



## Review article

## Antibiotic resistance in urban soils: Dynamics and mitigation strategies



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## ABSTRACT

Antibiotic resistance (AR) is a critical global health issue with significant clinical and economic implications. AR occurs when microorganisms develop mechanisms to withstand the effects of antibiotics, reducing treatment efficacy and increasing the risk of mortality and healthcare costs. While the connection between antibiotic use in clinical and agricultural settings and the emergence of AR is well-established, the role of urban soils as reservoirs and spreaders of AR is underexplored. This review examines the complex dynamics of AR in urban soils, highlighting the various sources of antibiotics, including domestic wastewater, industrial effluents, urban agricultural practices, but also microplastics and domestic animal excrements. The selective pressure exerted by these anthropogenic sources promotes the proliferation of antibiotic-resistant bacteria, particularly through horizontal gene transfer, which facilitates the transmission of resistance genes among soil microorganisms in urban environments. About that, the presence of antibiotics in urban soils poses a significant threat to public health by potentially transferring resistance genes to human pathogens through multiple pathways, including direct contact, food consumption, and water ingestion. Furthermore, AR in urban soils disrupts microbial community dynamics, impacting soil fertility, plant growth, and overall environmental quality. Therefore, this review aims to address gaps in understanding AR in urban soils, offering insights into its implications for human health and ecosystem integrity. By identifying these gaps and suggesting evidence-based strategies, this review proposes valid and sustainable solutions to mitigate and counteract the spread of AR in urban environments.

## 1. Introduction

Antibiotic resistance (AR) represents an alarming public health priority, both for its important clinical implications (i.e., increased morbidity, lethality, duration of the disease, development of complications, epidemics), and for the resulting economic consequences in the healthcare sector (Salam et al., 2023). Specifically, AR occurs when bacteria or other microorganisms develop the ability to resist the antibiotic effects, making these drugs less effective or even ineffective in treating infections (Serwecińska, 2020). In particular, this phenomenon occurs when bacteria undergo genetic modifications that enable them to survive the antibiotic action, and the use and abuse of antibiotics can accelerate the process of developing bacterial resistance (Bakkeren et al., 2020). AR emerges as a growing threat to human health and

environment, especially in urban soils (Anand et al., 2021). With the introduction of numerous and diverse artifacts over centuries, human activities have significantly altered the nature of urban soils. These soils are now vastly different from non-urban ones (Mónok et al., 2021). Moreover, starting from the Industrial Revolution in the 18th century, various pollutants such as lead from gasoline, nitrogen and sulfur oxides have been released into the environment significantly altering several pedological features of urban soils, such as pH, bulk density, carbon content and metal concentrations. Urban soils are located near buildings, industrial areas, city parks, landfills, peri-urban agricultural areas, etc. (Fig. 1). These soils are often degraded due to the strong surrounding anthropic pressures that modifies soil structure and functions (Li et al., 2018).

While the connection between the use of antibiotics in clinical and

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agricultural settings is widely studied (Mann et al., 2021), the role of urban soils as a reservoir and spreader of AR is a phenomenon that is still largely underestimated. Rapid urbanization and the growing anthropogenic impact on urban areas, have transformed soils into complex ecosystems, in which microorganisms play a crucial role, and where, the constantly increase of anthropogenic pressures introduce a complex contaminant mixture, including antibiotics and pharmaceuticals, favoring the development and spread of AR (Hou et al., 2021). The antibiotics contained in urban soils derive from various anthropogenic sources, such as domestic wastewater and from residential and hospital sewerage, that represent the main mechanisms through which antibiotics enter urban soils (Hassoun-Kheir et al., 2020; Kapley et al., 2023; Zhang et al., 2020). These wastewaters contain residues of drugs, including antibiotics, from medical treatments and veterinary therapies. Additionally, industrial effluents can contribute to soil pollution by antibiotics, as many industries produce and use such compounds in their manufacturing activities (Šimatović and Udiković-Kolić, 2020). Moreover, urban agricultural practices, such as the use of fertilizers containing animal waste treated with antibiotics or the direct application of antibiotics on crops, constitute another relevant source of contamination (Zalewska et al., 2021). Finally, the dispersion of antibiotics through solid waste, such as expired or unused drugs, can contribute to the accumulation of these compounds in urban soils (Lü et al., 2022).

In urban soils, the transmission of resistance genes occurs mainly through horizontal gene exchange processes between bacteria and other soil microorganisms (Lima et al., 2020). These genes can be carried by plasmids, mobile genetic elements that allow the transfer of genetic material between different organisms (Meng et al., 2022). The presence of antibiotics in urban environments creates a selective pressure that favors the proliferation of bacterial strains carrying resistance genes. The persistence of such genes is fueled by the stability of the plasmids and several environmental factors, including the presence of organic substances, soil pH and climatic conditions (Castañeda-Barba et al., 2024). This intricate system of gene transmission and persistence poses a significant threat to public health, as it can lead to the accumulation of resistant bacterial strains. One of the greatest concern is represented by possible transmission of these genes to human pathogens through various ways, including direct contact, consumption of contaminated food products and ingestion of contaminated water (Zainab et al., 2020). This can compromise the effectiveness of antibiotics used in medical practice, making infections more difficult to treat and increasing the risk of AR diseases spreading (Mancuso et al., 2021). Furthermore, AR in urban soils can alter microbial community dynamics, affecting soil food webs and compromising the ability of organic matter to decompose (Ezugworie et al., 2021). This can have negative consequences on soil

fertility, plant growth and the general quality of the urban environment.

