KNOCKING OUT AMR

MICROBIOLOGY SOCIETY

Antimicrobial Resistance (AMR) in Wastewater

What is AMR?

Antimicrobial resistance (AMR) occurs when disease-causing bacteria, viruses, fungi and parasites (pathogens) are no longer affected by the medicines that have been developed to target them, meaning they are resistant to the drugs [1,2]. Drug-resistant pathogens can cause infections that are difficult or impossible to treat [1]. These resistant micro-organisms increase the risk of disease spread and can lead to severe illness, disability and death [1].

This is why pathogens that are resistant to many drugs (multi-drug resistant) are often termed 'superbugs' [3]. AMR is a naturally occurring process, but the misuse and overuse of antimicrobials in humans, animals and plants have been the main drivers for the current health crisis [1,2].

A new report estimates that bacterial AMR will cause 39 million deaths between 2025 and 2050, equivalent to three deaths every minute [4]. AMR is a global problem which has significant costs for health, health systems and national economies [1,5,6]. Current estimates suggest the annual global cost of AMR is ~$900 billion/year [7]. AMR threatens our ability to treat common infections and to perform life-saving procedures including surgery, caesarean sections and cancer chemotherapy [1]. AMR also impacts the health of animals, plants and the environment in a One Health ecosystem, reducing productivity in farms and threatening food security [1].

The focus of this briefing is AMR in wastewater. Wastewater is a potential pathway for, and major contributor to, the spread of AMR [3]. Wastewater can also serve as a key tool to track and mitigate the spread of AMR.

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What is wastewater?

Wastewater is water that is not clean because it has already been used in the home, in a business, or as part of an industrial process [8].

Three main sectors contribute to wastewater:

- domestic wastewater from household activities;
- industrial wastewater generated via various sectors of industry (e.g. pharmaceutical, chemical and food);
- agricultural wastewater as a by-product of crop and livestock production [9].

Other sectors, such as the healthcare sector (e.g. hospitals), are also major contributors to wastewater [10,11].

The terms 'wastewater' and 'sewage' are often used interchangeably, but sewage is a type of wastewater, specifically referring to domestic wastewater and is often used to mean water containing human faecal waste [12]. However, in developed countries, a significant proportion of domestic, industrial and hospital wastewater will be transported and treated in the same sewers and wastewater treatment works (WWTWs) [13]. Throughout this briefing, the term 'wastewater' will encompass all types of wastewater, including sewage.

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How does wastewater get into our rivers and seas?

Wastewater can end up in our rivers and seas through different pathways, including:

- effluent (treated water) from WWTWs;
- combined sewer overflows, where untreated wastewater is discharged into waterways when the sewer system becomes overloaded, often during heavy rainfall;
- septic tanks [3].

Combined sewer overflows are exacerbated by various factors, including underinvestment in the sewage network and heavier storms due to climate change [14,15]. UK sewage infrastructure (e.g. pipes) dating back to the Victorian era is vulnerable to holes and cracks, and therefore wastewater leakage [3,14].

Untreated wastewater spills have become increasingly common in recent years, with millions of hours-worth of spills of untreated wastewater ending up in UK rivers and coastal water [3]. Many of these spills are caused by combined sewer overflows (2.6 million hours-worth in 2021), some water companies also routinely and illegally dump untreated wastewater [16,17]. According to the Rivers Trust data, 85% of river stretches in England fail to meet good ecological standards [18]. Meanwhile, Surfers Against Sewage reported that 1,924 people reported falling ill after entering UK waters in 2023, with around 60% of these cases linked to bathing waters classified as "excellent" [19].

Why is AMR in wastewater a problem?

How does AMR develop and spread in wastewater?

Micro-organisms in the environment can develop resistance by mutation or sharing antibiotic resistance genes (ARGs) with other micro-organisms (known as horizontal gene transfer), conferring resistance to previously sensitive/non-resistant organisms [20]. Wastewater may contain substances (e.g. antimicrobials and active pharmaceutical ingredients [APIs]) that can drive the selection of resistance [10,21,22]. Consequently, when wastewater containing resistance-driving substances enters the environment, this can lead to the spread of AMR [10,21].

UK policy landscape

Key recent developments in UK wastewater policy include:

- The new 5-year UK National Actional Plan (NAP) on AMR is the government's next step to achieve their ambitious target of ensuing AMR is controlled and contained by 2040 [21]. Commitment 1.3 involves implementing "effective waste management, wastewater treatment methods and agrochemical stewardship to minimise dissemination of AMR and AMR-driving chemicals into the environment" [21].
- The government have recently introduced legislation to tackle water bosses polluting Britain's rivers, lakes and seas [23,24]. The Water (Special Measures) Bill strengthens the power of regulators, allowing for tougher and faster action to be taken against water companies that damage the environment and fail their customers [23,24].

