Reducing the Emergence and Spread of Waterborne Antimicrobial Resistance (AMR) in Ethiopia from a One Health Perspective

INITIATIVE ON
One Health

David W Graham, Javier Mateo-Sagasta, Alemseged Tamiru Haile, Arshnee Moodley, Goraw Goshu and Mulugeta Kibret

December 17, 2024

INITIATIVE ON

One Health

CGIAR

David W Graham[1], Javier Mateo-Sagasta[2], Alemseged Tamiru Haile[3], Arshnee Moodley[4], Goraw Goshu[5] and Mulugeta Kibret[5]

1 Durham University, Durham, United Kingdom
2 International Water Management Institute, Colombo, Sri Lanka
3 International Water Management Institute, Addis Ababa, Ethiopia
4 International Livestock Research Institute, Kenya
5 Bahir Dar University, Bahir Dar, Ethiopia

Contents

List of figures


© Petterik Wiggers/IWMI

Summary

Antimicrobial resistance (AMR) is an increasing global health problem with serious impacts in Ethiopia. Environmental waters play a key role in the transmission and spread, and potentially in the development of resistance. The elevated presence of AMR and antimicrobials in Ethiopian water systems arises from inadequate waste management coupled with poorly regulated antimicrobial use (AMU) in the human, animal and agricultural sectors. The continued and inconsistent use of antimicrobials by healthcare providers and community-scale drug consumption drives AMR development in the gut of users, which spreads via wastes and water in Ethiopia. However, the massive use and misuse of antimicrobials is also common among animal health care providers, including unskilled and animal husbandry practitioners, which also results in waste releases and the environmental transmission and spread of AMR.

Surveillance should prioritize monitoring AMU and AMR, with a specific focus on water as a key conduit for AMR spread and a critical point for detection and control. However, monitoring studies must quantify the relative exposures from different AMR sources in parallel with health studies, i.e., One Health studies that provide integrated data that promote greater recognition and action of water environment in National Action Plans, which is currently not adequately supported in Ethiopia. Only through integrated studies across all sectors will develop solutions to locally and globally increasing AMR.

Strategies to mitigate AMR must involve: Encouraging prudent antimicrobial use and stewardship in humans and animal; Reducing inadequately treated fecal wastes to the environment: Strengthening standardized and integrated AMR surveillance and modelling; Championing water and One Health in National Action Plans for reducing AMR; Promoting sustainable "best buy" technologies and practices for water pollution control and health risk mitigation; Increasing training, education, and awareness; and Improving policy and institutional capacities to create an enabling environment for the effective implementation of all previous recommendations.

Antimicrobial resistance – A global problem with local impacts

Antimicrobial resistance (AMR) occurs when microorganisms are no longer susceptible to medicines used for their treatment, posing a global threat as important as climate change and biodiversity loss (UNEP 2023). AMR can develop in bacteria (also called antibiotic resistance, AR), viruses, protozoa and other microbes, including human, animal, and plant pathogens, and non-pathogenic commensal and environmental strains.

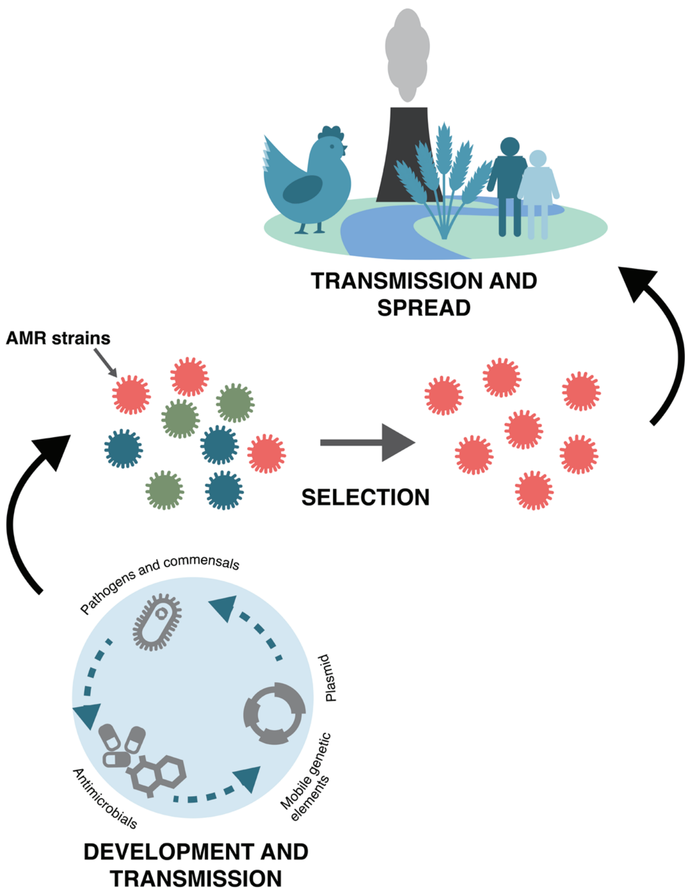
AMR predominantly arises when microbes are exposed to chemicals that cause them stress, such as antibiotics, disinfectants, heavy metals, and industrial and other pollutants (see Box 1). Such exposures kill the most susceptible strains, but some organisms survive, selecting for the strongest and most resistant strains that then proliferate through future generations (Figure 1). This natural selection process is ancient and natural (D'Costa et al. 2011), but human activity has accelerated AMR development due to antimicrobial use, creating new and even stronger AMR strains, giving rise to "superbugs" that are resistant to virtually all antimicrobial treatments (UNEP 2023, Knapp et al. 2010).

In parallel, pharmaceutical companies have stopped investing in antimicrobial research and development as costs are not adequately covered by returns (Global AMR R&D Hub 2021), largely due to rapid AMR development against new drugs upon entering the market. As such, no new class of antibiotics has been discovered since the 1970s (World Bank 2019), and relatively few antibacterials are under development, which aggravates the problem of AMR (Global AMR R&D Hub 2021).

