform environmental regulators where interventions could reasonably and effectively be implemented. However, it is substantially more complex to introduce discharge controls over the range of AMR-driving chemicals that could potentially enrich for ARGs. Moreover, it is currently without precedent to treat DNA and bacteriophage as an environmental pollutant - which it has now become.

### **4.1.1 Overlooked environmentally-relevant drivers of AMR**

The highest priority areas where the gaps in our understanding preclude evidence-based policy from proceeding are discussed in Section 4.3, Future Work. Areas that have been identified in only a few conceptual models of AMR in the environment are discussed below.

A growing body of literature in recent years have demonstrated landfills (Chen et al., 2017; Eggen et al., 2010; Musson and Townsend, 2009; Zhang et al., 2016) air (Echeverria-Palencia et al., 2017; Ferrey et al., 2018; Jones, 2020; Li et al., 2018; Pal et al., 2016; Seltenrich, 2015), landfill air (Li et al., 2020), and composting (Fischer et al., 2008; Gao et al., 2018; Gou et al., 2018; Wéry, 2014; Youngquist et al., 2016) as important sources of ARG-driving chemicals and ARGs. Air and composting have been particularly well documented in several recent studies highlighting emerging areas of hazard for AMR selection, dissemination and transmission. A poorly explored source of ARGs and ARBs is ballast water, which has been studied by only a few groups in a small number of harbours (Altug et al., 2012; Drake et al., 2007; Ng et al., 2015; Sloan, 2019). Ballast water hazards stems from the dissemination of potentially ARG-enriched water from one location to another, thereby potentially impacting the water quality at the destination port. The addition of chemicals for cleaning the ballast tanks could introduce ARG selection pressures, further increasing the hazard that ballast water represents.

## **4.2 Future schematics**

Schematics have routinely mixed the drivers of selection (e.g., human antibiotic use) with the pathways of dissemination (e.g., air, rivers) and the routes to transmission (e.g., food, bathing, hiking). Future risk assessment might benefit from schematics that isolate the sources of selection from dissemination and transmission, as they each represent opportunities to interrupt a particular driver of AMR. The merits of interrupting sources of selection are much easier to compare to other sources of selection—pathways of dissemination with each other—and routes to transmission with each other. Schematics of sources of selection, pathways of dissemination and routes of transmission still remain disconnected from what is ultimately needed, which is a schematic that conveys risk. The only way to convey risk within a schematic is to have access to data at an appropriate scale and resolution, which speaks to the content of Section 5.

## **4.3 Future work**

Knowledge of data sources to help inform future hazard and risk assessments will be essential in prioritising actions to help support the policy drivers identified in Section 1.2. Chronic sources of AMR selection and dissemination into the

environment will, arguably, need to be considered with haste. Clear example of chronic sources include:

- WWTPs
- animal farming and grazing
- composting
- azole fungicide use in crops
- land spreading of manure and biosolids.

Datasets recovered in Section 5 suggest there is data associated with WWTPs that can be more effectively aggregated on a national scale and made available in a timelier manner for the purpose of hazard and risk assessment. Addressing these barriers will be necessary to proceed with 'downstream' risk assessments, such as that associated with free/open swimming and bathing, shellfish, drinking water for farmed animals and humans, and wildlife exposure and dissemination of ARGs/ARBs.

Animal farming and grazing is important for its chronic release of manure containing antimicrobials, ARGs and ARBs. Animal farming and grazing has 'downstream' implications for hazard and risk assessment for humans who interact with the animals, wildlife, soil health, runoff into rivers, bioaerosol in the form of contaminated dust, slurry pits and subsequent land spreading, and direct exposure to ramblers on paths traversing farms. Data on the temporal and spatial location of animals is lacking, however, the use of complementary datasets to infer animal density, antimicrobial use, and grazing could be used in the interim. Nevertheless, considerably better data is needed to inform a robust hazard and risk assessment.

Composting facilities are important as they are known to have ideal conditions for the growth of azole-resistant *Aspergillus fumigatus* (*Afum*). *Afum* is an emerging healthcare threat that is, at least partially, caused by the use of azole fungicides in protecting fruit, the skin of which is composted, and from bulbs, which are dipped in azoles to preserve its 'shelf-life'. Widespread use of a mixture of azole fungicides in cereal farming represents another possible drivers of the growing crisis of drug-resistant *Afum*. Data sources appear adequate for understanding where composting facilities are and the kind of source material that is used. Data on dissemination and transmission of *Afum* and any other identified risks is absent and must be prioritised.

Land spreading of manure and biosolids from WWTPs are relevant because of the abundance of antimicrobials, ARGs and ARBs in both. The chronic discharge of manure and biosolids from farms and WWTPs makes land spreading among the more important AMR sources to hazard and risk assess (Hall et al., 2020). Data collection is needed for where land spreading is occurring, the composition of the material, the frequency of spreading, and the origin of the material to ensure any hazard or risk assessment is evidence based.

Groundwater can be significantly impacted from many surface activities, e.g., farming, land spreading, wastewater treatment/septic tanks, resulting in an elevated hazard for its future use as irrigation or potable water. Very little data

has been found to help inform a hazard assessment from AMR in groundwater, representing a high priority area for data collection.

A reduction in the discharge of AMR-driving chemicals into the environment will be key for reducing the environmental hazard from AMR. There are many stakeholders that can feasibly contribute to this source reduction, with some representing 'easy wins' and others requiring more sustained effort. Future work is needed to determine who these stakeholders are and to help determine a pathway for introducing maximum source reduction. These analyses must be performed in an interdisciplinary forum, as solutions to source reduction will range from vaccine development, to antibiotic stewardship, to laundry detergent formulation, just to name a few. Moreover, wastewater discharge targets, should they be implemented, will be much more easily achieved if a comprehensive suite of measures were undertaken to reduce AMR-driving chemical use at the source. Realistic estimates of what can be achieved through source reduction must be estimated to allow for the most cost-effective wastewater treatment intervention to be implemented.