Pathways and prevalence of AMR in wastewater

Drug-resistant micro-organisms and antimicrobial compounds are common contaminants in wastewater and sludge [25]. These contaminants originate from individual and domestic usage, pharmaceutical manufacturing, hospital effluents and agricultural activities [10,11,25].

Antibiotic-resistant micro-organisms have been detected within UK rivers and seas [3]. Currently, only the levels of *Escherichia coli* (*E. coli*) and Intestinal Enterococci are measured to assess the presence of faecal contamination and estimate health risks to people exposed to the water [3,26]. Sites contaminated with antibiotics are often also exposed to faecal waste, both of which can facilitate the development and spread of AMR [10,21,27]. While useful indicators for faecal contamination, *E. coli* and Intestinal Enterococci do not reflect overall bathing water quality. For example, the indicators fail to capture the risk of AMR spread, as they underrepresent the diverse range of antibiotic-resistant microorganisms present in UK waters [3,26].

On a global scale, testing of 258 rivers around the world revealed that 25.7% contained APIs at concentrations high enough to select for AMR [28]. Wastewater is therefore a significant environmental reservoir of AMR, and a source of exposure for animals, humans and plants [29]. Swimmers and surfers who frequently enter natural bodies of water are particularly vulnerable to infection with resistant microbes [19,30].

Pharmaceuticals are polluting England's national parks

- A 2024 study identified the presence of pharmaceuticals in the river water of all 10 national parks in England [31,32].
- At least one active pharmaceutical ingredient was detected at 52 out of 54 locations monitored across the ten parks, demonstrating widespread contamination [31,32].
- Although pharmaceutical pollution levels were generally lower in national parks compared to UK urban rivers, some rivers in national parks (Peak District and Exmoor) had higher concentrations of pharmaceuticals than rivers in London [31,32].
- Alarmingly, antibiotic concentrations in the Peak District and Exmoor were higher than levels thought to select for AMR in bacteria [31,32].

How is wastewater treated and how does that affect AMR?

WWTWs are facilities where wastewater is collected, and contaminants are removed using a range of chemical and biological processes [10].

An investigation from The National Chemical Investigations Programme demonstrated that WWTWs are effective at reducing the abundance of ARGs in treated effluent, with removal rates varying from 83% to 96% depending on the ARG type and treatment method used [33,34]. However, other studies have shown that despite a significant reduction in ARGs, WWTPs still release a substantial load of ARGs in their treated effluent [34]. For example, estimates suggest that treated wastewater can contain hundreds of thousands of ARGs per litre, leading to the release of approximately 11 billion ARGs into UK waters every day [14]. In fact, research has shown that the prevalence of some individual ARGs increase, rather than decrease, after wastewater treatment [33,34]. The conditions within WWTWs may therefore inadvertently lead to the development, transmission and multiplication of drug-resistant micro-organisms [3,10].

As the drivers and consequences of AMR are often exacerbated by poverty and inequality, low- and middle-income countries (LMICs) are disproportionately affected [1,35]. For example, LMICs often lack adequate wastewater treatment infrastructure, leading to lower wastewater treatment rates and a higher risk of waterborne AMR transmission [25,36,37,38].

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Wastewater as a tool to monitor AMR

While wastewater is a potential pathway for, and major contributor to, the spread of AMR, it can also be a tool to monitor AMR, as well as inform a targeted approach to mitigate its spread [3]. Wastewater-based epidemiology is a relatively cost-effective method for large-scale environmental AMR surveillance, which was utilised for timely intervention during the COVID-19 pandemic [39]. Wastewater can be used to monitor the prevalence and types of AMR in a population, both at the community level (i.e. WWTWs) and the building level (e.g. for vulnerable populations such as nursing homes, or relevant locations such as pharmaceutical facilities) [39,40,41].

As wastewater-based epidemiology allows for the comparison and monitoring of AMR prevalence across populations, the approach can be used as an early warning tool to inform policy and interventions, as well as prevent hospital outbreaks [39]. In addition, data on AMR spread can help clinicians determine the most effective antibiotics for a given population [39]. Finally, wastewater surveillance is essential for evaluating wastewater treatment technologies and their effectiveness at mitigating the environmental spread of AMR, both in the UK and globally [39].

Wastewater has been utilised as a tool for monitoring AMR in the UK, such as in the PATH-SAFE surveillance programme [42]. However, there are ways to strengthen these monitoring and surveillance efforts.

PATH-SAFE

- The Pathogen Surveillance in Agriculture, Food and Environment (PATH-SAFE) programme (2021–2025) was led by the Food Standards Agency, receiving £24m in funding to establish a UK-wide surveillance network for foodborne pathogens and AMR across the agri-food system [42].
- The programme consisted of four workstreams, one of which involved whole genome sequencing of wastewater to capture AMR data [43].

  PATH-SAFE developed methodologies and technologies for wastewater surveillance and analysis of genomic data, aiming to enhance surveillance practices and outcomes [43].
- PATH-SAFE exemplifies how high-level coordination and cross-departmental funding can support One Health surveillance [21]. Environmental sampling to improve AMR monitoring and surveillance needs to continue on a regular basis.