This review aims to explore the issue of AR in urban soils, with the aim of outlining the key mechanisms that drive its complex dynamics. Furthermore, we have reported the multiple sources of antibiotics in urban soils, analyzing the role of wastewater, industrial discharges, and urban agricultural practices in shaping a highly selective environment for antibiotic resistance. We will delve deeper into the transmission of resistance genes between soil microorganisms and the persistence of these genes in the urban environment, highlighting the possible threat posed by AR to human health and the whole ecosystem. Through this scientific investigation, we aim to provide a clear and updated overview of the continuously evolving phenomenon, identifying scientific gaps and suggesting the possible ways to address antibiotic resistance in urban soils, since only with an integrated and evidence-based approach we can mitigate the negative impacts of this silent threat and protect the health of our urban communities.

## 2. Antibiotic resistance sources in urban soils

In recent decades urban soils have been exposed to various stressors such as high temperatures, heat waves, floods, and the spread of organic and/or inorganic pollutants. These factors have facilitated the acquisition and dissemination of Antibiotic Resistance Bacteria (ARB), Antibiotic Resistance Genes (ARGs). For example, some researchers have described how heavy metals are involved in the acquisition of AR and its spread into urban soils (Vats et al., 2022), while others have observed that AR is more easily acquired by bacteria near a smelter industry (Yang et al., 2021).

The study of AR spread vectors in urban soils could play a key role to understand these mechanisms, supporting the development of new mitigation measures to counteract these phenomena. In this regard, several studies have described the possible AR spread vectors (Fig. 2) in the urban environment (Abbass et al., 2022), bringing back the main AR sources in wastewater, landfills, livestock manure, and last but not least, in domestic animal excrements and microplastics.

In the case of landfills, discharged wastewater contaminates surface water, which is then used for crop irrigation. This spreads AR on crop edible parts used for human and animal consumption. These irrigation practices are common in countries with limited wastewater remediation capacity, particularly arid regions such as North Africa and Middle East. Animal excrements are also a source of AR. As a result, both ARGs and ARBs can spread in the surrounding environment through airborne transmission and/or leaching into the water table.

Table 1 presents the most relevant antibiotics and ARGs identified in the primary AR sources in China and Italy. The antibiotics found various

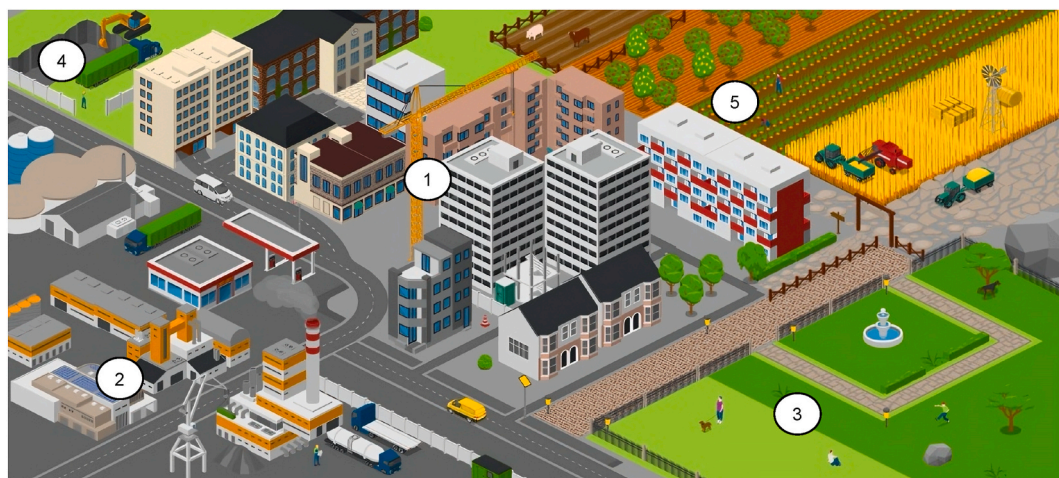


Fig. 1. Representation of an urban area. 1. Buildings; 2. Industrial area; 3. City parks/gardens; 4. Landfill; 5. Peri-urban agricultural area. Created in <https://icograms.com>.