Short-circuits in the sewage network that allows for frequent storming can eliminate society's best efforts to remove ARBs, ARGs, and AMR-driving chemicals from wastewater and rivers. Recent evidence has shown that combined sewer overflows can introduce orders of magnitude more ARBs into the receiving river than if the same flow had gone through a functional WWTP (Honda et al., 2020). Data collection on the frequency and volume of untreated sewage discharge into rivers is needed to ensure any hazard or risk assessment is evidence based. A holistic understanding of the range of barriers that prevent storming from occurring will need to be conducted, such as renewing pipes, planning permission, climate change, sustainable urban drainage, population growth.

## 5 Data sets for informing hazard and risk assessments

It is a non-trivial task to conduct a hazard and risk assessment of AMR in the environment given the deficiency of spatially and temporally-relevant data. In particular, the lack of data on transmission of resistance from the environment to the human microbiome is particularly apparent. It will be essential to use the existing data to inform strategies aimed at limiting AMR selection, dissemination and transmission. This section describes a non-exhaustive database of records that currently exist within England to help inform such an analysis.

England has extensive records on environmental status and the drivers of environmental change (e.g. pollution inputs to the environment) from regulatory monitoring and surveillance, from administrative records and targeted research activities. In recent years, the government has transformed the availability of environmental data, through the pursuit of an Open Data agenda and the development of web-based data collation and provision tools, such as the data.gov.uk portal. However, it remains the case that consistent access to data on the environment can be problematic. The datasets available are from a range of diverse sources, and the levels of “openness” and documentation can vary significantly. The discovery and identification of relevant datasets remain difficult, and information on the derivation and limitations of datasets is often hard to ascertain from the available information.

Identification of relevant datasets is a necessary first step towards the development of an understanding of the hazard characterisation of AMR in the environment. In many areas, the data available is likely to be adequate, or as good as is possible at a national scale. In other areas, data will be limited, and further data collation or modelling may be required.

This project approached this data identification activity by defining key areas relevant to the potential pathways for selection, dissemination and transmission identified from the literature review and existing understanding. Official portals were used as a starting point for dataset discovery, e.g. data.gov.uk, and the Environmental Information Data Centre (the UK freshwater and terrestrial sciences database). A Google search was required in most cases, even for the identification of government datasets and monitoring schemes. A previous Defra project (LM0308) undertook a similar exercise relating to datasets on catchment abstraction management and pollution and captured the information on datasets using the ISO-19115 metadata standard used by data.gov.uk. A similar approach was followed in this project for AMR-related datasets: the relevant metadata fields from the ISO-19115 standard were selected and used to capture dataset information within a simple spreadsheet. The fields used are listed below (appendix A). A number of additional headings were added, more specifically relevant to this project.

Seventy-three relevant datasets and reports were identified across the key areas identified. A completed list of datasets is provided electronically. Table 1, below, summarises the areas searched, and whether spatial datasets were identified to inform risk in this area.

**Table 1. Availability of datasets as they relate to AMR selection, dissemination and/or transmission hazards in England.**

Heading 1	Heading 2	Heading 3	Data available	
Human				
	NHS			
		GP prescribing	Yes	Open Prescribing already provides spatially explicit information on where active ingredients are prescribed. “PrAna dataset of active substance mapped by postcode / GP practice region, etc.” has processed this further and likely provides a quickest, cleanest option for accessing this data.
	High Risk Activities			
		Open Swimming	Yes	Crowd-sourced datasets of river swimming locations exist and there are plans for these to be made available for research (“wildswim.com map”), though no information on frequency of use is available. “MMO1064 Beach Activities Model” provides estimates of beach swimming frequency, though this is modelled based on facilities, etc..
		Beach Activities	Yes	“MMO1064 Beach Activities Model” provides estimates of beach use across a range of activities (paddle-activities, boating, surfing, scuba, fishing, etc.) though estimates are modelled based on physical information.

		Rambling	Some	Local authorities maintain datasets on public rights of way, which would be the ideal source, but there is no national collation of all areas. All digitally available datasets have been collated by Open Street Map community. OS products provide comprehensive coverage in some areas (urban areas and national parks) but not elsewhere.
		Proximity to high risk animals (farm animals, companion animals, bats, etc)	No	Species records exist, and data on livestock distribution, but information on likelihood of contact is not available.
		Other water sports (boating, surfing, etc.)	Yes	Beach only, not inland waters.
		Travel local/UK/International spreading AMR (e.g., gut carriage).	No	There is data on people travelling internationally, but spatial information on where people are from / spend time is not.
Sewage				
	Hospital			
		Sewage to local WWTP	Some	Locations of WWTPs will include hospitals.
		Sewage to hospital WWTP	Some	Where hospitals have their own waste disposal this will be listed within the Environmental Permitting Regulations data.
	Airport			
		Airline lavatory sewage disposal	No	There is little data on where airport sewage is treated, though this could be found on a case-by-case basis for larger airports.



	Wastewater treatment plant			
		Locations and capacities	Yes	EA datasets on UWWTD and effluent discharge locations provide detailed information.
	Sludge			
		Composting	Yes	EA Environmental Permitting datasets contain information suitably categorised to allow composting facilities to be identified. A specific extraction of a dataset on composting facilities is currently available to CEH.
		Anaerobic Digestion	Yes	The Anaerobic Digestion and Bioresources Association (ADBA) maintains a database of anaerobic digestion facilities. Locations and facility types are openly accessible. In addition Environmental Permitting datasets could provide the location of facilities and volumes of waste transferred.
	Effluent			
		River	Yes	EA consents to discharge datasets provide information on the licensed effluent. EA also maintains daily effluent volume time series data for ~3000 sites, derived from 15 minute data held by water companies. Spatial datasets on rivers are available (e.g. CEH digital rivers, EA Detailed River Network, OS Water Layer).

