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Healthcare waste management and antimicrobial resistance: a critical review

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ABSTRACT

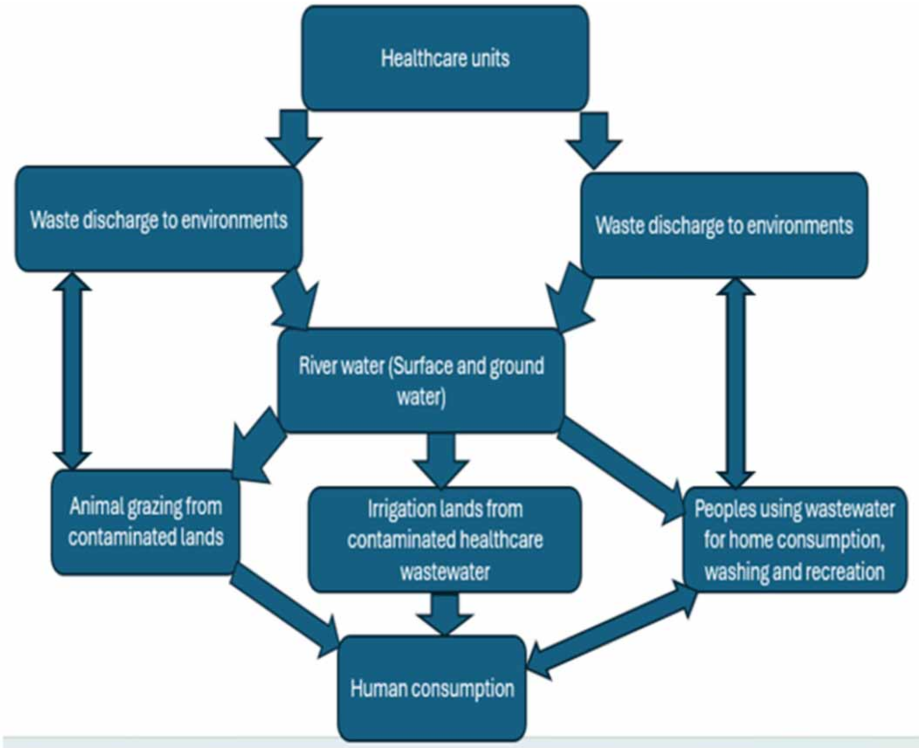
The rapid growth of populations and urbanization has led to a significant increase in healthcare waste, posing serious health risks. A search on Google Scholar identified seven relevant articles from Ethiopia that examine the relationship between improper waste management in healthcare facilities (HCFs) and the rise of antimicrobial resistance (AMR) genes. This review aims to highlight key concepts, evidence sources, and knowledge gaps specific to the Ethiopian context. The unsafe disposal of antibiotics through leaks and solid waste has contributed to what some are calling a 'silent pandemic,' raising concerns about emerging infectious diseases. Studies have revealed alarming rates of infectious agents and AMR in healthcare wastewater. Isolates of *C. jejuni, Escherichia coli, Enterococcus faecalis*, and *Enterococcus faecium* from various healthcare waste sites in Ethiopia demonstrate high levels of AMR genes. Additionally, research indicates that HCFs produce significant amounts of waste, with high per-person daily waste production rates. Leachate from landfills containing this waste can negatively affect soil health, biological activity, water quality, agriculture, animal health, and human well-being. To mitigate these risks, effective waste management practices and the promotion of alternative antimicrobial use are essential strategies for reducing the emergence of pandemic diseases in developing countries.

Key words: AMR, environments, healthcare waste, human, livestock

HIGHLIGHTS

- Healthcare waste poses significant risks to public health and the environment.
- Improper disposal of HCW contributes to the spread of antimicrobial resistance.
- Poverty and lack of policy regulations hinder effective HCW management.
- Rapid urbanization and geographical differences are challenges in the fight against waste management and AMR.
- Management of HCW is crucial for protecting public health and the environment.

GRAPHICAL ABSTRACT



1. INTRODUCTION

Healthcare, a rapidly expanding industry due to advancements in medical treatments and increasing chronic disease, generates substantial waste. This growth has led to a pressing need for effective waste management (Kenny & Priyadarshini 2021). HCW encompasses a wide range of materials from pharmaceuticals and medical supplies to laboratory specimens and research byproducts. Broadly, HCW is categorized into general (85%), infectious (10%), and chemical/radioactive (5%) waste, which pose significant environmental and health risks. Within the infectious waste category, sharps, pathological, cytotoxic, chemicals, pharmaceuticals, and radioactive substances represent particularly high-risk items, accounting for 15–25% of total healthcare waste (Padmanabhan & Barik 2019).

Healthcare waste is primarily generated by hospitals, medical centres, laboratories, veterinary clinics, research centres, mortuaries, blood banks, and nursing homes. High-income countries typically produce around 11 kg of hazardous waste per hospital bed per day, while low-income countries generate up to 6 kg (Janik-Karpinska *et al.* 2023). However, in many low-income countries, HCW is not properly segregated into hazardous and non-hazardous categories, which can significantly underestimate the actual amount of hazardous waste produced (Taslimi *et al.* 2020).

The municipal solid waste (MSW) generated by healthcare facilities (HCFs) in Ethiopia contains a significant number of antibiotic-resistant bacteria (ARB), antibiotic-resistant genes (ARGs), and hazardous metal-resistant genes (MGEs) (Teshome *et al.* 2020). The improper disposal of MSW in developing cities like Addis Ababa has severe consequences for the river ecosystems. The lack of appropriate waste management systems (WMS) exacerbates this issue (Anand *et al.* 2021).

Antibiotic-resistant (ABR) genes acquired by pathogens often have an environmental origin, even when antibiotics are used primarily for treating infectious diseases in humans and animals (Wang *et al.* 2022). The distribution of antimicrobial resistance (AMR) and ARGs within the environments are posing significant health risks to the humans and animals (Sanderson *et al.* 2016).

The spread of ARG may be a developing concern considering the expanding microbial resistance to antimicrobials that are being observed worldwide. The advancement and spread of ARG capable of giving AMR has been related to the broad utilization of antimicrobials in animals as well as humans (Pei *et al.* 2006). In agreement with this report, Yazie *et al.* (2019) reported that the percentage of hazardous HCW produced in Ethiopian HCFs is assumed to be at a highly increasing rate (Yazie *et al.* 2019).

In Ethiopia, various authors have highlighted the escalating challenges of AMR, including the role of infectious diseases in AMR development, the high mortality rates associated with AMR cases, and the ongoing debate between pharmacists and physicians regarding antibiotic overuse (Moges *et al.* 2014; Seboxa *et al.* 2015; Ibrahim *et al.* 2018; Gebremeskel *et al.* 2021). Systematic reviews and meta-analyses conducted in Ethiopia have identified *Campylobacter jejunum*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Staphylococcus aureus* as the most prevalent bacterial pathogens in humans, environments, food products, and animals, exhibiting resistance to cephalothin, cephalosporins, fluoroquinolones, and sulfamethoxazole-trimethoprim (Seboxa *et al.* 2015; Ibrahim *et al.* 2018; Gemeda *et al.* 2021; Fujita *et al.* 2022).

Several studies have demonstrated the detrimental effects of water pollution-related HCW on livestock, humans, and the environment in and around Addis Ababa (Mekuria *et al.* 2021; Erkossa *et al.* 2022; Hiruy *et al.* 2022). Despite the known risks, various surveys have revealed that rivers and streams in these areas are still used for small-scale irrigation, bathing, and consumption by both humans and livestock (WHO 2006). Additionally, agricultural water and soils contaminated by incinerator waste pose significant health risks to both farmers and consumers, as pathogens can be transferred from water to crops (WHO 2006).