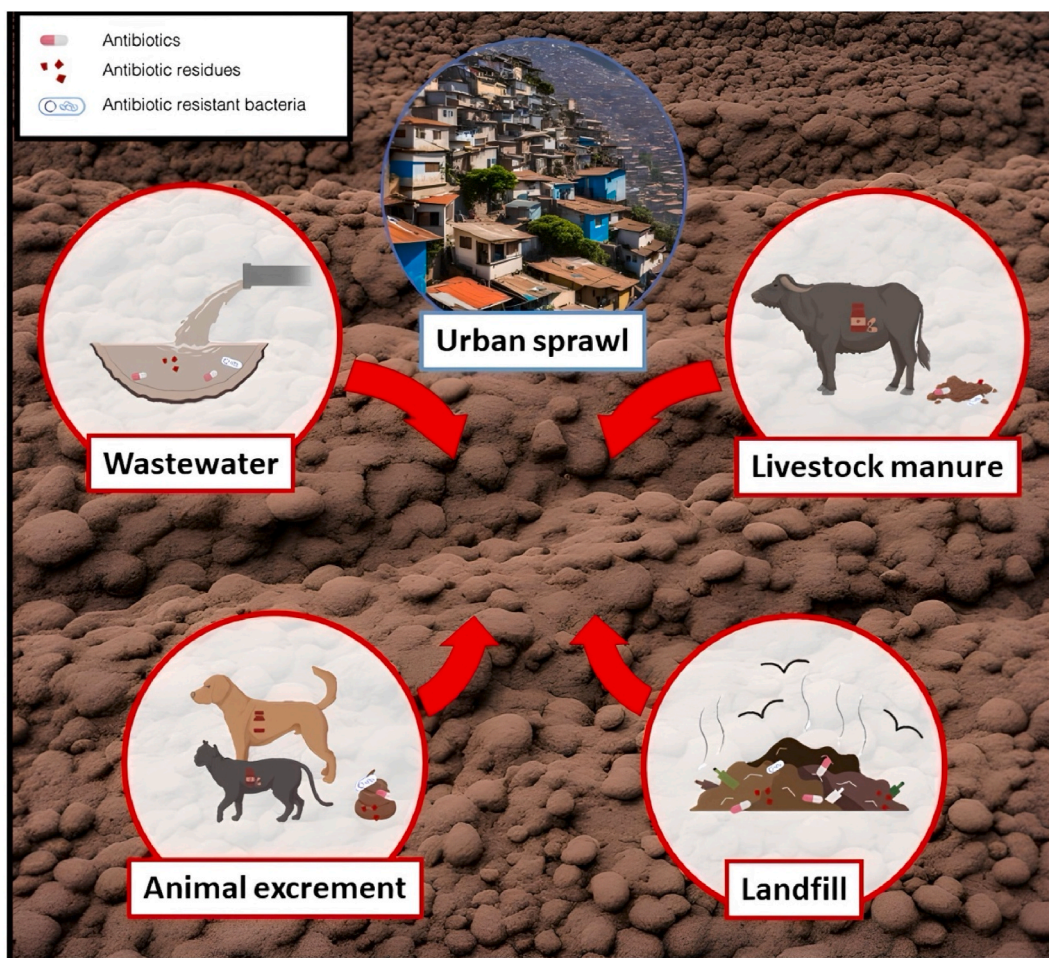


Fig. 2. Antibiotic resistance sources in urban soils.

studies primarily fall into to the classes of sulfonamides, fluoroquinolones, tetracyclines and macrolides. Sulfonamide resistance *sul* and tetracycline resistance *tet* genes were the most commonly observed in almost all AR sources. The absolute abundance values of *sul1* were consistent across different AR sources. In Italy, limited research has been conducted on the presence and quantification of antibiotics in wastewater. However, Sargenti et al., 2020 demonstrated the presence of antibiotics like erythromycin and sulphadiazine in a surface water body collected in central Italy (data not shown in Table 1), with detected concentrations below  $200 \text{ ng}\cdot\text{L}^{-1}$ . Furthermore (Frascaroli et al., 2021), reported high concentrations of antibiotics in municipal wastewater from several developing countries (data not showed in Table 1). For instance, in Durban (South Africa), approximately  $88,000 \text{ ng}\cdot\text{L}^{-1}$  of ciprofloxacin and  $20,500 \text{ ng}\cdot\text{L}^{-1}$  of metronidazole were detected. Similarly, in Machakos (Kenya) up to  $19,000 \text{ ng}\cdot\text{L}^{-1}$  of roxithromycin were present in municipal wastewater. Moreover, in studies conducted in recently established landfills (0–1 year), higher amounts of antibiotics were observed in Italy compared to China, while a lower absolute abundance of ARGs was found (Table 1). This significant difference in antibiotic concentrations in landfill leachates may depend on various factors, such as the use of more advanced systems for waste treatment, which could reduce the amount of antibiotics, or a more effective regulation in the management and drug disposal. Finally, a direct correlation between the ARGs absolute abundance and the antibiotic concentrations does not seem to exist. However, the presence of ARGs is generally correlated with the respective antibiotic groups (Berghlund, 2015). In fact, Table 1 shows a direct correspondence between the ARGs (e.g., *sul*, *tet*, etc.) and the detected antibiotics (e.g., sulfadiazine and

tetracycline).