		Land	No	Specific locations of sewage sludge application are not available, though should be registered.
		Lake	Yes	See rivers above. Lake spatial areas are available in the CEH / EA UK Lakes database.
		Beach	Yes	See rivers above.
	Combined sewer overflow (CSO)			
		Location & Discharge points & frequency of discharge	Yes	EA database on “Environmental Pollution Incidents” provides better spatial and temporary information on effluent releases than the water company reported “Event Duration Monitoring”. However some events will not be adequately captured.
Farm				
	Veterinary use of antibiotics/antimicrobials		Some	“Veterinary Antimicrobial Resistance and Sales Surveillance 2018” contains information on antimicrobial sales and use by animal types (including aquaculture and pets), and on surveillance of antimicrobial resistance. Supplementary information to the report contains further information on the methodologies used, and tables of information, but no datasets.
	Animal numbers		Yes	Datasets estimating livestock numbers to ~10km grid scale exist (e.g ADAS Farmscoper tool), generally based on remapping of data from the Junes Agricultural census. Animal and Plant Health Agency (APHA) Livestock Demographic Data Group population reports

				contain data at 1km resolution from more detailed reporting, but data is only provided at the county level on request.
	Animal feed			
		Animal feed industry (sources & waste streams)	Yes	Animal feed production statistics, by manufacturer, are available. EA Environmental Permitting data contains detailed information on industries and quantities of waste produced, e.g. the Waste Data Interrogator.
		Land and aquaculture feed use and disposal	No	There is no detailed information on where feed is used.
	Grazing/Pasture			
		Open defecation/manure	Yes	ADAS Manure GIS (produced for Defra) provides detailed (10km grids) on manure volumes by livestock type. Other work (e.g. on faecal coliform modelling) by EA may provide better information.
	Animal movement/transportation		Yes/No	APHA also have detailed information on animal transportation within the country and import/export. However this data may not be accessible.
	Manure			
		Composting	Some	Data available within the Waste Data Interrogator on volumes of “animal faeces, urine and manure (including spoiled straw), effluent, collected separately and treated off-site”.
		Anaerobic Digestion	Some	Data available within the Waste Data Interrogator on volumes of “animal faeces, urine and manure (including spoiled straw),

				effluent, collected separately and treated off-site".
	Slurry Pit			
		Land spread/Injection	No	No data identified
		Leaking/groundwater/surface water	No	No data identified
	Sheep Dip		No	No data identified
	Aquaculture		Yes	Locations of some aquaculture can be ascertained from EA discharge consents. CEFAS maintains a "Public register of Aquaculture Production Businesses in England and Wales".
		Antibiotics/Antiparasitics	Some	"Veterinary Antimicrobial Resistance and Sales Surveillance" includes data on use within aquaculture.
	Abattoir (waste stream)		Some	Limited information within the Waste Data Interrogator
Agriculture				
	Pesticide		Yes	CEH Land Cover plus Pesticides includes a number of fungicides, estimating distribution on a 1km grid using agricultural statistics and satellite-based crop mapping.
		Fungicide	Yes	CEH Land Cover plus Pesticides includes a number of fungicides, estimating distribution on a 1km grid using agricultural statistics and satellite-based crop mapping.
		Other	Yes	CEH Land Cover plus Pesticides includes a number of fungicides, estimating distribution

				on a 1km grid using agricultural statistics and satellite-based crop mapping.
	Herbicide		Yes	CEH Land Cover plus Pesticides includes a number of fungicides, estimating distribution on a 1km grid using agricultural statistics and satellite-based crop mapping.
		Glyphosate	Yes	CEH Land Cover plus Pesticides includes a number of fungicides, estimating distribution on a 1km grid using agricultural statistics and satellite-based crop mapping.
		Other	Yes	CEH Land Cover plus Pesticides includes a number of fungicides, estimating distribution on a 1km grid using agricultural statistics and satellite-based crop mapping.
	Orchards (apple, citrus, peach)			
		Antibiotic spraying	Some	Limited information from land cover mapping (orchards are included within a wider horticultural category and are difficult to identify. Data on ancient orchards is available, but these are limited in number and more likely to be organic.
Food				
	Crop			
		Contamination from manure/land spreading	Some	See manure above.
		Biocide use during handling	No	No datasets identified.
	Animal			

		Meat/fish grown with antibiotics/biocides (in meat)	No	No datasets identified.
	Food processing & waste stream		Some	Some data on processing streams and volumes for Manu industries within the Waste Data Interrogator.
	Food transportation (international)		No	No datasets identified.
	Shellfish bed		Yes	CEFAS "Public register of Aquaculture Production Businesses in England and Wales. EA maintains lists of shellfish areas and spatial datasets (though not currently publicly available).
Wildlife				
	Manure land spreading exposure		No	Species records exist but data on exposure would require modelling.
	Sewage effluent exposure in river		No	Species records exist but data on exposure would require modelling.
	Wildlife movement across local/national/world, spreading AMR (e.g., migrating birds)		No	Species records on migratory species exist, but not detailed spatial datasets on migration routes.
Companion Animal				
	Household companion animals (cats/dogs/rabbit/rodent)		Some	Pet Food Manufacturers "Pet Data Report 2017" provides overall numbers, with regional estimates, but not explicit spatial data.

	Recreational companion animals (horses, etc.)		Some	Papers exist with numerical estimates of horse numbers, but no specific datasets are available.
Industry				
	Pharmaceutical Manufacturing Waste		Some	Waste Data Interrogator includes data on volumes from a range of industries, though categories of waste can be quite wide.
	Agrochemical Industrial Waste		Yes	Waste Data Interrogator includes data on volumes from a range of industries, though categories of waste can be quite wide.
	Other Industrial Waste land and water(including metals & biocides)		Yes	Waste Data Interrogator includes data on volumes from a range of industries, though categories of waste can be quite wide. Pollutants are usually more specifically categorised.
	Historical Waste land and water (including metals and biocides)		Yes	Specific locations of historical waste sites are available within an EA dataset.
	Ballast water from ships		No	No datasets identified.
Solid Waste handling				
	Landfill (historical, pharma waste, metals) Incinerator		Some	Waste Data Interrogator and other Environmental Permitting datasets provide volumes produced from industries, and volume received by different types of waste sites (with locations).

		Leachate	No	No datasets identified.
	Composting (meat, food, crop waste streams)			
		Bioaerosols & land spreading	Some	See composting and anaerobic digestion facilities above. No data on land spreading sites available.



## 6 Appendix A: Dataset information fields

Fields against which information on datasets was captured, either from ISO-19115 metadata standard, or specific to this project (SC190010).

