Background
A significant proportion of antibiotics used in human and animal healthcare, agriculture and aquaculture end up in the environment after incomplete metabolism or after disposal. There is also evidence of serious antibiotic pollution from the facilities in which these medicines or their active pharmaceutical ingredients are produced. This spread of active substances is an important driver for emergence of antibiotic resistance (ABR) in the environment, by contributing to the antibiotic selection pressure on microorganisms.

The design most commonly used for wastewater treatment plants (WWTPs) is not fully effective in removing antibiotic residues and antibiotic resistance genes (ARGs). Instead, the effluent from WWTPs is rich in ARGs and antibiotic residues, and these pollutants eventually end up in the environment. Soil and water provide an ideal setting for the interaction of microorganisms, ARGs and antibiotic residues, which facilitates the emergence of ABR in the environment. This poses a significant risk to human, animal, and environmental health (One Health) and to global food security.

Although the Global Action Plan on Antimicrobial Resistance (GAP-AMR) advocates a One Health approach to contain ABR, the environmental dimension of ABR has largely been eclipsed by the human and animal/agricultural dimensions. However, in recent times, there has been renewed interest in addressing the issue of ABR in the environment, and there is an understanding that several behavioural change interventions can be effective in this domain. This workshop was aimed at evaluating various behavioural change actions, key actors in the space, strategies to incentivise positive changes in behaviour and bottlenecks associated therewith.

Approach
The interdisciplinary workshop, which had about 25 participants from all continents and from countries at all income levels, was structured to increase the knowledge base and facilitate greater interaction among attendees. Lenore Manderson, Distinguished Professor of Public Health and Medical Anthropology from the School of Public Health at the University of the Witwatersrand in South Africa, spoke on how social, cultural, and institutional factors drive antibiotic consumption and disposal across the world, especially in low- and middle-income countries (LMICs). She gave examples of the ways in which we can leverage a robust understanding of these factors to design behavioural interventions. Suraj K Tripathy, Associate Professor from the School of Biotechnology at the Kalinga Institute of Industrial Technology in India, explained his work on novel wastewater treatment technologies which reduce ARGs and residues in wastewater. He explained the cost-effectiveness of various methods and their efficacy in different settings.

The workshop participants were then divided into five breakout groups and each group deliberated on the identification of actions and innovations to change behaviour in relation to antibiotics and antibiotic-resistant bacteria in the environment. Breakout discussions lasted for one hour and findings were presented in the main session, in a pre-determined template. The summary of the workshop and the call to action outlining the recommendations were crystallised through an open discussion.

Recommendations
The workshop participants deliberated on possible entry points for reducing antibiotic residues and ABR in the environment. The scope of the discussion went beyond behavioural change interventions, as there was a consensus that the relevant fields of actions are part of a broader continuum. A multi-stakeholder, multi-modal strategy is required to contain the issue of antibiotic residues and ABR in the environment. A call to action on the environmental dimensions of ABR may include the following prioritised interventions and encompass the following range of stakeholders:
Prioritised interventions

Production and formulation of antibiotics: Reduce antibiotic pollution at source. Incentivise treatment of effluent in pharmaceutical plants and penalise defaulters, e.g., through differentiated taxes. Increase access to technologies for treating effluents from production facilities. Set up a global fund to incentivise sustainability measures in antibiotic production. Ensure transparency and oversight of antibiotic supply chains and systems to track the international movement of antibiotics.

Human antibiotic use: Prevent infections and encourage responsible antibiotic use – when antibiotics are needed – without compromising access to essential antibiotics in healthcare systems of poorer countries. Implement country-level measures to reduce incorrect prescription of antibiotics, including over-the-counter antibiotic sales. Improve prescribing competencies through access to relevant prescribing guidelines/algorithms and regulatory and enforcement capacity in countries, especially LMICs. Focus energy/resources to improve infection prevention and control, and water, sanitation and hygiene in potential hotspots for resistance generation, such as intensive care units in hospitals, healthcare facilities in general and homes of immune-compromised patients. Improve on-site wastewater treatment in hotspots like hospitals or ensure treatment in municipal wastewater treatment plants.

Farming, i.e., animal/agriculture/aquaculture antibiotic use: Encourage rational antibiotic use by banning use of antibiotics for growth promotion and unnecessary disease prophylaxis. Increase the capacity of farmers to adopt biosecurity measures for infection prevention. Ban the use in farming of highest-priority critically important antibiotics for human health (as per the WHO list). Encourage sustainable models of farming and food production that ensure responsible antibiotic use.