Consequently, several water-related health problems, including diarrhoea, dysentery, amoebiasis, ascariasis, and others, are prevalent in the region (WHO 2022). Studies (Amenu *et al.* 2013; Chala *et al.* 2021) demonstrate the detrimental effects of water pollution on humans, livestock, and the environment in and around Addis Ababa. Despite the pollution, contaminated rivers and streams in the region are still used for irrigating crops, particularly vegetables, and as a source of drinking water.

The objectives of this critical literature review are to assess the current state of healthcare waste management (HCWM), investigate the relationship between HCWM and AMR, identify the challenges and limitations of existing HCWM practices, and recommend strategies for improving HCWM in Ethiopia.

2. HEALTHCARE WASTE GENERATION STATUS IN ETHIOPIA

The amount of waste, particularly hazardous waste, generated by developed countries differs from that of low-income countries (WHO 2021). Hazardous waste, generated throughout the healthcare delivery process contains harmful chemicals that pose significant risks. Improperly managed HCWs can facilitate the transmission of over 30 hazardous blood-borne infections (Yazie *et al.* 2019). A meta-analysis of 17 publications conducted in Ethiopia revealed an alarmingly high proportion of hazardous waste generated in HCFs, which is up to 70% of the cases (Yazie *et al.* 2019). Additionally, heavy metals, another persistent toxic substance, are discharged from hospitals into the river system as wastewater, leading to various environmental and health problems (Akpor 2014).

HCFs in developing countries often discharge waste directly into water bodies. The Akaki River catchment area in Addis Ababa, Ethiopia, has become a particular concern due to its role as an urban effluent carrier and its contamination (Mekonnen & Hoekstra 2018). Assegide *et al.* (2022) discovered that trace metals in river samples from this area significantly contribute to surface water pollution (Assegide *et al.* 2022). Additionally, Gizachew *et al.* (2020) identified high levels of *E. coli* bacteria in the data, indicating faecal contamination in drinking water discharged from HCFs. These biological pollutants (Gizachew *et al.* 2020) can include microorganisms that cause infectious diseases like hepatitis A or E, dysentery, typhoid fever, cholera, and *E. coli* (Yohannes & Elias 2017).

Healthcare waste generated during healthcare activities poses a significantly higher risk of infection and injuries compared to municipal waste. In developing countries, HCW has often been overlooked and disposed of indiscriminately alongside municipal waste. The study revealed a substantial increase in hazardous HCW compared to the WHO standard of 85% non-hazardous waste, 10% hazardous waste, and 5% toxic waste (Hayleeyesus & Cherinete 2016; Tadesse 2024). Public hospitals generated a significantly higher proportion of total healthcare waste (59.22%) compared to private hospitals (40.48%) (Debere *et al.* 2013). The generated general or non-infectious and hazardous or infectious wastes in Ethiopia are shown in Table 1.

2.1. Types of healthcare waste and its challenges in management

Between 75 and 80% of the waste produced by healthcare establishments is general waste, like domestic waste. This waste primarily originates from administrative, housekeeping, and maintenance activities within HCFs (WHO 2014). In Ethiopia, there was a lack of segregation of HCW by type at the point of generation and a failure to disinfect infectious waste before disposal. Additionally, negligence, attitudinal problems, and low levels of awareness regarding safe HCWM practices were prevalent (Yazie *et al.* 2019). The United Nations Basel Convention classifies healthcare waste as the second most dangerous

Table 1 | Waste generated at various healthcare facilities of Ethiopia

Authors	General wastes (kg/day)	Hazardous wastes (kg/day)	Annual healthcare waste generation (kg/year)
Tadesse (2024)	37.26% (3.96 + 2.20	62.74% (6.68 + 4.29)	3,807.53
Tadesse & Kumie (2014)	38% (3.64 ± 1.45)	62% (5.97 ± 2.31)	–
Yazie *et al.* (2019)	–	21–70%	–
Hayleeyesus & Cherinete (2016)	–	34.9% (0.02–0.03) & 75% (1.23)	–
Gebremeskel *et al.* (2021)	52% (630.6)	24.7% (299.5)	48% (581.9)
Tesfahun *et al.* (2014)	0.25–2.77 (1.67)	52.2–63.4%	0.361–0.669%
Debere *et al.* (2013)	58.69%	41.31%	–

type of waste, after nuclear waste. The report of Janik-Karpinska *et al.* (2023) on the different types of infectious and non-infectious wastes generated from HCW is shown in Figure 1.

Solid waste refers to any type of discarded material, including refuse, junk, or waste. It can be categorized based on its source, such as e-waste, MSW, and HCFs waste (Padmanabhan & Barik 2019). Annually, over 2 billion tonnes of MSW are generated, contributing to air, water, and land pollution, which negatively impacts animal and human health. The contamination of air and water with toxic metals is a global environmental issue affecting hundreds of millions of people. Heavy metal contamination of food is also a significant concern for human and animal health. In this context, the concentration of heavy metals in food, air, and water resources is a critical area of evaluation (Ghorani-Azam *et al.* 2016).

3. ENVIRONMENTAL POLLUTION AS A CAUSE OF EMERGING ABR GENES

Antibiotics, when released into the environment, can have complex ecological consequences. The overuse of antibiotics in humans, livestock, and agriculture contributes to the increasing prevalence of ARGs, which further facilitates their spread in the environment. Environmental antibiotics pose a significant threat to both human and animal health. The improper use of antibiotics in healthcare, animal husbandry, and agricultural processing can result in antibiotic-resistant organisms (AROs). Antibiotics used for animals and crops can lead to the development and release of ARGs into the environment, posing a substantial health risk to humans (Koch *et al.* 2021).

Medical facilities, pharmaceutical companies, fisheries, and animal production and reproduction centres are recognized as significant hotspots for the dissemination of ARGs. Additionally, unstructured landfills, on-site sanitation facilities, funeral

Figure 1 | Standard waste composition in health facilities (Janik-Karpinska *et al.* 2023).

homes, and grave sites are often overlooked as sources of hazardous substances. These substances contribute to the spread of infectious diseases among humans and animals. The excessive and indiscriminate use of antibiotics to treat pathogenic microbial diseases, coupled with inadequate treatment of wastes containing non-metabolized drugs and their residues, is leading to increased environmental antibiotic concentrations, resulting in 'antibiotic pollution'. Antibiotic pollution is a growing global concern as it is a primary driver of ABR/AMR, which has severe global consequences and is contributing to a rise in human morbidity as shown in Figure 2 (Barathe *et al.* 2024).

3.1. ABR gene and the environment

ABR is a global health crisis driven by the transmission of germs and genes among humans, animals, and the environment. Despite the barriers that impede the movement of bacteria and genes, diseases often acquire new resistance factors from other species, limiting our ability to prevent and treat bacterial infections (Larsson & Flach 2022). The interconnectedness of humans, animals, and environments further exacerbates the risk of bacterial infections and AMR. Studies on various samples have revealed that municipal wastes are significant sources of ARGs and virulence genes for humans, animals, and the environment, with the environment serving as the primary reservoir (Sonola *et al.* 2022).