The result of this combination of factors is consequential. Bacterial AMR was directly or indirectly responsible for 4.7 million additional deaths worldwide in 2021 (Murray et al. 2022). Forecasts further show that at least 1.91 million deaths directly attributable to AMR and 8.22 deaths associated with AMR could occur globally in 2050 unless consequential preventative measures are taken (Naghavi et al. 2024) – on par with current rates of cancer deaths (O'Neill 2016). If not addressed now, AMR will reduce global GDPs by an estimated USD 3.4 trillion annually and push at least 24 million more people into extreme poverty over the next decade due to lost capacity to work (UNEP 2023). AMR, now referred to as the "silent pandemic," is among the leading threats to environmental sustainability and global health.

Increasing AMR is a global issue, with risks shared by all countries. However, AMR is particularly problematic in Ethiopia, which has the 170th highest age-standardized mortality rate resulting from AMR (per 100,000 people), among the ranking of 204 countries assessed, e.g., > 150 deaths per 100 000 population attributable to AMR in 2019 (Sartorius et al. 2024). In general, high rates of AMR are

Figure 1. How AMR is developed and selected, and monitoring priorities in order of importance in integrated surveillance studies aimed at reducing the transmission and waterborne spread of AMR. (Source: Authors)



MONITORING PRIORITIES IN INTEGRATED SURVEILLANCE

1. **Pathogenic AMR microorganisms**
2. **Non-pathogenic AMR microorganisms**
   Resistant organisms who can share AMR genes with pathogens, creating new resistant pathogens.
3. **AMR or mobile genetic transfer genes (MGE)**
   AMR genes and mobile genetic elements that indicate the potential for AMR and-or can mediate gene-sharing, respectively.
4. **Antimicrobials, heavy metals, and other chemicals**
   Antimicrobial levels usually relate to local use rate, whereas all three can increase the potential for AMR development.

How is AMR measured?

There is a diverse array of antimicrobials and an even greater diversity of AMR strains and antibiotic resistance genes (ARGs), making "AMR" difficult to define and quantify in most scenarios. Microbial culturing methods can quantify living AMR strains by growing the organisms in the presence of an antimicrobial on agar plates. Alternately, AMR can be quantified by measuring the abundance of ARGs within a system as an indicator of AMR organisms.

From a health protection perspective, quantifying living AMR pathogens is most important because they directly cause infectious disease (Figure 1). However, quantifying living non-pathogenic AMR strains also is useful because it reflects the abundance of strains that can potentially share their ARGs with pathogens. Quantifying ARGs and mobile genetic elements (MGEs) is also useful, especially in environmental samples. Genes do not indicate living AMR strains, but they do indicate the potential for AMR, which can be quantified more economically at mass scales using sequencing, genomics, and metagenomics. Microbial and genetic AMR data are best complemented with antimicrobial, pollutant and other metadata to help explain the causes and sources of AMR in different places.

> "Water plays a crucial role as a key connector between the arms of One Health. What happens to water upstream affects humans and animals downstream.

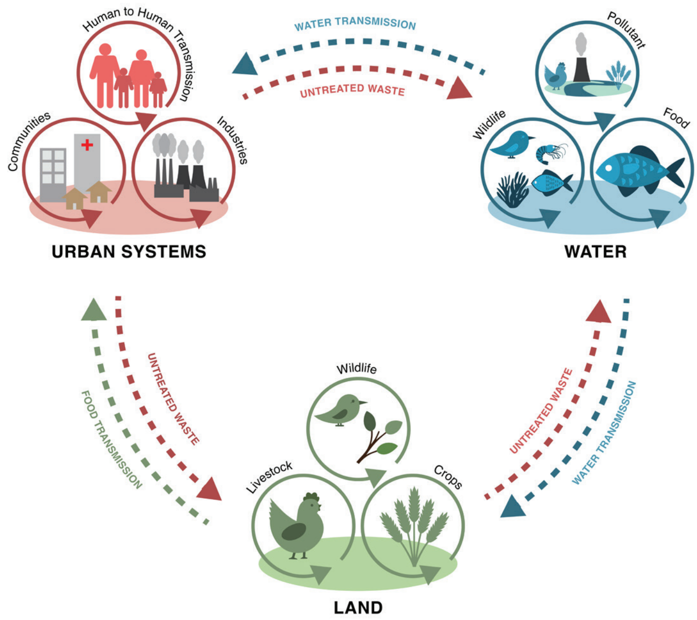
common in places with inadequate sanitation, poor water quality, greater industrial pollution, poor governance, and limited universal healthcare (Collignon et al. 2018, Graham et al. 2019b). As such, countries such as Ethiopia urgently need to develop holistic, One Health strategic plans to address their local AMR crisis (Berhe et al. 2021). The key is to prevent the development of AMR in the first place, based on more prudent use, but then mitigate the transmission and spread of residual AMR organisms and genes across human, animal, crop and food systems in the environment.

One Health and waterborne AMR in Ethiopia

The concept of One Health recognizes the interconnectedness of human, animal and environment health and emphasizes the importance of addressing health challenges through a holistic approach that integrates multiple disciplines and sectors.