Consumer campaigns: Engage consumer groups and build greater awareness among consumers regarding antibiotic use in humans and in farming. Design globally acceptable labelling and certification systems for antibiotic residues in food. Advocate for a system to better compensate farmers who use sustainable production methods. Encourage systems for consumers to choose products/antibiotics with less environmental impact.

Disposal of antibiotics or waste containing antibiotics: Institutionalise and incentivise waste collection and safe disposal at every possible opportunity and for every stakeholder and penalise systematic defaulters. Encourage and ensure the availability of antibiotic take-back systems in all countries for consumers and healthcare facilities. Introduce incentives for industries and/or farmers to achieve circular economy models to reduce antibiotic residue and ABR burden. Encourage treatment of all farm and hospital waste before it is discharged into the environment. Ensure availability of safe municipal waste treatment.

Antibiotic residues and antibiotic resistance in wastewater: Cut at source and create wastewater treatment facilities. Implement monitoring/surveillance programmes for antibiotic residues and ABR in sewage. Encourage research on cost-effective methods to remove/reduce antibiotic residues and ABR organisms.
Here, we present interventions that countries or organisations can use to prioritise actions to reduce antibiotic residues and antibiotic-resistant bacteria and resistance genes in the environment. The entities mainly involved in the mentioned interventions are the pharmaceutical industry, healthcare professionals and farmers. Other key stakeholders include legislators, policymakers, governmental agencies, international agencies, communication experts, academia and civil society, whose actions are essential to decrease antibiotic residues and resistance in the environment.

INTERVENTIONS

Production and formulation of antibiotics: Cut at source; incentivise treatment of effluent and penalise defaulters. Increase access to technologies for treating effluents from production facilities. Set up a global fund to incentivise sustainable wastewater treatment plant technologies for removal of antibiotic residues. Ensure transparency of antibiotic supply chains and systems to track the international movement of antibiotics.

Human antibiotic use: Prevent infections and encourage responsible antibiotic use – when antibiotics are needed – without compromising access to essential antibiotics in healthcare systems of poorer countries. Implement country-level measures to reduce incorrect prescription of antibiotics, including over-the-counter antibiotic sales. Improve prescribing competencies through access to relevant prescribing guidelines/algorithms. Focus regulatory capacity in countries, especially in low- and middle-income countries (LMICs). Focus energy/resources on improving infection prevention and control/water, sanitation and hygiene facilities. Increase at hotspot for resistance generation, such as intensive care units in hospitals and other healthcare facilities. Improve on-site wastewater treatment in hotspots like hospitals or ensure treatment in municipal wastewater treatment plants.

Farming, i.e., animal/agriculture/aquaculture antibiotic use: Encourage rational antibiotic use by banning use of antibiotics for growth promotion and unnecessary disease prophylaxis. Increase the capacity of farmers to adopt biosecurity measures for infection prevention. Ban the use in farming of highest-priority critically important antibiotics for human health. Encourage sustainable models of farming and food production that ensure responsible antibiotic use.

Consumer campaigns: Engage consumer groups and build greater awareness among consumers regarding infection prevention and antibiotic use in humans and in farming. Design globally acceptable labelling and certification systems for antibiotic residues in food.

Disposal of antibiotics or waste containing antibiotics: Institutionalise and incentivise waste collection and safe disposal at every possible opportunity and for every stakeholder, penalise systematic defaulters. Encourage the availability of antibiotic take-back systems from consumers and healthcare facilities in all countries. Introduce incentives for industries and/or farmers to achieve circular economy models to reduce antibiotic residue burden. All farm and hospital waste should be treated before it is discharged into the environment.


Antibiotic residues and antibiotic resistance in other waters: Build wastewater treatment facilities and monitoring/surveillance programmes for bacterial resistance in natural water bodies, especially near healthcare facilities and pharmaceutical manufacturing plants. Formulate realistic antibiotic residue guidelines for receiving waters. Facilitate universal and equitable access to safe drinking water.

STAKEHOLDERS

In addition to the stakeholders mainly involved in the aforementioned prioritised interventions – the pharmaceutical industry, healthcare professionals and farmers – the following are key stakeholders whose actions are essential to decrease antibiotic residues and antibiotic resistance in the environment. Listed are also suggested actions for them to take.