Transmission events of already prevalent resistant strains are more numerous, quantitative, and predictable, but the effects are limited. Understanding and managing the resistance dilemma requires quantifying routes and identifying causes and constraints for the environmental development and transmission of AMR (Larsson & Flach 2022). A key driver of the ancient and recent ongoing development of resistance mechanisms is thought to be the never-ending fight for resources among bacteria, including the natural synthesis of secondary metabolites that are identical to many antibiotics used today as medications (Davies & Davies 2010).

Various anthropogenic activities, including antibiotic usage in agriculture and aquaculture, non-human antibiotic applications, and waste disposal, contribute significantly to environmental reservoirs of resistance (Figure 3) and, likely, virulence genes and their harbouring organisms (Moura *et al.* 2010). The most common pathways for ARG transmission involve humans, domestic animals, and the environment. These transmissions can be direct or indirect through the external environment, often via faecal contamination. While individual transmission events have limited implications, the risks can

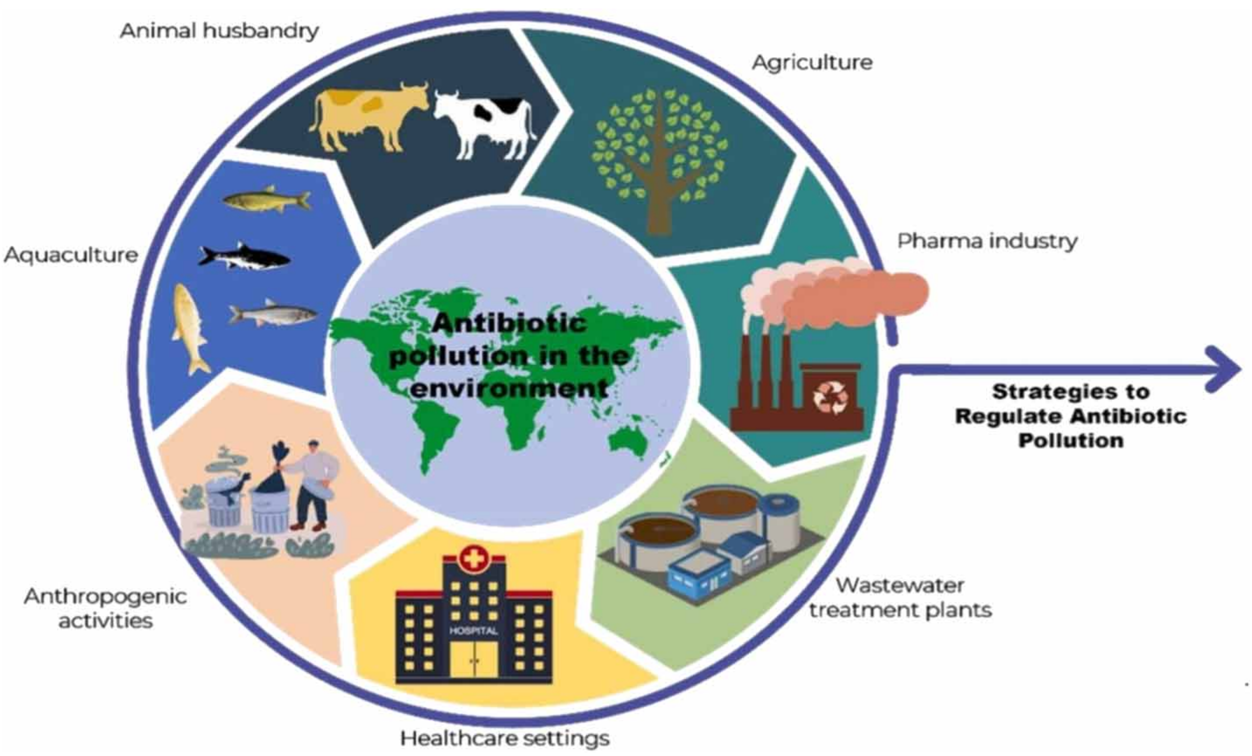


Figure 2 | Antibiotic pollution in the environment (*Source*: Barathe *et al.* 2024).

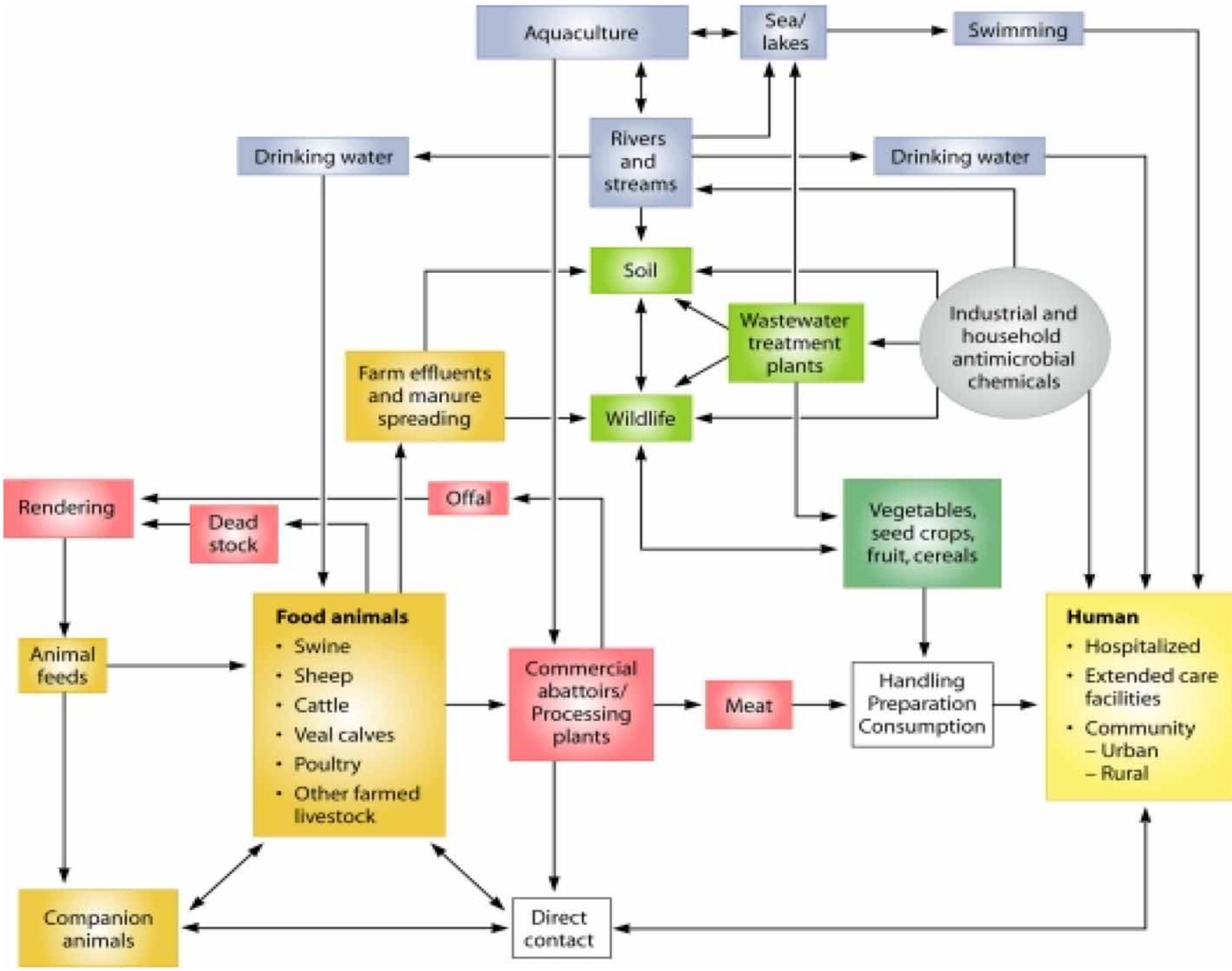


Figure 3 | Antibiotics and antibiotic resistance spread across agriculture, the community, hospitals, wastewater treatment, and other settings (*Source*: Bbosa *et al.* 2014).

generally be quantified. However, rarer and less predictable evolutionary processes occur when novel resistance components are acquired by infections through horizontal gene transfer (HGT) from the diverse ambient microbiota. Such transmission events can take place in the environment or within the human or animal microbiome, where single gene transfer events can have far-reaching and irreversible consequences (Larsson & Flach 2022).