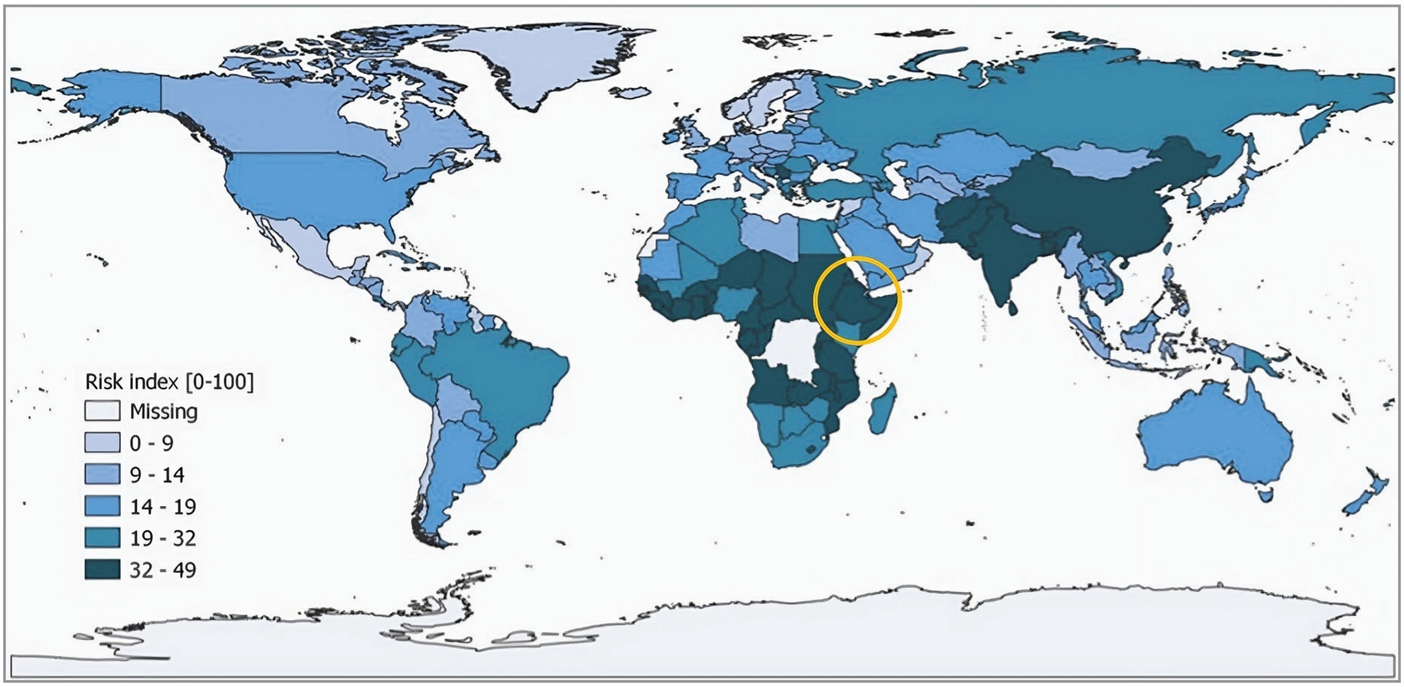
The development and selection of diverse AMR strains is occurring simultaneously across the One Health spectrum (see Figure 2), including within human and veterinary settings, crop and livestock production and other sectors that overuse or misuse antimicrobials and chemicals that drive resistance (Graham et al. 2019b, Scott et al. 2019, OHHLEP 2023).

Figure 2. AMR sources and sinks are highly interconnected, often linked by environmental pathways. (Source: Authors)



Water plays a crucial role as a key connector between the arms of One Health. What happens to water upstream affects humans and animals downstream. Hospitals, cities and farms (livestock, aquaculture and crops) discharge increasing loads of antimicrobial resistant bacteria (ARB) and ARGs to water bodies. Once in receiving waters, ARB and ARGs can be further transmitted and spread. Non-resistant bacteria in polluted aquatic environments can also gain resistance because of selection pressure if environmental levels of antimicrobials, heavy metals, and other pollutants are sufficiently high. Resistant pathogens could reach sites where there will be interactions between humans and animals that might lead to uptake, and disease outbreaks. Possible exposure routes include drinking water, recreational water activities, and untreated wastewater for irrigation (Abera et al. 2014, 2016; Jampani et al. 2024, 2022).

Figure 3. Predicted waterborne AMR exposure risk around the world in 2030. Ethiopia (circled below) is among the countries with the highest risk. Adapted from the World Economic Forum (WEF 2021).



Waterborne AMR tends to be most pronounced in places like Ethiopia, with less controlled antimicrobial use and inadequate water quality, sanitation and hygiene (WASH). On the basis of the projected AMR waterborne exposure risks in the future, Ethiopia is a country with among the greatest risks of waterborne AMR (Figure 3; WEF 2021), largely due inadequate WASH, but also highly levels of active pharmaceutical ingredient (APIs) in some local rivers. Despite these trends, waterborne AMR monitoring was not included in the recent Ethiopian NAP (MOH/MOA/EEC 2021).

In Ethiopian rivers, such as the Akaki River, AMR pollution can be very high (Hiruy et al. 2022, Belachew et al. 2018). In a recent global survey that included 137 rivers from 104 countries, the Akaki River in Addis Ababa ranked third in the world for APIs content at over 50 ug/L (Wilkinson et al. 2022). Such levels can select for ARGs in aquatic systems (Knapp et al. 2008). It is nevertheless unclear whether AMR in the Akaki is being more impacted by in situ activity of the chemicals themselves or due to AMR in untreated human, animal and hospital wastes along the river. This can only be determined through One Health-based studies on the river catchment.

While the One Health approach is vital for reducing cross-contamination between sectors (UNEP 2023); inadequate attention is currently being paid to the impact of AMR circulating in the Ethiopian environment on human and animal health systems (Tiseo et al. 2020, Baudoin et al. 2021).

Strategies to tackle waterborne AMR in Ethiopia

The United Nations has recommended One Health thinking and solutions (UNEP 2023), which is recognized in the recent 2021-2025 Ethiopian National Acton Plan (NAP) for reducing AMR (MOH/MOA/EEC 2021). Further, the 2024 UN General Assembly political declaration commits to "strengthen national capacities for sustainable, sector-specific, integrated and interoperable surveillance systems for antimicrobial resistance and antimicrobial use …" and specifically to commit to gather "… data on antimicrobial use across sectors and monitoring of water, sanitation and hygiene in healthcare facilities and community settings and the environment, and to share relevant information on emerging trends to inform decision making at all levels" (UNGA 2024).