### 2.1. Wastewater

In developing countries with limited water resources such as India and many African ones, only 28% of urban wastewater produced is treated and purified, whereas most untreated wastewater is directly used for agricultural field irrigation, posing enormous risks to human health due to the increase in antibiotic resistance genes of medical importance (Bougnom et al., 2020; Minhas et al., 2022). In fact, wastewater is an important reservoir and source of ARB and ARGs since includes antibiotic residues that contribute to the selection of both ARB and ARGs (Novo et al., 2013), and these residues derived mainly from their human use and subsequent excretion via urine and feces (Larsson and Flach, 2022). The study conducted in Germany by Voigt et al. (2020) has analyzed the antibiotic concentrations and microbial communities present in the wastewater, highlighting the presence of macrolides, sulfonamides and fluoroquinolones as the most common classes of drugs, and *Escherichia*, *Klebsiella*, *Enterobacter*, *Citrobacter* as the most common AR bacterial genera. Table 2 reports the more relevant antibiotics detected in municipal wastewater in various countries. Kenya and South Africa have shown very high concentrations of sulfamethoxazole and ciprofloxacin, respectively. Additionally, Kenya exhibited elevated levels of other antibiotics such as trimethoprim and amoxicillin. The presence of antibiotics in wastewater may be attributed to several factors, including the uncontrolled use of drugs both in human and veterinary medicine, as well as in agriculture, which lacks specific regulations. Furthermore, in the same countries, as in the case of Kenya

**Table 1**Occurrence of the most relevant antibiotics and ARGs in the main AR sources in urban soils. “–” = data not available; “\*\*\*” = expressed as  $\mu\text{g}\cdot\text{Kg}^{-1}$ .

Country	AR source	Antibiotics	Antibiotic concentrations [ng·L <sup>-1</sup> ]	ARGs	ARGs absolute abundance (copies·L <sup>-1</sup> )	ARGs relative abundance (copies per bacterial cells)	References	
China	Wastewater	Oxytetracycline	254.1	<i>sul1</i>	$1 \times 10^8$	$5 \times 10^{-2}$	Chen et al. (2020)	
		Norfloxacin	592.6	<i>sul3</i>	$1 \times 10^6$	$1 \times 10^{-3}$		
		Ofloxacin	298.8	<i>cmlA</i>	$1 \times 10^7$	$1 \times 10^{-2}$		
		Chloramphenicol	388.2	<i>int1</i>	$1 \times 10^6$	$1 \times 10^{-1}$		
		Clarithromycin	<50.0					
	Landfill (analysis of leachate in the dry season, in a recent area, 0–1 year)	Sulfamethoxazole	1300	<i>sul1</i>	$1 \times 10^{10}$	–	H. Liu et al. (2022a)	
		Sulfadimethoxine	100	<i>sul2</i>	$1 \times 10^{10}$	–		
		Tetracycline	<100	<i>int1</i>	$1 \times 10^{10}$	–		
		Erythromycin	500	<i>tetM</i>	$1 \times 10^{10}$	–		
		Roxithromycin	2000	<i>tetQ</i>	$1 \times 10^{10}$	–		
				<i>ermB</i>	$3 \times 10^{10}$	–		
	Livestock manure	Tetracycline, Chlortetracycline	2600*	<i>sul1</i>	–	$1 \times 10^{-1}$	Guo et al. (2021)	
		Oxytetracycline	400*	<i>sul2</i>	–	$2.8 \times 10^{-1}$		
		Sulfamethyldiazine	2100*	<i>tetM</i>	–	$2.5 \times 10^{-2}$		
		Sulfadiazine	130*	<i>tetO</i>	–	$4 \times 10^{-2}$		
	Animal excrements (dogs)	–	–					Yang et al. (2022)
					<i>sul1</i>	–	$1 \times 10^{-3}$	
					<i>sul2</i>	–	$1 \times 10^{-2}$	
				<i>cmlA</i>	–	$1 \times 10^{-4}$		
				<i>tetM</i>	–	$1 \times 10^{-2}$		
				<i>tetQ</i>	–	$1 \times 10^{-1}$		
Italy	Wastewater	–	–				Bonanno Ferraro et al. (2024)	
					<i>sul1</i>	$4.7 \times 10^8 - 1.2 \times 10^{10}$		$2.3 \times 10^{-3} - 2.0 \times 10^{-1}$
					<i>int1</i>			
					<i>tetA</i>	$4.3 \times 10^8 - 1.5 \times 10^{10}$		$9.8 \times 10^{-4} - 5.8 \times 10^{-2}$
					<i>bla<sub>TEM</sub></i>	$4.4 \times 10^7 - 1.8 \times 10^9$		$3.9 \times 10^{-5} - 1.0 \times 10^{-2}$
						$1.1 \times 10^7 - 2.5 \times 10^8$		$9.5 \times 10^{-7} - 2.4 \times 10^{-3}$
	Landfill (analysis of leachate in a recent area, 0–1 year)	Sulfamethoxazole	95816	<i>sul1</i>	$1 \times 10^8$	–	He et al. (2021)	
		Ciprofloxacin	7516	<i>sul2</i>	$1 \times 10^7$	–		
		Enrofloxacin	9074	<i>int1</i>	–	–		
		Roxithromycin	14862	<i>tetM</i>	$2.4 \times 10^7$	–		
	Livestock manure	Flumequine	–					Laconi et al. (2021)
		Enrofloxacin	–			<i>ermA</i>	$1 \times 10^{-13}$	
		Tylosin	–			<i>ermB</i>	$5 \times 10^{-3}$	
		Marbofloxacin	–			<i>bla<sub>TEM</sub></i>	$2.5 \times 10^{-5}$	
		Ampicillin	–			<i>qnrS</i>	$5 \times 10^{-16}$	
		Ciprofloxacin	–					