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How can we address AMR in wastewater?

We call on key stakeholders (policymakers, funding agencies, water companies, sector professionals and the general public) to:

Strengthen monitoring and surveillance

> **Establish regulations or guidelines for water companies to monitor and report the levels of antimicrobials, resistant micro-organisms and their resistance genes in the effluent discharge of WWTWs, as this is currently unregulated [10,44].**
- For example, the revised EU Urban wastewater treatment directive will require AMR monitoring at WWTWs [45]. Policymakers should extend this legislation to the UK, as otherwise the nation risks being left behind in terms of AMR surveillance.

> **Invest in advanced AMR monitoring strategies by equipping government authorities with better resources to conduct targeted and effective AMR surveillance [3]. Advanced AMR monitoring strategies are associated with clean waterways, for example in Iceland, Finland and Slovenia [3]. For this to be effective, stakeholders first need to establish clear aims for monitoring and surveillance to ensure that collected data is relevant and actionable for public health policy [46].**

> **Monitor and test for more antimicrobial resistant micro-organisms when establishing bathing water quality. Government authorities should utilise both phenotypic (bacterial growth) and genotypic (looking at genes) methods to better assess the risk of exposure for vulnerable groups such as swimmers and surfers [3,26].**
- Surveillance should also include the concentration of antibiotic residues [27].

Enhance treatment technologies and practices

> **Utilise existing wastewater treatment technologies to remove microbial contaminants, and therefore AMR, more effectively from treated wastewater by [47]:**
- Incorporating tertiary and quaternary treatment methods e.g. UV, membrane filtration, advanced oxidation processes and integrated processes [47,48].
- Combining treatment methods, which can significantly improve the removal of ARGs [47]. For example, ozonation and amorphous granular activated carbon, two advanced secondary treatment processes [48].

> **Improve the efficiency of existing wastewater treatment technologies in removing microbial contaminants (and therefore AMR) [47].**
- For example, operational adjustments such as prolonged sludge retention and hydraulic retention can be made during secondary treatment of wastewater to facilitate antibiotic removal [49,50].

> **Develop more effective wastewater treatment technologies for the removal of microbial contaminants (and therefore AMR) [47].**
- For example, simulations have demonstrated the efficiency of source separation-modified combined sewer systems, that separately treat toilet wastewater [51].

Improve stakeholder understanding of, and how to mitigate, the risks associated with AMR in wastewater

> **Launch educational awareness campaigns aimed at key stakeholders to improve their understanding of the significant role of wastewater in AMR and how to mitigate its spread.**

This should include campaigns aimed at:
- Sector professionals (e.g. NHS doctors, farmers and vets) to tackle systemic antibiotic overuse/misuse across all sectors by encouraging greater antimicrobial stewardship and appropriate antibiotic prescription/use to reduce the load of AMR contaminants entering the treatment system [3].
- The general public (e.g. patients, caregivers and community members) to tackle inappropriate antibiotic use and disposal by promoting best practices, such as disposing of any unused medicines at pharmacies.

The UK is working on improving stakeholder engagement. For example, in line with commitment 2.3 of the new UK NAP on AMR, government, civil societies and local partners will collaborate to publish an engagement guide on how to improve public understanding of, and how to mitigate, AMR risk [21]. However, this commitment could be taken a step further and establish specific engagement activities, such as workshops, to effectively raise awareness [21].

> **Multisector promotion of One Health and cross-sector collaboration to address AMR. One Health is an integrated and unifying approach which recognises that human, animal and ecosystem health are intrinsically connected [21]. Wastewater, as both a component of the environment and a by-product of human and animal activity, reflects the overlap of these interconnected systems. As a result, One Health is an excellent framework to improve stakeholder understanding of, and how to mitigate, the risks associated with AMR in wastewater.**
- The new UK NAP on AMR takes a One Health approach, however, the plan could go further by establishing specific One Health commitments [21].

Conclusion

Wastewater is commonly contaminated with antimicrobial resistant micro-organisms and antimicrobial compounds. Upon entering our environment, such as rivers and seas, contaminated wastewater therefore serves as a pathway for, and major contributor to, the spread of AMR in the UK and worldwide. Importantly, wastewater serves not only as a vehicle for AMR but also as a critical tool for tracking and mitigating its spread.

There are various interventions to tackle AMR in wastewater, including strengthening monitoring and surveillance, improving stakeholder engagement and enhancing treatment technologies and practices. We urge stakeholders to adopt a combination of interventions tailored to local contexts, recognising the interconnected and cross-sectoral nature of AMR and its presence in wastewater.

Glossary

AMR
Antimicrobial resistance.

APIs
Active pharmaceutical ingredients.

ARGs
Antibiotic resistance genes.

NAP
National Action Plan.

PATH-SAFE
Pathogen Surveillance in Agriculture, Food and Environment.

WWTWs
Wastewater treatment works.

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