Both the UNGA declaration, which Ethiopia was a signatory, and the Ethiopian NAP commit to integrated action against AMR, but solutions must be planned and supported across sectors, including surveillance on AMR in water environments. However, operationalizing and funding environmental action is lacking in Ethiopia, especially integrated AMR surveillance based on One Health. This is especially important for Ethiopia because Ethiopia lacks universal WASH – and is where waterborne AMR exposures are among the highest in the world and almost certainly have consequential impact on high levels of AMR in healthcare systems.

Addressing the challenge of AMR and developing science-informal One Health-based solutions in Ethiopia requires a series of multifaceted actions. The actions include policy guidance, surveillance, data collection, increased awareness of waterborne and environmental AMR in the country, and the use of alternative therapeutics in healthcare. Examples for consideration in Ethiopia include:

- **Encourage prudent AMU and stewardship:**
  With few new antimicrobials, emphasis in healthcare has shifted to stronger antimicrobial stewardship, which is a systematic approach to educate and support health care professionals to follow evidence-based guidelines for prescribing and administering antimicrobials, reduce use of broad-spectrum antimicrobials, and explore alternative and adjunct therapies. For example, a move towards vaccines instead of antimicrobials has proved promising in animal health protection, which should be considered in human healthcare to reduce dependency on antimicrobials and subsequent AMR. The promotion of WASH in households and livestock and aquaculture value chains can also reduce AMR infections and reduce the need of antimicrobials.

- **Strengthen standardized and integrated AMR surveillance and modelling:**
  There is little knowledge regarding the relative importance of different pathways of AMR transmission and spread in Ethiopia. AMR can be developed almost anywhere, but the proportion of AMR infections due to environmental exposures versus clinical or other exposures is largely unknown. Speculation suggests that more than 50% of AMR infections in countries with poor water quality, including Ethiopia, may result from food or waterborne transmission (Laxminarayan and Chaudhury 2016), but this requires local validation. The extent that various sources, such as untreated human waste, agricultural activities or industrial wastes, contribute to waterborne AMR is also a knowledge gap in Ethiopia.

“ For example, a move towards vaccines instead of antimicrobials has proved promising in animal health protection, which should be considered in human healthcare to reduce dependency on antimicrobials and subsequent AMR.

Local integrated surveillance studies that provide standardized data on human and animal health, antimicrobial use, and environmental and exposure from across sectors are needed to address these knowledge gaps (Beyene et al. 2023, Liguori et al. 2022). The use of genetic and other source-tracking methods (e.g., Ott et al. 2021, Hendriksen et al. 2019) can also help identify the priority AMR pollution sources. Improving the modelling of AMR transport and fate in Ethiopian water bodies is also crucial (Jampani et al. 2024, Jampani et al. 2022) to understand the role of water, evaluate potential mitigation measures, provide specific policy guidance and set priority interventions.

Operational action depends on Ethiopia's capacity, which is currently still limited. However, valuable work is still possible using available methods in tandem, such as microbial culturing of AMR strains, background data on sample context (e.g., water quality), and quantification of ARGs across sources and studies (Denku et al. 2022).

- **Champion water and One Health in National Action Plans for reducing AMR**

Ethiopia's most recent NAP (2021 to 2025) promoted a One Health approach, which is commendable (MOH/MOA/EEC 2021). Environmental factors, including waste management and water quality, were stated as important to AMR but were only minimally described or funded in operational surveillance planning. This may have resulted from the fact that water professionals, experts who are needed to plan and operationalize environmental monitoring, where not apparently included in NAP development. The inclusion of experts on water and environmental AMR is urgently needed in future NAP development and implementation, especially those involved with existing environmental monitoring programs (Mateo-Sagasta et al. 2024). However, value from environmental monitoring will only be gained by coupling such monitoring with parallel monitoring of the other One health sectors (human and animal health systems), as stated previously.

- **Promote sustainable "best buy" technologies and practices for water pollution control and health risk mitigation:**

There are multiple potential sources of ARB, antimicrobials and other drivers of AMR into water bodies. These include cities, industries, livestock, crops and aquaculture. Figure 4 shows how AMR can spread in a dysfunctional watershed, and how to transition to cleaner and safer watersheds. Prevention of AMR at the source is critical, including reduced use of antimicrobials, adoption of good sanitation and hygiene practices, and behavior change at the source and improved waste and wastewater management.

Implementing prevention and containment measures across sectors will progressively enhance environmental water quality (Figure 4), thereby reducing the broader spread of AMR. This, in turn, decreases the demand for antimicrobials, creating a downward spiral in antimicrobial use, which in turn, reduces new AMR development. Based on the high API levels and other pollutants observed in the Akaki River, reducing demand for antimicrobials and industrial chemicals is critically needed in Ethiopia.