**Table 2**Antibiotic prevalence and their concentration (expressed as ng·L<sup>-1</sup>) in wastewater, in different countries. Fayaz et al. (2024).

Antibiotics	Country					
	USA	Iran	Kenya	Singapore	South Africa	Canada
Norfloxacin	60	8	2800	–	143	–
Ciprofloxacin	690	–	3000	3496	88011	2500
Doxycycline	20	–	2700	–	–	45
Sulfamethoxazole	250	–	49300	1172	1172	3100
Trimethoprim	430	–	5600	–	–	810
Amoxicillin	90	6	4600	3746	3746	–
Azithromycin	–	16	–	272	–	–
Erythromycin	–	9	–	143	–	690

inefficient disposal of medications due to the lack of effective waste management services results in them being frequently discarded into sewers or landfills, ultimately entering the wastewater system.

Moreover, in countries with limited water resources, the reuse of wastewater, after the disinfection and purification treatments, could be an efficient solution to counteract the scarcity of water resources. However, also in this case, the reuse of municipal wastewater for the irrigation of public gardens or agricultural fields could also facilitate the spread of ARB and ARGs (Hong et al., 2013), being present either ARGs,

or ARB, albeit in minor quantities compared to untreated wastewater. Currently, the legislation and guidelines do not specify limits for the concentrations of ARGs or ARB occurring in reused water (Hong et al., 2018).

## 2.2. Landfills

Due to population growth and human activities, an additional source and reservoir of ARB and ARGs is certainly to be found in solid municipal waste landfills, to which only few studies have been actually published. In this regard, Wu et al. (2015) evaluated the concentrations of 20 antibiotics and 6 ARGs in two Shanghai transfer stations (Hulin and Xupu) and in a landfill tank in two separate months, detecting higher levels of antibiotics in the leachate of the transfer stations ( $985 \pm 1965$  ng·L<sup>-1</sup>), in particular in Hulin. In addition, macrolides ( $3561 \pm 8377$  ng·L<sup>-1</sup>), quinolones ( $975 \pm 1608$  ng·L<sup>-1</sup>) and sulfonamides ( $402 \pm 704$  ng·L<sup>-1</sup>) were identified as the most common antibiotic classes in the three analyzed sites. Furthermore, He et al. (2021) have focused their work on four different landfill sites in Northern Italy, investigating the concentrations of five classes of antibiotics (Chloramphenicol, Sulfonamide, Quinolones, Tetracyclines and Macrolides), over 34 years, evaluating any correlations with the development of resistance. In this study concentrations of some antibiotics whose use is now banned or limited in Italy, were found that would seem to determine the long-term

development of ARGs, and in the investigated landfills, nine ARGs were found, and their abundance was similar among the four landfills.

### 2.3. Livestock manure

Since the end of the Second World War and the economic boom of the 1960s and 1970s, cities and many industrial activities have expanded into agricultural areas where soils were already rich in ARB. Furthermore, in the last two decades some of these industrial activities have been discontinued, increasing the surface area of degraded and abandoned soils, consequently leading to the spread of AR.

AR diffusion in agricultural soils is related to the use of antibiotics in animal husbandry, typically added to feed or administered through injections, with the goal of reducing diseases and improving productivity. This practice has been, and continues to be, a significant source of AR spread into the environment (Castanon, 2007). Animal manure is widely used to fertilize agricultural soil, due to its high nutrient and organic matter content. However, Van Boeckel et al. (2015) reported that the excessive use of animal husbandry drugs, such as antibiotics, is a growing concern. They estimated that 63,151 tons of antibiotics were consumed in livestock farming in 2010, with a global increase of 67% by 2030. After antibiotics are ingested by animals, they are poorly absorbed in the intestine, and are excreted into the environment without degradation maintaining their active form as metabolites (Lima et al., 2020). As a result, the animal manure becomes a significant reservoir and hotspot for ARB and ARGs. These antibiotics if not efficiently degraded, can reach the environment (e.g. soil or watercourses) thereby inducing resistance in the occurring microbial communities (S. Li et al., 2023a,b). Furthermore, manure can be a source of pathogenic bacteria that can compromise human health. In fact, Pachepsky et al. (2006) detected the main pathogens transmitted by manure and in addition to the uncommon bacteria, *Campylobacter*, several strains of *E. Coli*, *Salmonella* and *Yersinia enterocolitica* were found. Moreover, to highlight the ARB in the manure, Huygens et al. (2021) assessed the presence of antibiotic residues and bacteria (*E. Coli* and *Salmonella* spp.) resistant to them, in 25 samples of beef cow manure and 9 samples of calf slurry for fattening from different farms in Belgium: *Salmonella* was not detected in any of the samples tested. In contrast, *E. coli* was present in 8/9 samples of calf slurry for fattening, with 70% of the isolates resistant to ampicillin, sulfamethoxazole, trimethoprim and tetracycline, and in 22/25 samples of beef cattle manure where less than 20% of the isolates showed resistance to these antibiotics.