Field to be captured	Origin of this metadata field	Description of field
Heading 1	SC190010	See sheet "search areas"
Heading 2	SC190010	See sheet "search areas"
Heading 3	SC190010	See sheet "search areas"
Title	ISO19115	Title of the dataset
URL	ISO19115	Main URL to online dataset or information about this dataset, or website, etc.
Informative for	SC190010	Could provide information on selection, dissemination, transmission
Priority	SC190010	Priority for inclusion in environmental AMR map [1 (high confidence of relevance), 2 (medium confidence of relevance) 3 (low confidence of relevance)]
Comment	SC190010	Comment on this priority
Description	ISO19115	<p>The description should describe the data resource in question, NOT the project/activity which produced it.</p> <p>The description is an 'executive summary' that allows the reader to determine the relevance and usefulness of the resource. The text should be concise but should contain sufficient detail to allow the reader to ascertain rapidly the scope and limitations of the resource.</p>
Resource status	ISO19115	e.g. (freely) available, controlled, unavailable, restricted
Reference dates	ISO19115	Date created / published / released

Version	ISO19115	Where known
Temporal extent	ISO19115	If applicable. For example: start and end date (could just be year of either)
Contacts	ISO19115	Author / publisher, etc.
Format(s)	ISO19115	File format
Use constraints	ISO19115	Legal / licence restrictions
Spatial extent	ISO19115	Probably UK / GB / England (etc.) / North East England, etc. would be suitable and more useful than lat long bounding box at this point
Spatial representation types	ISO19115	Raster (gridded data), polygon, point
Lineage	ISO19115	Summary of how the dataset was derived, including useful caveats or limitations of this, e.g if a dataset was modelled, some indication if the underlying data is known to have limitations such as in the spatial resolution or accuracy
Resource maintenance	ISO19115	Frequency of updates, e.g. annual, irregular, not planned
Additional information	ISO19115	Multiple entries: related website, dataset, citations of this dataset, etc. with name, description and URL
Service	ISO19115	Any web services related to this data, e.g. download, Web Feature Service, as this will help speed up access to the dataset
Conformity	SC19010	Whether the existing dataset metadata complies with data standards.

## 7 References

- Addison, J.B. (1984). Antibiotics in sediments and run-off waters from feedlots. *Residue Rev* 92, 1–28.
- Ahlstrom, C.A., Bonnedahl, J., Woksepp, H., Hernandez, J., Olsen, B., and Ramey, A.M. (2018). Acquisition and dissemination of cephalosporin-resistant *E. coli* in migratory birds sampled at an Alaska landfill as inferred through genomic analysis. *Sci. Rep.* 8, 7361.
- Altug, G., Gurun, S., Cardak, M., Ciftci, P.S., and Kalkan, S. (2012). The occurrence of pathogenic bacteria in some ships' ballast water incoming from various marine regions to the Sea of Marmara, Turkey. *Mar. Environ. Res.* 81, 35–42.
- Amos, G.C.A., Zhang, L., Hawkey, P.M., Gaze, W.H., and Wellington, E.M. (2014). Functional metagenomic analysis reveals rivers are a reservoir for diverse antibiotic resistance genes. *Vet. Microbiol.* 171, 441–447.
- Amos, G.C.A., Gozzard, E., Carter, C.E., Mead, A., Bowes, M.J., Hawkey, P.M., Zhang, L., Singer, A.C., Gaze, W.H., and Wellington, E.M.H. (2015). Validated predictive modelling of the environmental resistome. *ISME J.* 9, 1467–1476.
- Arnold, K.E., Williams, N.J., and Bennett, M. (2016). “Disperse abroad in the land”: the role of wildlife in the dissemination of antimicrobial resistance. *Biol. Lett.* 12.
- Bengtsson-Palme, J., Hammarén, R., Pal, C., Östman, M., Björlenius, B., Flach, C.-F., Fick, J., Kristiansson, E., Tysklind, M., and Larsson, D.G.J. (2016). Elucidating selection processes for antibiotic resistance in sewage treatment plants using metagenomics. *Sci. Total Environ.* 572, 697–712.
- Boerlin, P., and Reid-Smith, R.J. (2008). Antimicrobial resistance: its emergence and transmission. *Anim. Health Res. Rev.* 9, 115–126.
- Boerlin, P., and White, D.G. (2013). Antimicrobial resistance and its epidemiology. In *Antimicrobial therapy in veterinary medicine*, S. Giguère, J.F. Prescott, and P.M. Dowling, eds. (Hoboken, NJ: John Wiley & Sons, Inc), pp. 21–40.
- Centre for Disease Control (2019). Antibiotic Resistance Threats in the United States (2019 AR Threats Report) (U.S. Department of Health and Human Services, CDC).
- Chen, Q.-L., Li, H., Zhou, X.-Y., Zhao, Y., Su, J.-Q., Zhang, X., and Huang, F.-Y. (2017). An underappreciated hotspot of antibiotic resistance: The groundwater near the municipal solid waste landfill. *Sci. Total Environ.* 609, 966–973.
- Comber, S., Gardner, M., Jones, V., and Ellor, B. (2015). Source apportionment of trace contaminants in urban sewer catchments. *Environ. Technol.* 36, 573–587.