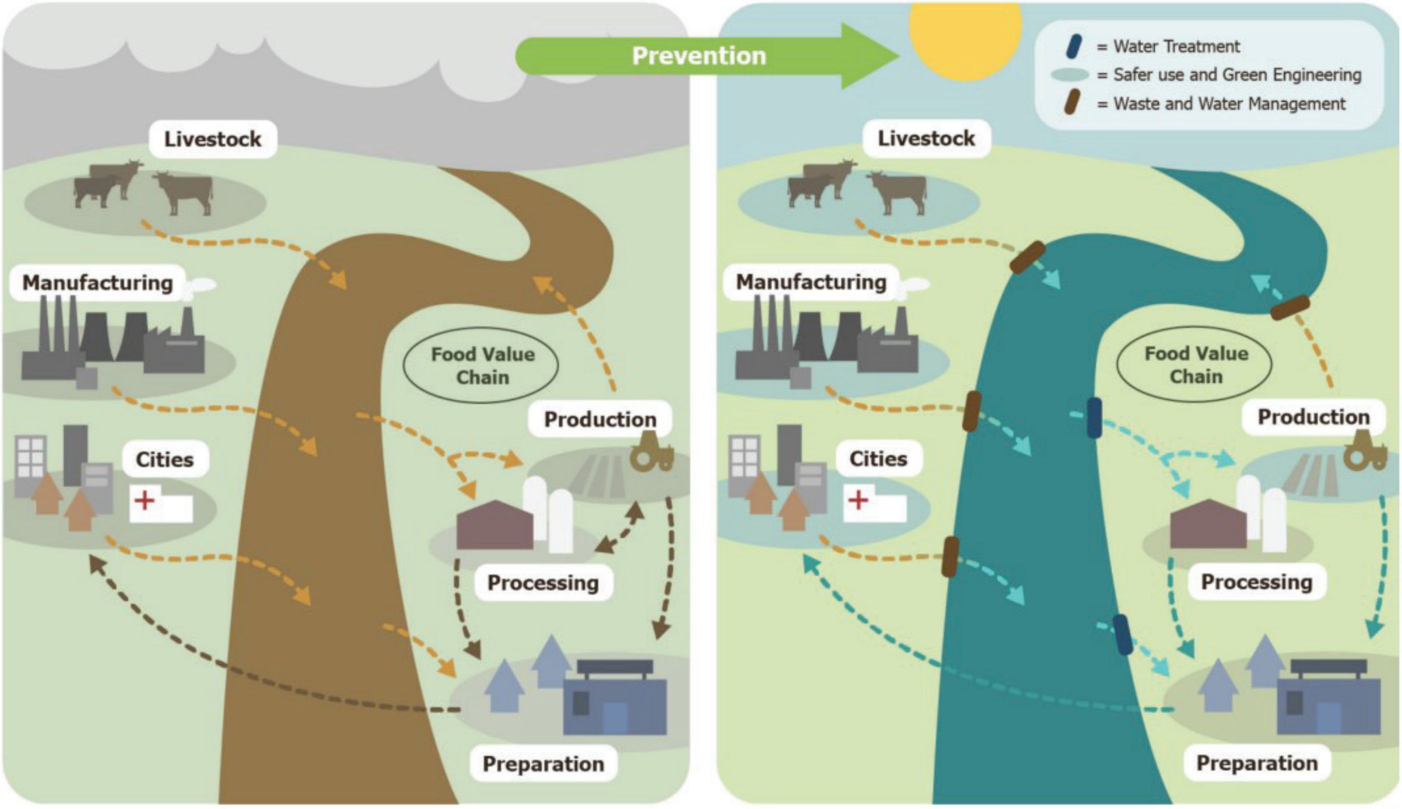
There are multiple mature technologies for water pollution control and new technology development and implementation is not necessarily the best immediate solution in low-income countries, like Ethiopia. The World Health Organization recommends the "best buy" principle be used in choosing the most appropriate waste and wastewater treatment technology for a particular location (WHO/FAO/WOAH 2020). This principle encourages technologies that provide the greatest "cost-benefit" in reducing AMR with the available resources. This means technological development, such as in waste treatment, would improve in smaller steps, progressing as more resources become available. In principle, initial action would be to fully implement WASH and fecal waste containment, but then progress to small-scale decentralized wastewater treatment plants (WWTPs) and ultimately to full-scale WWTPs (Graham et al. 2019a).

> "There are multiple mature technologies for water pollution control and new technology development and implementation is not necessarily the best immediate solution in low-income countries, like Ethiopia.

It is essential to co-select and co-develop with local stakeholders the business models that can facilitate the adoption of proven technologies to treat waste from cities (Otoo and Drechsel 2018), livestock (Sathiskumar et al. 2024) and other sources.

Finally, it is also important to work on risk management when polluted water is used downstream. This includes drinking water source protection and water treatment but also the safe management of water during food production, processing and preparation in crops (FAO 2019), livestock and aquaculture value chains.

Figure 4. What a One Health approach to preventing AMR transmission and spread across the environment would look like in Ethiopia (Source: Authors).



- **Increase training, education, and awareness and improve policy and institutional capacities.**

  All previous recommendations can show a positive impact, but they need an enabling environment for effective implementation. This must be driven by expanded training and education on a technical level, but also include educational initiatives and awareness campaigns for the wider public, especially on the critical role polluted water on AMR spread when WASH is inadequate.

  However, the above must be done in tandem with investment in the essential infrastructure for AMR surveillance and monitoring. Such investment is needed in increased laboratory capacity, but also data networks that will allow information to be gained, stored, and integrated from different One Health sectors, allowing more holistic and informed decision-making by policymakers.

  Such an integrated system, in parallel to training and education, must be underpinned by increased governmental awareness, which is needed to trigger political action. However, integration and awareness must not solely fall on the shoulders of the government, but include active involvement of the public and industry, of solutions are to become sustainable.


© Apollo Habtamu/IWMI

References

Abera, B.; Kibret, M.; Goshu, G.; Yimer, M. 2014. Bacterial quality of drinking water sources and antimicrobial resistance profile of Enterobacteriaceae in Bahir Dar city, Ethiopia. *Journal of Water, Sanitation and Hygiene for Development* 4: 384–390. https://doi.org/10.2166/washdev.2014.105.

Abera, B.; Kibret, M.; Mulu, W. 2016. Extended-Spectrum beta (β)-Lactamases and antibiogram in Enterobacteriaceae from clinical and drinking water sources from Bahir Dar City, Ethiopia. *PLOS ONE* 11: e0166519. https://doi.org/10.1371/journal.pone.0166519.