Another concern associated with the ARB and ARGs spread is their possible transmission from the waste treatment system in the landfill to the air. In fact, Li et al. (2020) isolate from the air (leeward zone) 41 ARB strains that had a specific nucleotide sequence (*bla*<sub>TEM-1</sub>) also found in strains present in landfill leachate, detecting this direct correlation between solid waste treatment systems and ARGs transmission in the air. In another study, instead, it was detected the ARGs spread both in the air within the farm structures and in the surrounding environment, confirming the dispersion of these genes over significant distances (up to 10 km), highlighting, also, an association of the clinically relevant pathogens with the ARGs, indicating potential risks to human health (Bai et al., 2022).

### 2.4. Domestic animal excrements and microplastics

The spread of ARGs and ARMs, in urban gardens and parks, depends mainly by the animal excrements of dogs and cats. Indeed, Yang et al. (2022) showed that the feces of dogs and cats present a high abundance of ARGs, with a greater presence in the dog feces compared to those of cats, where the bacterial community was characterized mainly by the genera *Firmicutes*, *Desulfobacterota*, and *Proteobacteria*. Furthermore, they also highlighted possible airborne spread in the surrounding area, in addition to direct spread in the soil. Finally, microplastics (sizes between 1 and 1000 µm) can also contribute to the dispersion of pathogens

and ARGs (Wu et al., 2023; Zhou et al., 2024). In fact, microplastics become vectors on which microorganisms, carrying AR, can develop biofilms for adhering on the surfaces and facilitating, in this way, gene exchange and AR spread. Moreover, it was estimated that density of ARB, present on microplastics, was approximately 100–5000 times higher than that of the surrounding environment (Junaid et al., 2022). Moreover, it has been also highlighted that microplastics can incorporate chemicals and additives, further increasing the transmission of ARGs. For instance, it has been discovered that the adsorption of Cu or Zn ions on plastic coating materials can drastically increase the surface enrichment of ARGs (e.g. macrolidene, lincoamine, streptomycin) (Flach et al., 2017).

### 2.5. Key factors affecting urban AR worldwide

The abundance and diffusion of AR in urban areas are also associated with geographical region and socio-economic status. The resistome present in the urban context is strongly correlated to country-specific characteristics and antibiotic usage practices. A meta-analysis conducted by (Wu et al., 2024) on 20 countries, distributed all around the world, reveals that samples collected from New Zealand contained the highest abundance of ARGs, with Nigeria following closely. The large number of ARGs identified in the above mentioned countries is due to presence of booming animal husbandry industries in New Zealand, while poor healthcare and education are the primary sources of AR in the case of Nigeria. On the contrary, Munk et al. (2022) in an other meta-analysis study demonstrate how European and North American countries present a better and more homogeneous situation regarding the ARGs distribution. This situation is ascribed, by the same authors, to high standards of public and private healthcare assistance and data collection and management.