3.2. Wastewater treatment plants as a source of ABR genes

The widespread use of antibiotics has led to the accumulation of ARGs in the environment, with domestic wastewater serving as a significant reservoir for ARGs and resistant bacteria (Shen *et al.* 2023). Wastewater treatment plants (WWTPs) are the primary facilities for collecting and treating municipal household sewage. Biological treatment processes can effectively remove most contaminants from wastewater, including nitrogen, phosphorus, and organic pollutants (Zhou *et al.* 2023). However, the growth and reproduction of microorganisms during biological treatment can create ideal conditions for the dissemination of ARGs, resulting in high concentrations of antibiotics and ARGs within WWTPs (Łuczkiewicz *et al.* 2010; Novo & Manaia 2010). Consequently, municipal WWTPs are key reservoirs and hotspots for the propagation and spread of ARGs (Guo *et al.* 2017).

A study by Łuczkiewicz *et al.* (2010) on faecal coliforms ($n = 153$) and enterococci ($n = 199$) isolates from a municipal WWTP using activated sludge technology revealed the WWTP as a hotspot for AMR gene development. The most prevalent enterococci species were *Enterococcus faecium* (60.8%) and *Enterococcus faecalis* (22.1%), followed by *Enterococcus hirae* (12.1%), *Enterococcus casseliflavus/gallinarum* (4.5%), and *Enterococcus durans* (0.5%), all of which are major human pathogens. Enterococci exhibited high resistance to nitrofurantoin (53%) and erythromycin (44%), with lower resistance to ciprofloxacin (29%) and tetracycline (20%). Among *E. coli* isolates from the WWTP, the most common resistance patterns were to ampicillin (34%), piperacillin (24%), and tetracycline (23%) (Łuczkiewicz *et al.* 2010; Okoye *et al.* 2022).

Antimicrobial drugs are classified as emerging micropollutants of concern due to their potential for serious ecotoxicological consequences, even at low concentrations and long-term exposure. Currently, there is no standardized regulatory framework defining acceptable antibiotic levels in environmental water quality criteria. This lack of regulation has led to the widespread indiscriminate discharge of antimicrobials into urban WWTPs at potentially active concentrations. The release of antibiotics into water bodies, often bypassing the effectiveness of WWTPs, is contributing to the development of AMR and poses potential health risks. The emergence of clinically significant multiple ABR in untreated hospital effluents and WWTPs has been linked to the ongoing exposure of bacteria to antibiotics (Mutuku *et al.* 2022).

ABR can be transmitted and propagated among bacteria through intra- and interspecies horizontal gene transfer (HGT). WWTPs receive wastewater contaminated with a diverse array of contaminants, including antibiotics and chemicals from various sources. These facilities harbour a vast and diverse microbial population, creating ideal conditions for the dissemination and reproduction of AMR. Current WWTPs are not designed to remove micropollutants, ARB, or ARGs, resulting in their persistence in the effluent (Uluseker *et al.* 2021).

WWTPs are also significant producers of ARGs, which can alter the resistomes of microbial communities in various habitats within the receiving river environment. However, the extent to which different ecosystems are affected and whether ARGs, like certain chemical pollutants, can accumulate or become enriched in the river ecology remains unclear (Lee *et al.* 2023). The potential environmental releases and its major sources are listed in Table 2 (UNEP 2022).

3.3. Derivers of ABR genes

In the battle against AMR, it is crucial to address the interconnectedness of all four domains: human health, animal health, agriculture, and ecosystems. However, resistance management is fraught with challenges due to various global sociocultural and economic factors. The spread of resistant bacteria and their resistance genes in soil and surrounding ecosystems has been linked to several pathways, including WWTPs, agricultural waste, and hospital effluent. A number of factors contribute to the exacerbation of AMR, including improper treatment, recycled wastewater, and the overuse of antibiotics without proper regulation (Irfan *et al.* 2022a, 2022b).

ARGs and AMRs have been frequently detected in a variety of sources, including humans, animals, food, plants, soils, and water. While the primary selective pressure driving the emergence of resistance is difficult to isolate, it is widely acknowledged that the misuse of antibiotics in the veterinary, medical, and agricultural sectors is a key contributing factor (Holmes *et al.* 2016). Significant dietary changes associated with increased population density may be another major contributor to resistance. Additionally, global sanitation and water pollution issues stemming from hospital and pharmaceutical waste, sewage, and manure runoff exacerbate the problem (Irfan *et al.* 2022a, 2022b).

3.3.1. Excessive use of antibiotics

The alarming rate of AMR emergence has been accelerated by the overuse and misuse of currently available antimicrobials (Figure 4). Healthcare professionals treating newborns, children, and individuals with specific diseases or syndromes in both human and animal populations are more likely to prescribe antibiotics inappropriately. Previous studies have revealed excessive antibiotic use in primary care settings, with up to 55% of patients in South Africa (Gasson *et al.* 2018), 88% in Pakistan (Sarwar *et al.* 2018), 61% in China (Wang *et al.* 2023), and 15.4% in Canada (Schwartz *et al.* 2020) receiving unnecessary antibiotic prescriptions. Furthermore, in Louisiana, USA, up to 60% of antibiotic prescriptions given to patients with acute respiratory tract infections in primary care settings were clinically inappropriate (Milani *et al.* 2019).

ABR is a worldwide issue that affects not only humans but also domestic and wild animals and ecosystems. Clinical, biological, social, political, economic, and environmental factors are its main sources of resistance development. All of these factors contribute to the environmental presence of AMR bacteria (Figure 4) (Irfan *et al.* 2022a, 2022b). The pathways for the AMR in different social and ecological measures were also justified by different authors. Global consumption of veterinary antibiotics in 2017 amounted to about 85,330 tons (OIE 2022). By 2030, the use of antibiotics in animal production for food will rise by 11.5% (Rasheed *et al.* 2014). Out of 160 countries studied for antimicrobial use, 26 still used antibiotics as growth promoters in agricultural settings in 2019 (OIE 2022).