- Comber, S., Gardner, M., Sörme, P., Leverett, D., and Ellor, B. (2017). Active pharmaceutical ingredients entering the aquatic environment from wastewater treatment works: A cause for concern? *Sci. Total Environ.* *613-614*, 538–547.
- Davies, J., and Davies, D. (2010). Origins and evolution of antibiotic resistance. *Microbiol. Mol. Biol. Rev.* *74*, 417–433.
- Day, M.J., Hopkins, K.L., Wareham, D.W., Toleman, M.A., Elviss, N., Randall, L., Teale, C., Cleary, P., Wiuff, C., Doumith, M., et al. (2019). Extended-spectrum  $\beta$ -lactamase-producing *Escherichia coli* in human-derived and foodchain-derived samples from England, Wales, and Scotland: an epidemiological surveillance and typing study. *Lancet Infect. Dis.* *19*, 1325–1335.
- Department of Health (2019). Contained and controlled: The UK's 20-year vision for antimicrobial resistance (UK Department of Health).
- Dobbs, F.C., Goodrich, A.L., Thomson, F.K., and Hynes, W. (2013). Pandemic serotypes of *Vibrio cholerae* isolated from ships' ballast tanks and coastal waters: assessment of antibiotic resistance and virulence genes (*tcpA* and *ctxA*). *Microb. Ecol.* *65*, 969–974.
- Dorado-García, A., Smid, J.H., van Pelt, W., Bonten, M.J.M., Fluit, A.C., van den Bunt, G., Wagenaar, J.A., Hordijk, J., Dierikx, C.M., Veldman, K.T., et al. (2018). Molecular relatedness of ESBL/AmpC-producing *Escherichia coli* from humans, animals, food and the environment: a pooled analysis. *J. Antimicrob. Chemother.* *73*, 339–347.
- Drake, L.A., Doblin, M.A., and Dobbs, F.C. (2007). Potential microbial bioinvasions via ships' ballast water, sediment, and biofilm. *Mar. Pollut. Bull.* *55*, 333–341.
- Durão, P., Balbontín, R., and Gordo, I. (2018). Evolutionary mechanisms shaping the maintenance of antibiotic resistance. *Trends Microbiol.* *26*, 677–691.
- Echeverria-Palencia, C.M., Thulsiraj, V., Tran, N., Ericksen, C.A., Melendez, I., Sanchez, M.G., Walpert, D., Yuan, T., Ficara, E., Senthilkumar, N., et al. (2017). Disparate Antibiotic Resistance Gene Quantities Revealed across 4 Major Cities in California: A Survey in Drinking Water, Air, and Soil at 24 Public Parks. *ACS Omega* *2*, 2255–2263.
- Eggen, T., Moeder, M., and Arukwe, A. (2010). Municipal landfill leachates: a significant source for new and emerging pollutants. *Sci. Total Environ.* *408*, 5147–5157.
- European Commission (2017). A European 'One Health' Action Plan against Antimicrobial Resistance (AMR) (European Commission).
- Ferrey, M.L., Coreen Hamilton, M., Backe, W.J., and Anderson, K.E. (2018). Pharmaceuticals and other anthropogenic chemicals in atmospheric particulates and precipitation. *Sci. Total Environ.* *612*, 1488–1497.
- Fischer, G., Albrecht, A., Jäckel, U., and Kämpfer, P. (2008). Analysis of airborne microorganisms, MVOC and odour in the surrounding of composting

- facilities and implications for future investigations. *Int J Hyg Environ Health* 211, 132–142.
- Frimodt-Møller, J., and Løbner-Olesen, A. (2019). Efflux-Pump Upregulation: From Tolerance to High-level Antibiotic Resistance? *Trends Microbiol.* 27, 291–293.
- Frost, I., Van Boeckel, T.P., Pires, J., Craig, J., and Laxminarayan, R. (2019). Global geographic trends in antimicrobial resistance: the role of international travel. *J Travel Med* 26.
- Fukuda, K., Limmathurotsakul, D., Okeke, I.N., Shetty, N., van Doorn, R., Feasey, N.A., Chiara, F., Zoubiane, G., Jinks, T., Parkhill, J., et al. (2018). Surveillance and Epidemiology of Drug Resistant Infections Consortium (SEDRIC): Supporting the transition from strategy to action. [version 2; peer review: 3 approved]. *Wellcome Open Res.* 3, 59.
- Gao, M., Qiu, T., Sun, Y., and Wang, X. (2018). The abundance and diversity of antibiotic resistance genes in the atmospheric environment of composting plants. *Environ. Int.* 116, 229–238.
- Gardner, M., Comber, S., Scrimshaw, M.D., Cartmell, E., Lester, J., and Ellor, B. (2012). The significance of hazardous chemicals in wastewater treatment works effluents. *Sci. Total Environ.* 437, 363–372.
- Gardner, M., Jones, V., Comber, S., Scrimshaw, M.D., Coello-Garcia, T., Cartmell, E., Lester, J., and Ellor, B. (2013). Performance of UK wastewater treatment works with respect to trace contaminants. *Sci. Total Environ.* 456-457, 359–369.
- Gerhard, W.A., and Gunsch, C.K. (2020). Higher normalized concentrations of tetracycline resistance found in ballast and harbor water compared to ocean water. *Mar. Pollut. Bull.* 151, 110796.
- Gou, M., Hu, H.-W., Zhang, Y.-J., Wang, J.-T., Hayden, H., Tang, Y.-Q., and He, J.-Z. (2018). Aerobic composting reduces antibiotic resistance genes in cattle manure and the resistome dissemination in agricultural soils. *Sci. Total Environ.* 612, 1300–1310.
- Gouliouris, T., Raven, K.E., Moradigaravand, D., Ludden, C., Coll, F., Blane, B., Naydenova, P., Horner, C., Brown, N.M., Corander, J., et al. (2019). Detection of vancomycin-resistant *Enterococcus faecium* hospital-adapted lineages in municipal wastewater treatment plants indicates widespread distribution and release into the environment. *Genome Res.* 29, 626–634.
- Graham, D.W., Knapp, C.W., Christensen, B.T., McCluskey, S., and Dolfing, J. (2016). Appearance of  $\beta$ -lactam Resistance Genes in Agricultural Soils and Clinical Isolates over the 20th Century. *Sci. Rep.* 6, 21550.
- Greig, J., Rajić, A., Young, I., Mascarenhas, M., Waddell, L., and LeJeune, J. (2015). A scoping review of the role of wildlife in the transmission of bacterial pathogens and antimicrobial resistance to the food Chain. *Zoonoses Public Health* 62, 269–284.