Baudoin, F.; Hogeveen, H.; Wauters, E. 2021. Reducing antimicrobial use and dependence in livestock production systems: A social and economic sciences perspective on an interdisciplinary approach. *Frontiers in Veterinary Science* 8: 584593. https://doi.org/10.3389/fvets.2021.584593.

Belachew, T.; Mihret, A.; Legesse, T.; Million, Y.; Desta, K. 2018. High level of drug resistance by gram-negative bacteria from selected sewage polluted urban rivers in Addis Ababa, Ethiopia. *BMC Research Notes* 11: 524. https://doi.org/10.1186/s13104-018-3622-0.

Berhe, D.F. et al. 2021. Prevalence of antimicrobial resistance and its clinical implications in Ethiopia: A systematic review. *Antimicrobial Resistance & Infection Control* 10: 168. https://doi.org/10.1186/s13756-021-00965-0.

Beyene, A.M.; Andualem, T.; Dagnaw, G.G.; Getahun, M.; LeJeune, J.; Ferreira, J.P. 2023. Situational analysis of antimicrobial resistance, laboratory capacities, surveillance systems and containment activities in Ethiopia: A new and One Health approach. *One Health* 16: 100527. https://doi.org/10.1016/j.onehlt.2023.100527.

Collignon, P.; Beggs, J.J.; Walsh, T.R.; Gandra, S.; Laxminarayan, R. 2018. Anthropological and socioeconomic factors contributing to global antimicrobial resistance: A univariate and multivariable analysis. *The Lancet Planetary Health* 2: e398–e405. https://doi.org/10.1016/S2542-5196(18)30186-4.

D'Costa, V.M. et al. 2011. Antibiotic resistance is ancient. *Nature* 477: 457–461. https://doi.org/10.1038/nature10388.

Denku, C.Y.; Ambelu, A.; Mitike, G. 2022. Enteric bacterial pathogens and their antibiotic-resistant patterns from the environmental sources in different regions of Ethiopia: A laboratory-based cross-sectional study. *Health Science Reports* 5: e521. https://doi.org/10.1002/hsr2.521.

FAO (Food and Agriculture Organization of the United Nations); WHO (World Health Organization). 2019. Safety and quality of water used in food production and processing – Meeting report. Microbiological Risk Assessment Series 33. Rome, Italy: Food and Agriculture Organization of the United Nations. Available at https://www.who.int/publications/i/item/9789241516402

Global AMR R&D Hub. 2021. Estimating global patient needs and market potential for priority health technologies addressing antimicrobial resistance. Available at https://globalamrhub.org/wp-content/uploads/2021/08/EAG-Report_FINAL_20082021.pdf (accessed on February 14, 2024).

Graham, D.W.; Giesen, M.J.; Bunce, J.T. 2019a. Strategic approach for prioritising local and regional sanitation interventions for reducing global antibiotic resistance. *Water* 11: 27. https://doi.org/10.3390/w11010027."

Graham, D.W. et al. 2019b. Complexities in understanding antimicrobial resistance across domesticated animal, human, and environmental systems. *Annals of the New York Academy of Sciences* 1441: 17–30. https://doi.org/10.1111/nyas.14036.

Hendriksen, R.S.; Bortolaia, V.; Tate, H.; Tyson, G.H.; Aarestrup, F.M.; McDermott, P.F. 2019. Using genomics to track global antimicrobial resistance. *Frontiers in Public Health* 7: 242. https://doi.org/10.3389/fpubh.2019.00242.

Hiruy, A.M.; Mohammed, J.; Haileselassie, M.M.; Acharya, K.; Butte, G.; Haile, A.T.; Walsh, C.; Werner, D. 2022. Spatiotemporal variation in urban wastewater pollution impacts on river microbiomes and associated hazards in the Akaki catchment, Addis Ababa, Ethiopia. *Science of The Total Environment* 826: 153912. https://doi.org/10.1016/j.scitotenv.2022.153912.

IHME (Institute for Health Metrics and Evaluation). 2022. The burden of antimicrobial resistance (AMR) in Ethiopia. Seattle, Washington: Institute for Health Metrics and Evaluation. Available at https://www.healthdata.org/sites/default/files/2023-09/Ethiopia.pdf (accessed on February 26, 2024).

Jampani, M.; Gothwal, R.; Mateo-Sagasta, J.; Langan, S. 2022. Water quality modelling framework for evaluating antibiotic resistance in aquatic environments. *Journal of Hazardous Materials Letters* 3: 100056. https://doi.org/10.1016/j.hazl.2022.100056.

Jampani, M.; Mateo-Sagasta, J.; Chandrasekar, A.; Fatta-Kassinos, D.; Graham, D.W.; Gothwal, R.; Moodley, A.; Chadag, V.M.; Wiberg, D.; Langan, S. 2024. Fate and transport modelling for evaluating antibiotic resistance in aquatic environments: Current knowledge and research priorities. *Journal of Hazardous Materials* 461: 132527. https://doi.org/10.1016/j.jhazmat.2023.132527.

Knapp, C.W.; Engemann, C.A.; Hanson, M.L.; Keen, P.L.; Hall, K.J.; Graham, D.W. 2008. Indirect evidence of transposon-mediated selection of antibiotic resistance genes in aquatic systems at low-level oxytetracycline exposures. *Environmental Science & Technology* 42: 5348–5353. https://doi.org/10.1021/es703199g.

Laxminarayan, R.; Chaudhury, R.R. 2016. Antibiotic resistance in India: Drivers and opportunities for action. *PLOS Medicine* 13: e1001974. https://doi.org/10.1371/journal.pmed.1001974.

Liguori, K.; Keenum, I.; Davis, B.C.; Calarco, J.; Milligan, E.; Harwood, V.J.; Pruden, A. 2022. Antimicrobial resistance monitoring of water environments: A framework for standardized methods and quality control. *Environmental Science & Technology* 56: 9149–9160. https://doi.org/10.1021/acs.est.1c08918.