Table 2 | The major pollution sources affecting AMR in the environment to waste effluent

Major sources	Type and nature of potential environmental releases
Poor sanitation, swage, and waste effluent	• Preventable use of antimicrobials due to disease burden caused by poor water, sanitation, and hygiene (WASH) conditions • Lack of sanitation or poorly functioning sanitation or fragmented systems (e.g. open defaecation, poorly contained pit latrines, septic tanks, and sewers) that contaminate water sources and spread AMR • Effluent from septic tanks and WWTPs • Fecal sludge and wastewater biosolids • Releases from unused drugs disposed of in toilets, bins, or waste dumps • Leaching from open waste dumps, urban runoff
Effluent and waste from pharmaceutical manufacturing	• High concentration of antimicrobials in untreated effluent • Residual antimicrobials in solid wastes discharge from pharmaceutical fermentation manufacturing • Resistant microbes in effluent if biological treatment is applied
Effluent and waste from healthcare facilities	• Antimicrobial products and residues in hospital solid wastes • Resistance microbes (including those with more abundant and diverse ARGs) and antimicrobial residues (particularly antimicrobial compounds of last resort) in hospital wastewater (effluent)
Use of antimicrobials and manure in crop production	• Fungicides, herbicides, heavy metals, and antibiotics used in the production of food, feed, and raw materials • Untreated manure and wastewater that may contain pharmaceutical residues, ARGs, and resistance microbes intentionally applied to soil and crops • Inappropriate disposal of unused antimicrobials (i.e. fungicides)
Releases, effluent, and waste in the animal production	• Manure and effluent from aquatic and terrestrial animal production, that may contain pharmaceutical residues, ARGs, and resistance microbes • Application of antibiotics and parasiticides in aquaculture that go directly to the water environment

Source: Environmental dimensions of AMR. Summary for policymakers (UNEP 2022).

3.3.2. Biocides

Biocides are antimicrobial agents commonly used in various settings and industries, including HCFs, beauty brands, home furnishing additives, agricultural applications like wheel and foot rinses, and industrial processes like the prevention of fouling and souring in piping systems and oil wells (e.g. hydraulic fracturing) (Kahrilas *et al.* 2015). Common biocides include ecdylene, formaldehyde, chlorhexidine, triclosan, and quaternary ammonium compounds (QACs). Other examples include stearalkonium chloride, isothiazolium-benzalkonium chloride, cetrimonium chloride/bromide, and cetylpyridinium chloride (Buffet-Bataillon *et al.* 2012).

Unlike antibiotics, biocides typically target multiple sites (Poole 2002). A biocide's effectiveness is often concentration-dependent, with minimal effects at low concentrations (Hugo & Longworth 2011). Resistance to biocides can arise if the antibiotic acts on a single target site and the cell's adaptive mechanisms prevent it from reaching that target. The mode of action of biocides is still not fully understood, especially at low or sub-inhibitory doses. The general mode of action of a biocide can be characterized based on the bacterial structure it best targets. Biocides can interact with bacterial cells at one, two, or all three levels of the cell membrane, cytoplasmic membrane, and other cytoplasmic components to exert their antimicrobial effect (McDonnell & Russell 1999).

3.4. The ecological risks to the occurrence of emerging ABR genes

There are many different types of environmental systems that contain ARB, ARGs, and the associated mobile genetic elements (MGEs). These systems include soils, non-marine aquatic systems, plants, wildlife, and airborne bioaerosols. ABR in environmental systems is widely acknowledged to present serious risks to human health and ecology (Gwenzi *et al.* 2022). The study conducted on the ecological risk assessment of antibiotics in the soil environment in typical chicken farms in Hangzhou, China, showed that the total concentration of fluoroquinolones was much higher than those of sulphonamides and tetracycline in chicken manure than in soil samples (Zha *et al.* 2023).

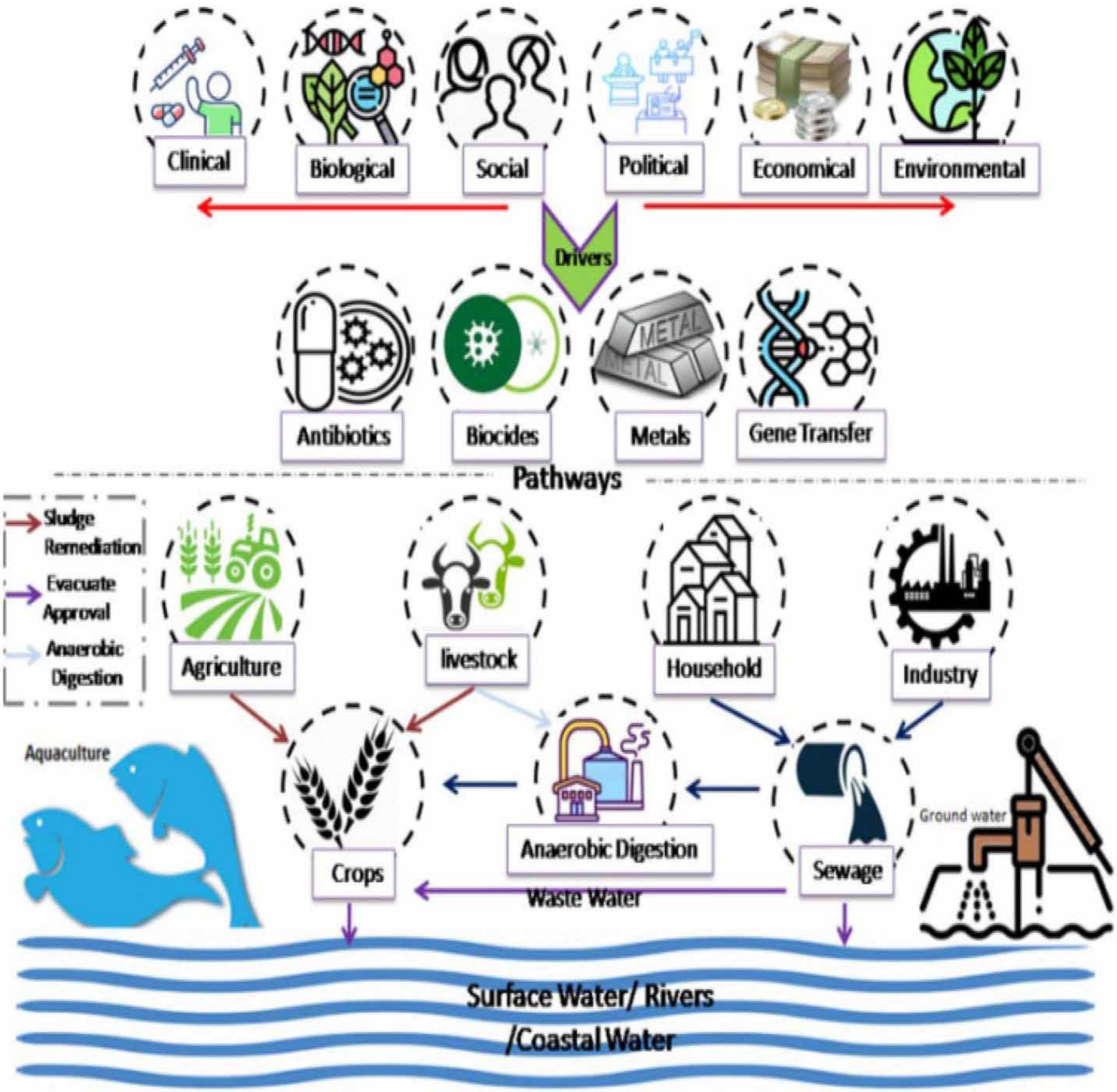


Figure 4 | Different drivers and passways for AMR development (*Source:* Irfan *et al.* 2022a, 2022b).

As a result of so many antimicrobials used in medicine and animal husbandry, they are constantly released into the environment. This damages the ecosystem and encourages the development and spread of ABR. The high number of ARG and bacteria raises the possibility that pathogenic bacteria in the ecosystem will develop resistance and expands the window of opportunity for human contact with AMR pathogens (Wang *et al.* 2023). A framework for comprehending the threats of AMR to ecological and environmental health at different levels or hierarchies of biological organization is put forth, which is known as the ecosystem cascade or hierarchical concept. Overall, the current viewpoint demands immediate investigation to produce empirical data regarding the threats that AMR poses to ecological and environmental health in environmental systems (Gwenzi *et al.* 2022).