- Gullberg, E., Albrecht, L.M., Karlsson, C., Sandegren, L., and Andersson, D.I. (2014). Selection of a multidrug resistance plasmid by sublethal levels of antibiotics and heavy metals. *MBio* 5, e01918–14.
- Hall, M.C., Mware, N., Gilley, J., Bartelt-Hunt, S.L., Snow, D.D., Schmidt, A., Eskridge, K., and Li, X. (2020). Influence of setback distance on antibiotics and antibiotic resistance genes in runoff and soil following the land application of swine manure slurry. *Environ. Sci. Technol.*
- He, Y., Yuan, Q., Mathieu, J., Stadler, L., Senehi, N., Sun, R., and Alvarez, P.J.J. (2020). Antibiotic resistance genes from livestock waste: occurrence, dissemination, and treatment. *npj Clean Water* 3, 4.
- HM Government (2019). Tackling antimicrobial resistance 2019–2024: The UK's five-year national action plan (HM Government).
- Holmes, A.H., Moore, L.S.P., Sundsfjord, A., Steinbakk, M., Regmi, S., Karkey, A., Guerin, P.J., and Piddock, L.J.V. (2016). Understanding the mechanisms and drivers of antimicrobial resistance. *Lancet* 387, 176–187.
- Honda, R., Tachi, C., Yasuda, K., Hirata, T., Noguchi, M., Hara-Yamamura, H., Yamamoto-Ikemoto, R., and Watanabe, T. (2020). Estimated discharge of antibiotic-resistant bacteria from combined sewer overflows of urban sewage system. *npj Clean Water* 3, 15.
- Huijbers, P.M.C., Blaak, H., de Jong, M.C.M., Graat, E.A.M., Vandenbroucke-Grauls, C.M.J.E., and de Roda Husman, A.M. (2015). Role of the environment in the transmission of antimicrobial resistance to humans: A review. *Environ. Sci. Technol.* 49, 11993–12004.
- International Environmental AMR Forum (2018). Initiatives for Addressing 'Antimicrobial Resistance in the Environment' Current: Situation and Challenges (Wellcome Trust, U.S. CDC, UK Science & Innovation Network).
- Jones, M. (2020). Review of airborne antimicrobial resistance (Environment Agency of England).
- Jones, V., Gardner, M., and Ellor, B. (2014). Concentrations of trace substances in sewage sludge from 28 wastewater treatment works in the UK. *Chemosphere* 111, 478–484.
- Kashuba, E., Dmitriev, A.A., Kamal, S.M., Melefors, O., Griva, G., Römling, U., Ernberg, I., Kashuba, V., and Brouchkov, A. (2017). Ancient permafrost staphylococci carry antibiotic resistance genes. *Microb. Ecol. Health Dis.* 28, 1345574.
- Kirchhelle, C. (2018). Pharming animals: a global history of antibiotics in food production (1935–2017). *Palgrave Commun.* 4, 96.
- Knapp, C.W., Dolfing, J., Ehlert, P.A.I., and Graham, D.W. (2010). Evidence of increasing antibiotic resistance gene abundances in archived soils since 1940. *Environ. Sci. Technol.* 44, 580–587.
- Knöppel, A., Näsvall, J., and Andersson, D.I. (2017). Evolution of Antibiotic Resistance without Antibiotic Exposure. *Antimicrob. Agents Chemother.* 61.

- Kovalakova, P., Cizmas, L., McDonald, T.J., Marsalek, B., Feng, M., and Sharma, V.K. (2020). Occurrence and toxicity of antibiotics in the aquatic environment: A review. *Chemosphere* 251, 126351.
- Kurenbach, B., Marjoshi, D., Amábile-Cuevas, C.F., Ferguson, G.C., Godsoe, W., Gibson, P., and Heinemann, J.A. (2015). Sublethal exposure to commercial formulations of the herbicides dicamba, 2,4-dichlorophenoxyacetic acid, and glyphosate cause changes in antibiotic susceptibility in *Escherichia coli* and *Salmonella enterica* serovar Typhimurium. *MBio* 6.
- Larsson, D.G.J., Andremont, A., Bengtsson-Palme, J., Brandt, K.K., de Roda Husman, A.M., Fagerstedt, P., Fick, J., Flach, C.-F., Gaze, W.H., Kuroda, M., et al. (2018). Critical knowledge gaps and research needs related to the environmental dimensions of antibiotic resistance. *Environ. Int.* 117, 132–138.
- Leonard, A.F.C., Singer, A., Ukoumunne, O.C., Gaze, W.H., and Garside, R. (2018a). Is it safe to go back into the water? A systematic review and meta-analysis of the risk of acquiring infections from recreational exposure to seawater. *Int. J. Epidemiol.* 47, 572–586.
- Leonard, A.F.C., Zhang, L., Balfour, A.J., Garside, R., Hawkey, P.M., Murray, A.K., Ukoumunne, O.C., and Gaze, W.H. (2018b). Exposure to and colonisation by antibiotic-resistant *E. coli* in UK coastal water users: Environmental surveillance, exposure assessment, and epidemiological study (Beach Bum Survey). *Environ. Int.* 114, 326–333.
- Leonard, A.F.C., Garside, R., Ukoumunne, O.C., and Gaze, W.H. (2020). A cross-sectional study on the prevalence of illness in coastal bathers compared to non-bathers in England and Wales: Findings from the Beach User Health Survey. *Water Res.* 176, 115700.
- Li, J., Cao, J., Zhu, Y.-G., Chen, Q.-L., Shen, F., Wu, Y., Xu, S., Fan, H., Da, G., Huang, R.-J., et al. (2018). Global survey of antibiotic resistance genes in air. *Environ. Sci. Technol.* 52, 10975–10984.
- Li, L., Wang, Q., Bi, W., Hou, J., Xue, Y., Mao, D., Das, R., Luo, Y., and Li, X. (2020). Municipal solid waste treatment system increases ambient airborne bacteria and antibiotic resistance genes. *Environ. Sci. Technol.* 54, 3900–3908.
- Liu, A., Fong, A., Becket, E., Yuan, J., Tamae, C., Medrano, L., Maiz, M., Wahba, C., Lee, C., Lee, K., et al. (2011). Selective advantage of resistant strains at trace levels of antibiotics: a simple and ultrasensitive color test for detection of antibiotics and genotoxic agents. *Antimicrob. Agents Chemother.* 55, 1204–1210.
- Ludden, C., Raven, K.E., Jamrozy, D., Gouliouris, T., Blane, B., Coll, F., de Goffau, M., Naydenova, P., Horner, C., Hernandez-Garcia, J., et al. (2019). One Health Genomic Surveillance of *Escherichia coli* Demonstrates Distinct Lineages and Mobile Genetic Elements in Isolates from Humans versus Livestock. *MBio* 10.
- Lv, B., Cui, Y., Tian, W., Li, J., Xie, B., and Yin, F. (2018). Abundances and profiles of antibiotic resistance genes as well as co-occurrences with human bacterial pathogens in ship ballast tank sediments from a shipyard in Jiangsu Province, China. *Ecotoxicol. Environ. Saf.* 157, 169–175.