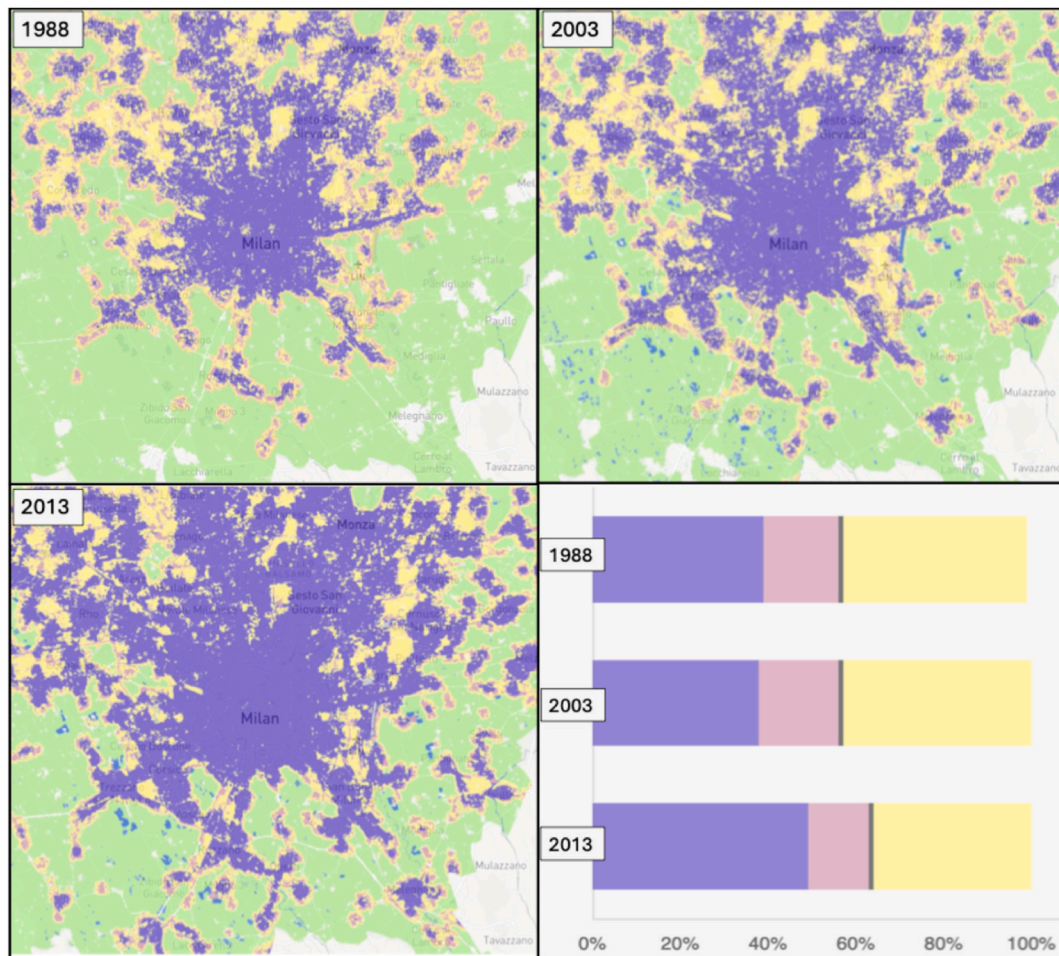
As illustrated above in the case of New Zealand, one of the main causes of the ARGs spread is the animal farming. About that, a case of study (Meng et al., 2023) conducted in the area of the Harbin city (Heilongjiang province, China) showed that the main source of AR, among the five point sources considered (e.g., pharmaceutical industry, residential area, farm, etc.) was the pig farm. In particular, the authors highlighted how the main vectors for AR diffusion are airborne dust and discharged wastewater. In fact, these two matrices carried the highest relative abundances of targeted ARGs ( $5.34 \times 10^{-1}$  number of copies per bacterial biomass, in the dust, and  $3.59 \times 10^{-1}$  in the wastewater).

Furthermore, all AR sources, discussed above, have a different impact on their spread in urban soils. However, the urbanization of agricultural and rural lands is likely one of the main causes of AR diffusion. The expansion of the urban area of Milan, Northern Italy, from 1988 to 2013, is shown in Fig. 3. It is noteworthy, that this city experienced a 10% increase in urbanization in particular in areas that were previously rural or peri-urban, and used for agricultural activities. Similarly, cities like Beijing (China), New York (USA), or Lagos (Nigeria) underwent a significant urbanization increase in the same period (<http://atlasofurbanexpansion.org>). Moreover, the uncontrolled and unplanned urban sprawl is likely one of the most critical issues to address. In fact, it is very common to find shantytowns on the outskirts of cities where wastewater treatment plants and sanitation facilities are lacking, thus creating hotspots for AR diffusion (Nadimpalli et al., 2020).

## 3. ARB and ARGs transmission

Urbanization intensifies the spread of the AR phenomenon in the soil environment (Zhu et al., 2019). In urban contexts human exposure to ARB is greater because of farming, gardening, recreational activities, and pollution. In fact, several studies suggest that dust in crowded public places contains harmful bacteria and genes that make bacteria resistant to antibiotics. Since dust easily meets people, many residents are exposed to dust and the potentially harmful bacteria and genes carried along. These ARB and ARGs could enter the human body through the





**Fig. 3.** Urban expansion of Milan (Italy) since 1988 to 2013. Violet = urban built-up; Yellow = urbanized open space; Pink = peri-urban built up; Green = rural area; Grey = rural built up.

skin, both digestive and respiratory system, posing a threat to human health. Feng et al. (2022) found that different public places show varying amounts of these harmful genes, but they remain stable throughout different seasons, indicating a long-term presence in the dust in various public spaces.