The 'Environmental component,' 'Evolutionary component,' and 'Human compartment' are interconnected, with the ultimate fate of the entire system determined by the impact on the human compartment (Vassallo *et al.* 2021). As outlined in Ben *et al.* (2019), applying these concepts to risk assessment involves two primary objectives: measuring exposure to AMR and estimating the number of infectious diseases caused by specific AMR isolates from a particular environment (Ben *et al.* 2019). To achieve this, an evolutionary fitness test on the same ARBs can help predict potential future trajectories. This information can aid in determining the likelihood of an increase in infectious diseases in the future. Figure 5 proposes a conceptual framework for risk assessments of ABR to human health that incorporates this new component. The 'Evolutionary component' would necessitate a specific section of analysis focused on the evolution of microorganisms in a particular environment. This analysis would evaluate the long-term effects on the persistence and selection of ARBs and ARGs (Ben *et al.* 2019).

4. STATUS OF ABR GENES IN ETHIOPIA

Healthcare waste in Ethiopia poses a significant threat to AMR. Due to limited resources, inadequate infrastructure, and ineffective WMS, multi-drug-resistant (MDR) bacteria proliferate in healthcare settings. In addition, nearly half (49.2%) of the bacteria were identified as extended spectrum beta lactamase (ESBL) producers. However, despite exhibiting complete resistance to beta-lactam antibiotics, 11.8% of them did not test positive for ESBL production. The characterization of *E. coli* revealed that 30.6 and 5.6% of them carried *bla*CTX-M group 1 type-15 and *bla*NDM genes, respectively (Gashaw *et al.* 2024).

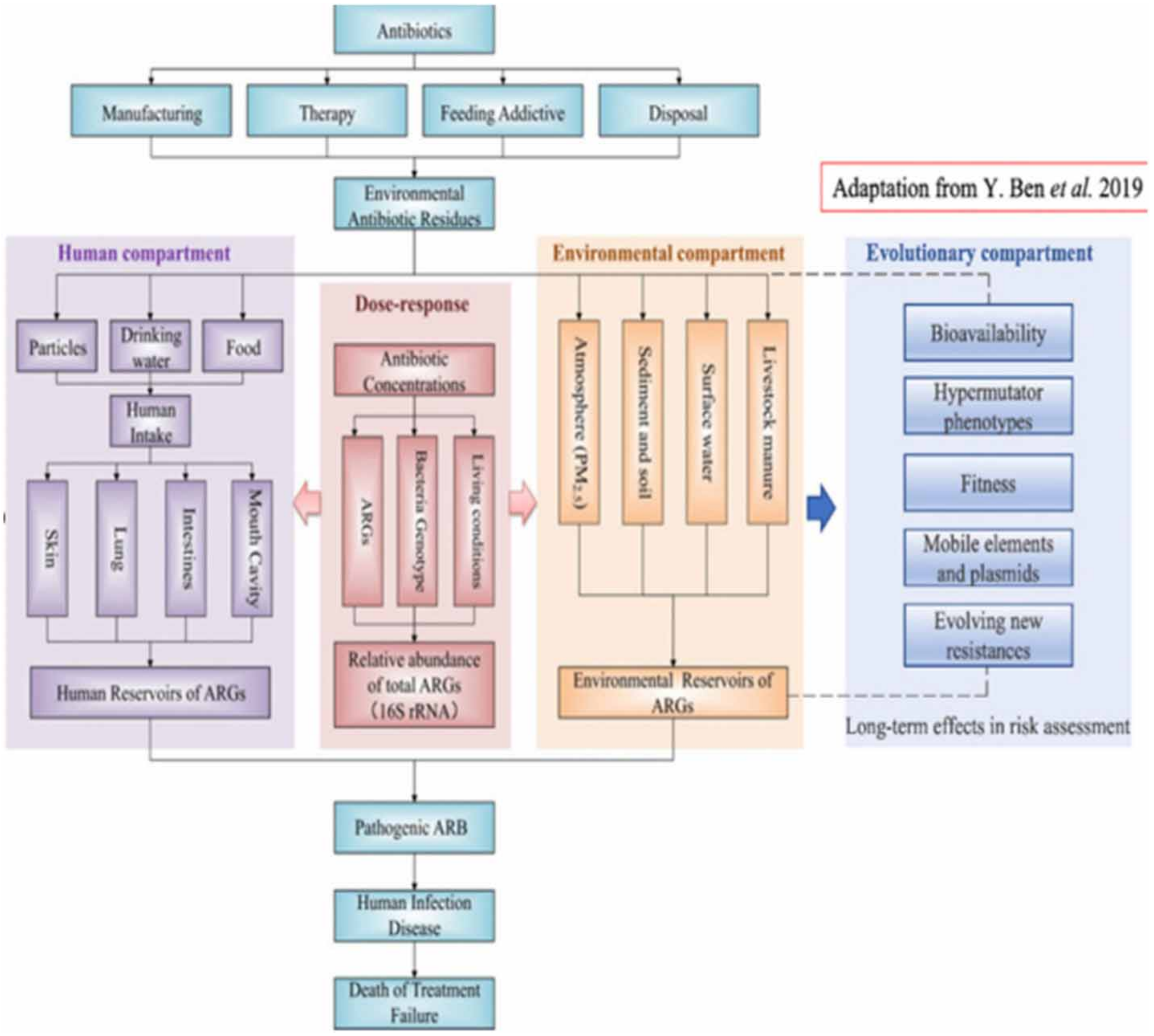


Figure 5 | Conceptual frame work for risk assessment of ARG (*Source:* Vassallo *et al.* 2021).

Hospital waste, particularly wastewater, contains high levels of ARB like *E. coli*, *Klebsiella pneumoniae*, and *Staphylococcus aureus* (Mekengo *et al.* 2021). The improper disposal of antibiotics and other pharmaceuticals contributes to environmental contamination, fostering the development and spread of AMR. This is a pressing public health concern as infections caused by ARB are challenging to treat, leading to prolonged hospital stays and increased healthcare costs (Ugoeze *et al.* 2024).

Ethiopia's National AMR Action Plan aims to address these challenges by improving waste management practices, enhancing AMR surveillance, and implementing antimicrobial stewardship programmes. However, limitations such as poor laboratory infrastructure, logistical difficulties, and insufficient funding hinder the effective implementation of these interventions.

Addressing these challenges requires a multifaceted approach, including standardizing and reporting AMR diagnoses, increasing financial investment, and improving education and training for healthcare workers. In addition, integrated one-health approaches should be prioritized to have deep knowledge of the sources of organisms. By addressing these issues, Ethiopia can effectively combat AMR and improve public health outcomes (Alhassan & Abdallah 2024).

Global research at Washington University analysed 471 million individual records or isolates from 7,585 study–location–years to create the most comprehensive set of AMR estimates to date. While a subset of relevant data for this, the status in the Ethiopian case is presented in Table 3. Improving data reliability is crucial for future analyses. By implementing new strategies for data preparation, utilizing more accessible data, and incorporating additional systematic literature reviews, we can enhance the overall analysis.

ABR burden in 2019 in Ethiopia reported that there were 21,200 deaths attributable to AMR and 85,300 deaths associated with ARGs. Ethiopia has the 35th highest age-standardized mortality rate per 100,000 population associated with AMR across 204 countries (Figure 6) and first compared to secondary infections like maternal and neonatal disorders, cardiovascular diseases, respiratory infections and tuberculosis, enteric infections, and neoplasms (Figure 7) (healthdata.org).