Mateo-Sagasta, J.; Haile, A.T.; Beza, H.M. 2024. Water at the forefront of One Health in Ethiopia, October. Available at https://hdl.handle.net/10568/155458 (accessed on December 21, 2024).

MOH/MOA/EFC. 2021. Antimicrobial resistance prevention and containment strategic plan: The One Health approach 2021-2015 Third Edition. Ministry of Health, Ministry of Agriculture, and the Environment, Forest and Climate Change Commission Ethiopia. Available at http://www.fmhaca.gov.et/wp-content/uploads/2022/02/Ethiopian-AMR-PC_Strategic-Plan-2021_2025.pdf (accessed on March 9, 2024).

Murray, C.J.L. et al. 2022. Global burden of bacterial antimicrobial resistance in 2019: A systematic analysis. *The Lancet* 399: 629–655. https://doi.org/10.1016/S0140-6736(21)02724-0.

Naghavi, M. et al. 2024. Global burden of bacterial antimicrobial resistance 1990–2021: A systematic analysis with forecasts to 2050. *The Lancet* 404: 1199–1226. https://doi.org/10.1016/S0140-6736(24)01867-1.

OHHLEP (One Health High-Level Expert Panel). 2023. 10th Meeting of the One Health High-Level Expert Panel (OHHLEP). Available at https://www.who.int/publications/m/item/10th-meeting-of-the-one-health-high-level-expert-panel-(ohhlep) (accessed on August 10, 2024).

O'Neill, J. 2016. Infection prevention, control and surveillance: Limiting the development and spread of drug resistance. Review on Antimicrobial Resistance. Available at https://amr-review.org/sites/default/files/Health%20infrastructure%20and%20surveillance%20final%20version_LR_NO%20CROPS.pdf (accessed on December 14, 2023).

Otoo, M.; Drechsel, P., eds. 2018. *Resource recovery from waste: business models for energy, nutrient and water reuse in low- and middle-income countries*. London New York: earthscan from Routledge, Routledge Taylor & Francis Group.

Ott, A.; O'Donnell, G.; Tran, N.H.; Mohd Haniffah, M.R.; Su, J.-Q.; Zealand, A.M.; Gin, K.Y.-H.; Goodson, M.L.; Zhu, Y.-G.; Graham, D.W. 2021. Developing surrogate markers for predicting antibiotic resistance "hot spots" in rivers where limited data are available. *Environmental Science & Technology* 55: 7466–7478. https://doi.org/10.1021/acs.est.1c00939.

Sartorius, B. et al. 2024. The burden of bacterial antimicrobial resistance in the WHO African region in 2019: A cross-country systematic analysis. *The Lancet Global Health* 12: e201–e216. https://doi.org/10.1016/S2214-109X(23)00539-9.

Sathiskumar, A.; Singha, R.; Agide, Z.; Peña, G.; Ruiz-Bastidas, R.C.; Taron, A.; Mateo-Sagasta, J. 2024. Resource recovery from livestock waste: A compilation of business cases from the Global South, November. Available at https://hdl.handle.net/10568/159573 (accessed on December 21, 2024).

Scott, H.M. et al. 2019. Critically important antibiotics: criteria and approaches for measuring and reducing their use in food animal agriculture. *Annals of the New York Academy of Sciences* 1441: 8–16. https://doi.org/10.1111/nyas.14058.

Tiseo, K.; Huber, L.; Gilbert, M.; Robinson, T.P.; Van Boeckel, T.P. 2020. Global trends in antimicrobial use in food animals from 2017 to 2030. *Antibiotics* 9: 918. https://doi.org/10.3390/antibiotics9120918.

UNEP (United Nations Environment Programme). 2023. *Bracing for superbugs: strengthening environmental action in the One Health response to antimicrobial resistance*. Geneva, Switzerland: United Nations Environment Programme. Available at https://www.unep.org/resources/superbugs/environmental-action (accessed on February 14, 2024).

UNGA (United Nations General Assembly). 2024. Political Declaration of the High-level Meeting on Antimicrobial Resistance. United Nations General Assembly. Available at https://www.un.org/pga/wp-content/uploads/sites/108/2024/09/FINAL-Text-AMR-to-PGA.pdf (accessed on December 10, 2024).

WEF (World Economic Forum). 2021. *Antimicrobial resistance and water: the risks and costs for economies and societies*. Geneva, Switzerland: World Economic Forum.

WHO/FAO/WOAH. 2020. Technical brief on water, sanitation, hygiene and wastewater management to prevent infections and reduce the spread of antimicrobial resistance. World Health Organization, Food and Agriculture Organization of the United Nations, and World Organisation for Animal Health. Available at https://www.who.int/publications/i/item/9789240006416 (accessed on February 14, 2024).

Wilkinson, J.L. et al. 2022. Pharmaceutical pollution of the world's rivers. *Proceedings of the National Academy of Sciences*, 119:e2113947119. https://doi.org/10.1073/pnas.2113947119.

World Bank. 2019. *Pulling together to beat superbugs: knowledge and implementation gaps in addressing antimicrobial resistance*. Washington DC: World Bank. https://doi.org/10.1596/37098.


ETHIOPIA

Glossary

Source: Compiled by the authors

Active Pharmaceutical Ingredient (API) – Active pharmaceutical ingredients (APIs) are chemical compounds that exert a direct biological or other impactful influence in diagnosing, curing, alleviating, treating or preventing diseases, or modify the structure or function of the human or animal body.

Antibiotic Resistance Gene (ARG) – An antibiotic resistance gene (ARG) is a segment of DNA that encodes for traits that allow microorganisms to withstand the effects of specific antibiotics, reducing or eliminating the drugs' effectiveness in treating infections caused by those organisms.