- Maddamsetti, R., and Lenski, R.E. (2018). Analysis of bacterial genomes from an evolution experiment with horizontal gene transfer shows that recombination can sometimes overwhelm selection. *PLoS Genet.* *14*, e1007199.
- Magi, G., Marini, E., and Facinelli, B. (2015). Antimicrobial activity of essential oils and carvacrol, and synergy of carvacrol and erythromycin, against clinical, erythromycin-resistant Group A Streptococci. *Front. Microbiol.* *6*, 165.
- Maier, L., Pruteanu, M., Kuhn, M., Zeller, G., Telzerow, A., Anderson, E.E., Brochado, A.R., Fernandez, K.C., Dose, H., Mori, H., et al. (2018). Extensive impact of non-antibiotic drugs on human gut bacteria. *Nature* *555*, 623–628.
- Mao, D., Luo, Y., Mathieu, J., Wang, Q., Feng, L., Mu, Q., Feng, C., and Alvarez, P.J.J. (2014). Persistence of extracellular DNA in river sediment facilitates antibiotic resistance gene propagation. *Environ. Sci. Technol.* *48*, 71–78.
- Marshall, B.M., and Levy, S.B. (2011). Food animals and antimicrobials: impacts on human health. *Clin. Microbiol. Rev.* *24*, 718–733.
- McCann, C.M., Christgen, B., Roberts, J.A., Su, J.-Q., Arnold, K.E., Gray, N.D., Zhu, Y.-G., and Graham, D.W. (2019). Understanding drivers of antibiotic resistance genes in High Arctic soil ecosystems. *Environ. Int.* *125*, 497–504.
- Murray, A.K., Zhang, L., Yin, X., Zhang, T., Buckling, A., Snape, J., and Gaze, W.H. (2018). Novel Insights into Selection for Antibiotic Resistance in Complex Microbial Communities. *MBio* *9*.
- Murray, A.K., Zhang, L., Snape, J., and Gaze, W.H. (2019). Comparing the selective and co-selective effects of different antimicrobials in bacterial communities. *Int. J. Antimicrob. Agents* *53*, 767–773.
- Musson, S.E., and Townsend, T.G. (2009). Pharmaceutical compound content of municipal solid waste. *J. Hazard. Mater.* *162*, 730–735.
- Ng, C., Le, T.-H., Goh, S.G., Liang, L., Kim, Y., Rose, J.B., and Yew-Hoong, K.G. (2015). A comparison of microbial water quality and diversity for ballast and tropical harbor waters. *PLoS One* *10*, e0143123.
- Overballe-Petersen, S., Harms, K., Orlando, L.A.A., Mayar, J.V.M., Rasmussen, S., Dahl, T.W., Rosing, M.T., Poole, A.M., Sicheritz-Ponten, T., Brunak, S., et al. (2013). Bacterial natural transformation by highly fragmented and damaged DNA. *Proc. Natl. Acad. Sci. USA* *110*, 19860–19865.
- Le Page, G., Gunnarsson, L., Trznadel, M., Wedgwood, K.C.A., Baudrot, V., Snape, J., and Tyler, C.R. (2019). Variability in cyanobacteria sensitivity to antibiotics and implications for environmental risk assessment. *Sci. Total Environ.* *695*, 133804.
- Pal, C., Bengtsson-Palme, J., Kristiansson, E., and Larsson, D.G.J. (2016). The structure and diversity of human, animal and environmental resistomes. *Microbiome* *4*, 54.
- Palmer-Young, E.C., Sadd, B.M., and Adler, L.S. (2017). Evolution of resistance to single and combined floral phytochemicals by a bumble bee parasite. *J. Evol. Biol.* *30*, 300–312.



- Perron, G.G., Whyte, L., Turnbaugh, P.J., Goordial, J., Hanage, W.P., Dantas, G., and Desai, M.M. (2015). Functional characterization of bacteria isolated from ancient arctic soil exposes diverse resistance mechanisms to modern antibiotics. *PLoS One* 10, e0069533.
- Rascovan, N., Telke, A., Raoult, D., Rolain, J.M., and Desnues, C. (2016). Exploring divergent antibiotic resistance genes in ancient metagenomes and discovery of a novel beta-lactamase family. *Environ. Microbiol. Rep.* 8, 886–895.
- Rodríguez-Verdugo, A., Gaut, B.S., and Tenailon, O. (2013). Evolution of *Escherichia coli* rifampicin resistance in an antibiotic-free environment during thermal stress. *BMC Evol. Biol.* 13, 50.
- Seltenrich, N. (2015). Dust Emissions from Cattle Feed Yards: A Source of Antibiotic Resistance? *Environ. Health Perspect.* 123, A96–A96.
- Shuyler, L.R. (1973). National animal feedlot waste research program. E.P.A.-R2-73-157 (Environmental Protection Agency).
- Singer, A., Shaw, H., Rhodes, V., and Hart, A. (2016). Review of antimicrobial resistance in the environment and its relevance to environmental regulators. *Front. Microbiol.* 7, 1728.
- Singer, A., Colizza, V., Schmitt, H., Andrews, J., Balcan, D., Huang, W., Keller, V., Aless, Ro, V., and Williams, R. Ecotoxicity risks during influenza pandemic.
- Singer, A.C., Colizza, V., Schmitt, H., Andrews, J., Balcan, D., Huang, W.E., Keller, V.D.J., Vespignani, A., and Williams, R.J. (2011). Assessing the ecotoxicologic hazards of a pandemic influenza medical response. *Environ. Health Perspect.* 119, 1084–1090.
- Singer, A.C., Xu, Q., and Keller, V.D.J. (2019). Translating antibiotic prescribing into antibiotic resistance in the environment: A hazard characterisation case study. *PLoS One* 14, e0221568.
- Sloan, C. (2019). Characterizing Antibiotic and Heavy Metal Resistance Genes from Bacteria in Commercial Ship Ballast Water Discharged into the Duluth-Superior Harbor.
- Smith, S., Wang, J., Fanning, S., and McMahon, B.J. (2014). Antimicrobial resistant bacteria in wild mammals and birds: a coincidence or cause for concern? *Ir. Vet. J.* 67, 8.
- Swann, M.M., Baxter, K.L., and Field, H.I. (1969). Report of the Joint Committee on the Use of Antibiotics in Animal Husbandry and Veterinary Medicine. H.M. Stationery Office.
- Swift, B.M.C., Bennett, M., Waller, K., Dodd, C., Murray, A., Gomes, R.L., Humphreys, B., Hobman, J.L., Jones, M.A., Whitlock, S.E., et al. (2019). Anthropogenic environmental drivers of antimicrobial resistance in wildlife. *Sci. Total Environ.* 649, 12–20.
- Tarabai, H., Valcek, A., Jamborova, I., Vazhov, S.V., Karyakin, I.V., Raab, R., Literak, I., and Dolejska, M. (2019). Plasmid-Mediated mcr-1 Colistin Resistance in *Escherichia coli* from a Black Kite in Russia. *Antimicrob. Agents Chemother.* 63.