5. MITIGATION AND CONTROL STRATEGIES FOR ABR DEVELOPMENT

The literature still lacks information on the ways in which the One-Health approach is related to the interplay between the administration of antibiotics in food-producing animals, susceptibility in the biosphere, potential negative effects on human and livestock welfare, and many related environmental complications. Owing to the complexity of the issue and the dearth of pertinent information on the pathways and mechanisms connected to the genomic, biochemical, and community levels, assessing the risks that antimicrobial therapy poses to human health and animal welfare in the community from antimicrobial administration in veterinary medicine appears to be difficult. Regarding the impact that reception habitat has on the destiny of AMR, MDR, and ARGs, there is significantly less information available (Irfan *et al.* 2022a, 2022b).

ABR is becoming a more widespread problem worldwide and is linked to higher rates of morbidity and death in both clinical and community settings. The emergence of superbugs and the spread of AMR to various environmental niches have made effective control measures even more challenging (Swami 2014). The worldwide threat posed by AMR necessitates cooperative action to create efficient AMR combat strategies. Fourteen actions are suggested by the center of disease control (CDC) to stop AMR in a medical setting (CDC 2013) (Figure 8). At several levels, a cooperative approach is necessary. Various strategies can be used to address AMR at the global, governmental, local, hospital, individual, and patient levels.

ABR ought to be a fundamental part of professional education for pharmacists, medical professionals, and agricultural sectors. Apart from providing professional training, public education initiatives ought to aim at raising awareness. Research has demonstrated that interactions between physicians and pharmaceutical companies can influence physician prescriptions and

Table 3 | Data inputs for Ethiopia by source type

Source type	Sample size	Sample size unit
Mortality surveillance (minimally invasive tissue sampling [MITS])	189	Deaths
Literature studies	6,222	Cases/isolates/susceptibility tests
Microbial or laboratory data with/without outcome	52,021	Isolates

Source: healthdata.org.

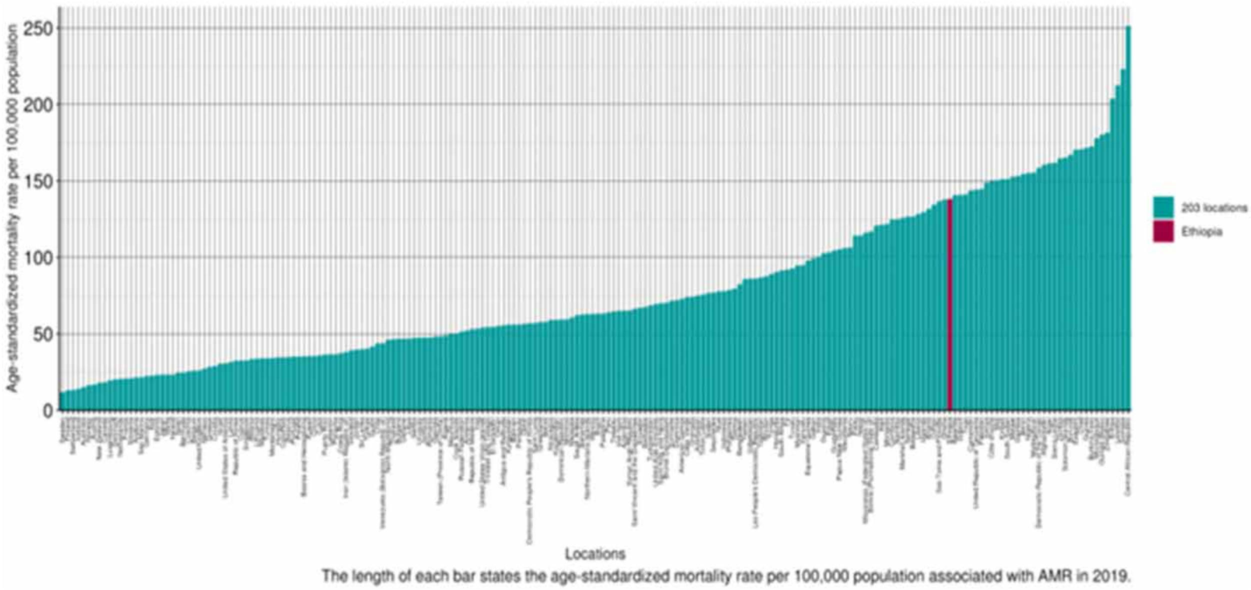


Figure 6 | Age-standardized mortality rate associated with AMR in 2019 for 204 locations (*Source*: Healthdata.org).

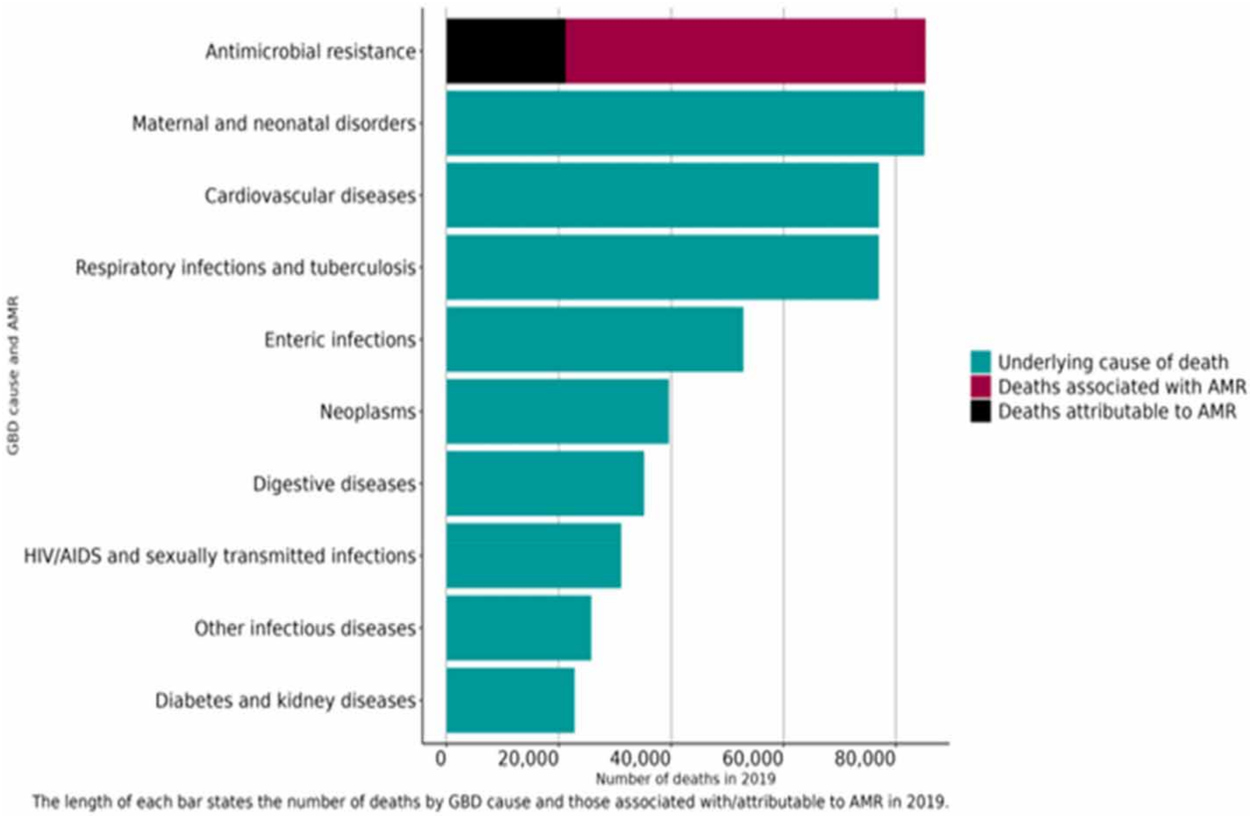


Figure 7 | Placing AMR in context with other causes of death in 2019, Ethiopia (*Source:* Healthdata.org).

that pharmaceutical company promotions can influence patients' requests for prescription drugs (Ahmed *et al.* 2015). Antimicrobial stewardship has helped optimize the benefits of existing antimicrobials and reduced the development of resistance in recent years, leading to improved therapeutic outcomes (Kakkar *et al.* 2020).