Legislators/policymakers/governmental agencies/international agencies: Mobilise public opinion around the issue of antibiotic residues and bacterial resistance in environment. Improve the visibility of the issue in policy circles. Encourage commitments from international groupings like OECD/G20/G7 and pharmaceutical industry bodies. Develop templates for Smart Regulation of antibiotic use in various sectors. Frame sustainability criteria for public procurement of antibiotics. Launch an international surveillance system for antibiotic residues and bacterial resistance in the environment.

Communication experts: Create a coordinated strategy to develop communication materials which approach antibiotic residues and bacterial resistance as an environmental and ecological issue. Increase science communication capacity in LMICs. Develop policy briefs ahead of important international meetings on health or environment. Mainstream conversations on taboo subjects like human excreta and waste, which are important vehicles for resistance and residues.

Academia: Take the lead in development and piloting of technologies for removing antibiotic residues, resistant bacteria and resistance genes from water and effluents, including hybrid water treatment technologies. Develop innovative methods and strategies for source separation and source concentration to reduce antibiotics in effluents. Advocate for best practices and create an evidence base for policy action. Perform comprehensive analyses of evidence on antibiotic residues and bacterial resistance in the environment and validity/feasibility of various interventions.

Civil society: Improve the dialogue between the industry, governments and the public. Set up sustainability norms for pharmaceutical producers and advocate to ensure adherence. Perform advocacy regarding prioritisation of decreasing antibiotic residues and bacterial resistance in environment. Increase awareness of the potential impact on the environment of antibiotic residues and encourage pro-environment behaviours.
and ARGs from wastewater. Improve access to safe sanitation facilities in LMICs. Ensure pre-treatment of waste generated in hospitals and healthcare facilities.

**Antibiotic residues and antibiotic resistance in other waters:** Build wastewater treatment facilities. Implement monitoring and surveillance programs for antibiotic residues and ABR in natural water bodies, especially near healthcare facilities and pharmaceutical manufacturing plants. Formulate realistic antibiotic residue guidelines for receiving waters. Facilitate universal and equitable access to safe drinking water.

**Stakeholders**

In addition to the stakeholders mainly involved in the aforementioned prioritised interventions – the pharmaceutical industry, healthcare professionals and farmers— the following are key stakeholders whose actions are essential to decrease antibiotic residues, ARB and ARGs in the environment. Listed are also suggested actions for them to take.

**Legislators/policymakers/governmental agencies/international agencies:** Mobilise public opinion around the issue of antibiotic residues and ABR in environment. Improve the visibility of the issue in policy circles. Encourage commitments from international groupings like OECD/G20/G7 and pharmaceutical industry bodies. Develop templates for Smart Regulation of antibiotic use in various sectors. Frame sustainability criteria for public procurement of antibiotics. Set up sustainability norms for pharmaceutical producers. Formulate realistic antibiotic residue guidelines for receiving waters. Launch an international surveillance system for ABR in the environment.

**Communication experts:** Create a coordinated strategy to develop communication materials which approach ABR as an environmental and ecological issue. Increase science communication capacity in LMICs. Develop policy briefs ahead of important international meetings on health and/or environment. Mainstream conversations on taboo subjects like human excreta and waste, which are important vehicles for resistant bacteria, ARGs and antibiotic residues.

**Academia:** Take the lead in developing and piloting of technologies for removing antibiotic residues and ARGs from water and effluents, including hybrid water treatment technologies. Develop innovative methods and strategies for source separation and source concentration to reduce antibiotics in effluents. Advocate for best practices and create an evidence base for policy action. Perform comprehensive analyses of evidence regarding ABR in the environment and validity/feasibility of various interventions. Develop and evaluate risk evaluation and risk assessment methods with a One Health approach.

**Civil society:** Improve the dialogue between the industry, governments and the public. Set up sustainability norms for pharmaceutical producers/formulators and advocate to ensure adherence. Increase advocacy regarding prioritisation of decreasing antibiotic residues and ABR in environment. Increase awareness of the potential impact on the environment of antibiotic residues and ABR and encourage pro-environment behaviours.

**Acknowledgements**

This brief is one in a series of eight policy briefs produced as an outcome of the digital 2021 Uppsala Health Summit “Managing Antimicrobial Resistance Through Behavior Change.” Uppsala Health Summit is an international arena for dialogue, exploring possibilities and implementation challenges associated with advancement in medicine and public health. You can find the entire series of briefs and more information about Uppsala Health Summit at www.uppsalahealthsummit.se.

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