Antimicrobial Resistance (AMR) – Antimicrobial resistance (AMR) develops when bacteria, viruses, fungi and parasites develop a resistance to the effects of antimicrobial drugs. AMR renders antibiotics and other antimicrobial medications ineffective, making infections challenging or even impossible to manage.

Antimicrobial Use (AMU) – Antimicrobial use (AMU) involves using medicines like antibiotics, antivirals, antifungals and antiparasitics to prevent and treat infections in humans, animals and plants. AMU also includes use for other purposes, such as growth promotion in food animal production.

Antimicrobials – Medications used to address infectious ailments across humans, animals and plants. They encompass a range of therapeutic agents, including antibiotic, antiviral, antifungal and antiparasitic agents. Antibiotics are drugs specific to bacterial infections.

Best-buy Technologies – The most cost-effective and efficient technologies or solutions available in a particular resource context, emphasizing value for money and optimal performance.

Development of AMR – The process by which bacteria, viruses, fungi or parasites acquire resistance to antimicrobial drugs. Development can occur naturally via genetic mutations or be accelerated by selective pressures imposed by the improper or overuse of antibiotics, antivirals, antifungals or antiparasitics.

Exposure Risk – Exposure risk is the probability that individuals or populations will encounter potential AMR microorganisms. Characterizing AMR exposures (ARGs and AMR microbes) identifies possible health risks that depend on the pathways of exposure. Not all exposures pose consequential health risks.

Gene – A gene is a segment of DNA that contains the instructions for building and maintaining living organisms. Genes serve as the basic units of heredity, carrying genetic information from one generation to the next, including resistance genes (ARGs) that can confer AMR in microorganisms.

Genome – A genome is the entire set of genes within an organism's DNA, containing the instructions for its development, functioning and reproduction.

Growth P-promoters – Growth promoters are substances or agents administered to enhance the growth and productivity of animals, often in the context of animal farming or agriculture. These can include antibiotics or other compounds that stimulate growth.

Health Risk – The health risk of AMR depends on the duration and concentration of exposures to AMR microorganisms, and the pathways of exposure. Pathways range from direct ingestion to proximal exposures. The risk of acquiring AMR pathogens varies based on available pathways and local behavior.

Infrastructure – Physical resources and nonphysical systems that underpin civil existence, such as sewer lines, wastewater treatment plants, roads and other urban and rural systems.

Integrated AMR surveillance – This type of integrated surveillance is the coordinated monitoring and data collection on AMR organisms, genes, antimicrobials use, and metadata, spanning humans, animals and the environment. This approach recognizes the interconnectedness of health in these domains, aiming to provide a comprehensive understanding and address AMR collectively.

Metagenome – A metagenome refers to the collective genetic material derived from a diverse community of microorganisms, such as bacteria, viruses and fungi, present in a particular environment or sample.

Microbial Culturing – Growing microorganisms present in clinical, veterinary and environmental samples on selective solid media. For AMR isolates, selective media contains antimicrobial agents to determine microbial susceptibility to those agents and their physical AMR traits. Sequencing of organism DNA can be used to determine the genetic basis of their observed resistance.

National Action Plans (NAPs) – NAPs are comprehensive strategies developed by governments to address growing challenges, such as AMR. AMR NAPs should outline coordinated efforts and policies involving healthcare, agriculture and other relevant sectors to promote responsible use of antimicrobials, enhance surveillance, raise awareness and implement measures to mitigate and control antimicrobial resistance at the national level.

One Health – One Health is an inclusive strategy that aims to harmonize and enhance the health of people, animals and the environment. It recognizes the interconnectedness of human health, animal health, plant health and the broader environment, emphasizing their interdependence must be considered in overall well-being of all elements.

Pathogen – A pathogen is a microorganism, such as a bacterium, virus, fungus or parasite that causes disease or illness in its host organism.

Sequencing – Sequencing refers to the process of determining the precise order of nucleotides (A, T, C and G) in a DNA or RNA molecule, providing insight into the genetic information encoded within that molecule. It can be used to characterize the genomes of individual microorganisms or whole microbial communities and can support integrated AMR surveillance.

Spread of AMR – The dissemination or proliferation of resistant microorganisms or genes across populations, environments or geographical regions. The spread of AMR extends local transmission events to wider scales and is often results from contaminated food and water. Efforts to control and mitigate the spread of AMR often involves creating barriers that block AMR from migrating away for their point of development.

Transmission of AMR – The transfer of resistant microorganisms or genes between individuals, animals or environments. Transmission can occur through various means, such as direct contact, contaminated food and water, or the exchange of genetic material, leading to AMR spread. Understanding and controlling transmission pathways is key to managing and preventing the wider spread of AMR.

WASH – WASH, i.e., water, sanitation and hygiene, is a collective term for practices aimed at ensuring access to clean water, proper sanitation facilities and good hygiene practices. WASH programs address public health concerns by promoting safe water sources, adequate sanitation infrastructure, and hygiene education to prevent waterborne diseases and improve overall well-being.

Acknowledgements

This work was carried out under the CGIAR Initiative on One Health. We would like to thank all funders who support this research through their contributions to the CGIAR Trust Fund (www.cgiar.org/funders).

Suggested Citation

Graham, D. W.; Mateo-Sagasta, J.; Haile, A. T.; Moodley, A.; Goshu, G.; Kibret, M. 2024. *Reducing the emergence and spread of waterborne antimicrobial resistance (AMR) in Ethiopia from a One Health perspective*. Colombo, Sri Lanka: International Water Management Institute (IWMI). CGIAR Initiative on One Health. 20p.

International Water Management Institute

INTERNATIONAL LIVESTOCK RESEARCH INSTITUTE

Durham University

Javier Mateo-Sagasta, Senior Researcher & Coordinator, Water Quality, IWMI, *J.Mateo-Sagasta@cgiar.org*

Alemseged Tamiru Haile, Senior Researcher, IWMI, *A.T.Haile@cgiar.org*

INITIATIVE ON
One Health