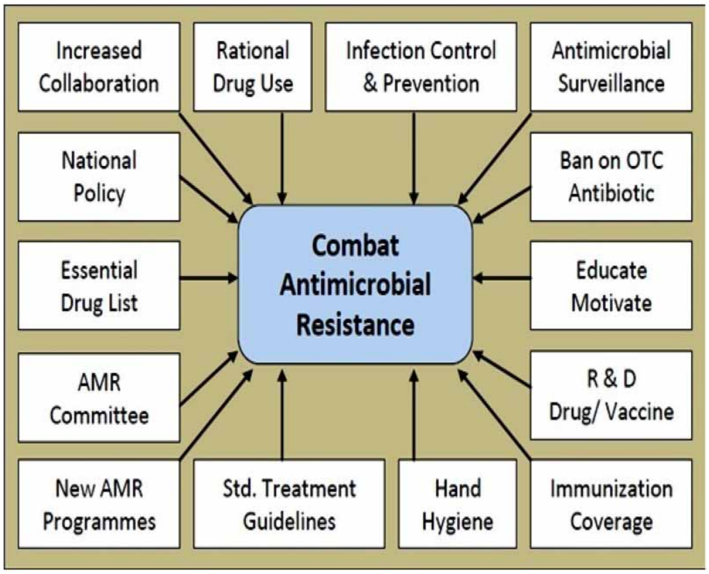


Figure 8 | Approaches for combating AMR (*Source*: Swami 2014). Std, standard; R & D, research and development; OTC, over the counter.

Nonetheless, the last 30 years have seen a decline in antimicrobial development, necessitating the adoption of novel tactics to combat AMR. Prospects for reducing resistance include the combined or singular application of efflux activity inhibition, quorum quenching, biofilm disruption, antimicrobial peptides, nano-antibiotics, lytic bacteriophage particles, clustered regularly interspaced short palindromic repeats (CRISPR)-Cas9 technology, and mutant selection window (MSW) closing (Adefisoye & Olaniran 2023). These authors also suggest that CRISPR-Cas9 technology be optimized as a crucial instrument for AMR prevention and control (Adefisoye & Olaniran 2023).

6. CURRENT PRACTICES AND POLICIES FOR HCWM IN ETHIOPIA

HCWM in Ethiopia involves various practices and policies aimed at ensuring the safe and effective disposal of medical waste. Key practices include segregation at source using designated containers, daily collection of infectious waste, and the use of personal protective equipment (PPE). While vaccination against Hepatitis B is prevalent among healthcare workers, access to this preventive measure remains a challenge due to cost and market availability (Tiruneh *et al.* 2024).

To guide HCWM, the Federal Ministry of Health has developed a comprehensive manual outlining procedures for segregation, storage, transportation, and disposal. Training and awareness programs are ongoing to educate healthcare workers on proper waste management practices. Additionally, regulatory frameworks are in place to ensure compliance with waste management standards, although enforcement can be hindered by resource constraints (Health-Care-March-New-Cover (ephi.gov.et)).

In addition, Ethiopia has established policies and practices for the management of medical waste. However, there is still much to be done to ensure their effective implementation across the country. Improving education and awareness, providing infrastructure support, and strengthening enforcement efforts are vital in addressing the challenges of medical waste management in Ethiopia. By prioritizing these efforts, Ethiopia can better protect the health of its citizens and the environment (HICLOVER Incinerator(HICLOVER.COM) (gudaos.net)).

7. STRATEGIES FOR IMPROVING HCWM IN ETHIOPIA

Segregation of wastes at the point of generation, using appropriate collection materials, and pre-treatment of infectious waste before disposal should be implemented. Healthcare workers and waste handlers should receive comprehensive training on these practices (Tadesse & Kumie 2014). To effectively improve HCWM in Ethiopia, several strategies can be implemented (Yazie *et al.* 2019; Gizalew *et al.* 2021; Tiruneh *et al.* 2024):

- Strengthen policy and regulation: develop comprehensive policies outlining responsibilities for HCFs and ensure strict enforcement of existing regulations and guidelines.
- Capacity building and training: provide regular training programmes for healthcare workers on proper waste management techniques and conduct awareness campaigns to educate both healthcare workers and the public.
- Infrastructure and resources: equip HCFs with necessary waste management tools and regularly maintain and upgrade waste management facilities.
- Waste segregation and disposal: implement strict segregation of waste at the point of generation and utilize safe disposal methods such as incineration, autoclaving, and secure landfilling.
- Monitoring and evaluation: conduct regular audits and inspections of HCFs and establish feedback mechanisms for continuous improvement.
- Community involvement: engage local communities in waste management initiatives and encourage partnerships between government, private sector, and non governmental organizations (NGOs).

8. KEY FINDINGS AND INSIGHTS

Healthcare waste, generated during the provision of healthcare services, poses a significant threat to human health, animal well-being, and the environment. This review identified poor waste management and excessive medical waste generation as key contributors to the rise of ABR. In Ethiopia, healthcare waste presents significant risks to public health and the environment. Many of the microbes isolated from healthcare waste have developed ABR, increasing the risk of zoonotic diseases in developing countries, including Ethiopia. Economic factors, such as poor infrastructure, rapid urbanization, a lack of regulations, and improper disposal of medical waste, contribute to these risks. Additionally, WWTPs and waste from animal farms are primary sources of ABR gene development, driven by excessive antibiotic use in healthcare, agriculture, and biocides used in various institutions. Research on HCWM highlights the detrimental impacts of improper disposal, particularly in developing countries like Ethiopia. These impacts extend to wildlife, water quality, plants, and disease transmission. Despite the severity of these issues, a lack of policy action and regulations regarding healthcare waste handling and its economic implications is evident. To address these challenges, collaborative one-health approaches, including mitigation strategies and policy measures, are crucial in developing countries.

In line with concluding remarks from the review, and to address the challenges associated with HCWW and AMR, the following points are proposed.

- A One-Health approach, focusing on mitigation strategies for AMR and toxic substances.
- Implementing effective WMS, promoting responsible antibiotic use, and fostering interdisciplinary collaboration.
- Strengthening regulations and policies,
- Investing in infrastructure and facilities,
- Promoting public awareness,
- Adopting sustainable waste management practices,
- Enhancing regional cooperation
- Conducting further research,
- Developing innovative technologies,
- Investing in training and capacity building, and
- Addressing the economic and social costs associated with AMR and HCWM.

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DATA AVAILABILITY STATEMENT

All relevant data are included in the paper or its Supplementary Information.

CONFLICT OF INTEREST

The authors declare there is no conflict.

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