- Tell, J., Caldwell, D.J., Häner, A., Hellstern, J., Hoeger, B., Journal, R., Mastrocco, F., Ryan, J.J., Snape, J., Straub, J.O., et al. (2019). Science-based Targets for Antibiotics in Receiving Waters from Pharmaceutical Manufacturing Operations. *Integr Environ Assess Manag* 15, 312–319.
- Torres, R.T., Fernandes, J., Carvalho, J., Cunha, M.V., Caetano, T., Mendo, S., Serrano, E., and Fonseca, C. (2019). Wild boar as a reservoir of antimicrobial resistance. *Sci. Total Environ.* 135001.
- Tyrrel, S.F., and Quinton, J.N. (2003). Overland flow transport of pathogens from agricultural land receiving faecal wastes. *J. Appl. Microbiol.* 94 *Suppl*, 87S–93S.
- UN Environment Programme (2017). *Frontiers 2017: Emerging Issues of Environmental Concern*.
- United Nations (2017). *Towards a Pollution Free Planet. Report of the Executive Director. Environment Assembly of the United Nations Environment Programme (United Nations Environment Programme)*.
- Veterinary Medicines Directorate (2019). *UK Veterinary Antibiotic ' Resistance and Sales Surveillance Report: UK - VARSS 2018 (Veterinary Medicines Directorate)*.
- Wang, R., van Dorp, L., Shaw, L.P., Bradley, P., Wang, Q., Wang, X., Jin, L., Zhang, Q., Liu, Y., Rieux, A., et al. (2018a). The global distribution and spread of the mobilized colistin resistance gene *mcr-1*. *Nat. Commun.* 9, 1179.
- Wang, Y., Lu, J., Mao, L., Li, J., Yuan, Z., Bond, P.L., and Guo, J. (2018b). Antiepileptic drug carbamazepine promotes horizontal transfer of plasmid-borne multi-antibiotic resistance genes within and across bacterial genera. *ISME J.* 13, 509–522.
- Wang, Y., Lu, J., Zhang, S., Li, J., Mao, L., Yuan, Z., Bond, P.L., and Guo, J. (2019). Non-antibiotic pharmaceuticals can enhance the spread of antibiotic resistance via conjugation. *BioRxiv*.
- Wéry, N. (2014). Bioaerosols from composting facilities--a review. *Front. Cell Infect. Microbiol.* 4, 42.
- Wistrand-Yuen, E., Knopp, M., Hjort, K., Koskiniemi, S., Berg, O.G., and Andersson, D.I. (2018). Evolution of high-level resistance during low-level antibiotic exposure. *Nat. Commun.* 9, 1599.
- Wong, A. (2017). Epistasis and the evolution of antimicrobial resistance. *Front. Microbiol.* 8, 246.
- World Health Organisation (2015). *Global Action Plan on Antimicrobial Resistance*.
- Wu, J., Huang, Y., Rao, D., Zhang, Y., and Yang, K. (2018). Evidence for environmental dissemination of antibiotic resistance mediated by wild birds. *Front. Microbiol.* 9, 745.
- Wuthiekanun, V., Mayxay, M., Chierakul, W., Phetsouvanh, R., Cheng, A.C., White, N.J., Day, N.P.J., and Peacock, S.J. (2005). Detection of *Burkholderia*

- pseudomallei in soil within the Lao People's Democratic Republic. *J. Clin. Microbiol.* **43**, 923–924.
- Youngquist, C.P., Mitchell, S.M., and Cogger, C.G. (2016). Fate of Antibiotics and Antibiotic Resistance during Digestion and Composting: A Review. *J Environ Qual* **45**, 537–545.
- Zhang, S., Wang, Y., Song, H., Lu, J., Yuan, Z., and Guo, J. (2019). Copper nanoparticles and copper ions promote horizontal transfer of plasmid-mediated multi-antibiotic resistance genes across bacterial genera. *Environ. Int.* **129**, 478–487.
- Zhang, X.-H., Xu, Y.-B., He, X.-L., Huang, L., Ling, J.-Y., Zheng, L., and Du, Q.-P. (2016). Occurrence of antibiotic resistance genes in landfill leachate treatment plant and its effluent-receiving soil and surface water. *Environ. Pollut.* **218**, 1255–1261.
- Zhao, Y., Cocerva, T., Cox, S., Tardif, S., Su, J.-Q., Zhu, Y.-G., and Brandt, K.K. (2019). Evidence for co-selection of antibiotic resistance genes and mobile genetic elements in metal polluted urban soils. *Sci. Total Environ.* **656**, 512–520.
- Zhou, Z.-C., Feng, W.-Q., Han, Y., Zheng, J., Chen, T., Wei, Y.-Y., Gillings, M., Zhu, Y.-G., and Chen, H. (2018). Prevalence and transmission of antibiotic resistance and microbiota between humans and water environments. *Environ. Int.* **121**, 1155–1161.

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