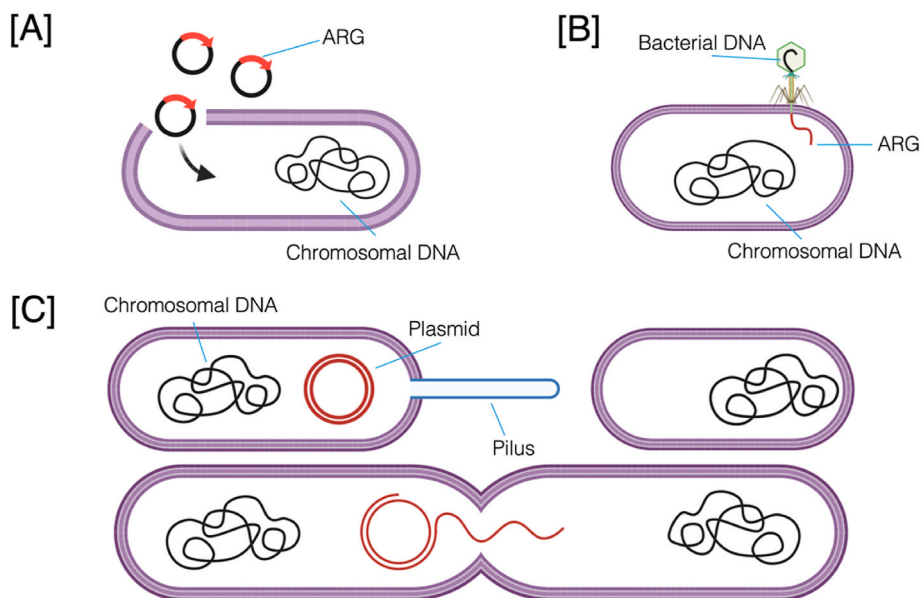
In urban soil, the risk of antibiotic resistance dissemination, increased by manure fertilization and the reuse of treated wastewater containing ARB or ARGs, extends to groundwater and crops. This scenario has far-reaching consequences for the environment, food chain and human health, making infections increasingly challenging to treat. This increasing risk is linked to the presence of Mobile Genetic Elements (MGEs) within bacteria inhabiting these environments (Partridge et al., 2018). MGEs, associated with AR, play a pivotal role in promoting resistance by capturing, accumulating, and disseminating resistance determinants within or between cells. This process involves both intracellular and intercellular mobility (Domingues et al., 2015). Intracellular mobility encompasses the random transmission of MGEs, along with associated genes, to different regions of the same or different DNA molecules, including elements like Transposons and Insertion Sequences (IS). Typically existing in multiple copies in the genome, MGEs contribute to diversity through homologous recombination. Plasmids and Integrative Conjugative Elements (ICEs) are integral to the molecular mechanisms governing the transmission of ARGs among microorganisms (Partridge et al., 2018).

The AR among harmful bacteria poses an escalating threat to public health, with Horizontal Gene Transfer (HGT) identified as a pivotal factor in propagating this phenomenon in the environment (Fletcher,

2015). The HGT facilitates the transfer of ARGs from friendly and environmental bacteria to pathogenic ones through three several mechanisms: *transformation*, *transduction* and *conjugation* (Fig. 4).

*Transformation* (Fig. 4 – A) is a process where bacteria can uptake, integrate, and utilize external DNA fragments, often in the form of plasmids. For this mechanism to occur successfully, there must be available external DNA, the recipient bacteria must be in a receptive state, and the transferred DNA must be stabilized by integrating into the recipient genome or forming a circular structure (Villa et al., 2019). *Transduction* (Fig. 4 – B), on the other hand, involves bacteriophages – viruses that infect bacteria – playing a crucial role in transferring beneficial genes through transduction, thereby assisting in the survival and dissemination of these genes (Modi et al., 2013). Several studies indicate that bacteriophages may play a significant role in the ARGs spread, exemplified by the presence of specific of them in bacteriophages isolated from rivers and urban sewage water (Anand et al., 2021).

*Conjugation* (Fig. 4 – C) involves the transfer of DNA between cells through direct contact, facilitated by specific mechanisms encoded by genes on self-replicating plasmids or integrative elements within the chromosome. This exchange occurs across various environments, including insects, soil, water, and in the context of pathogens within food and healthcare settings (Bethke et al., 2020; Partridge et al., 2018; Villa et al., 2019).



**Fig. 4.** Mechanisms of horizontal gene transfer. (A) *Transformation* - it is the uptake, integration, and functional expression of naked fragments of extracellular DNA. (B) *Transduction* - bacteriophages can transfer bacterial DNA from a previously infected bacterium to closely related bacteria. (C) *Conjugation* - it is a process requiring cell to cell contact via cell surface pili or adhesins, through which DNA is transferred into bacteria from other microbes.

#### 4. The different role of microbial groups in urban soils

Different microbial groups can contribute negatively or positively to the spread of ARGs into the urban soils.

Currently urban soil microbiota is still poorly characterized and very few studies are available in the scientific literature. Some of these studies, conducted in China and the Southwestern USA, showed that the microbial community dynamics were affected by low, moderate and high urbanization gradients (Chen et al., 2021; M. Li et al., 2023b). Soils in highly urbanized areas had a lower abundance of arbuscular mycorrhizal and saprotrophic fungi, but a higher number of human pathogen bacterial taxa. Therefore, it is possible to infer that the bacterial communities of these soils are enriched of AR due to the reasons mentioned above. Moreover, some data available in the scientific literature describe the microbiota of certain urban soils sampled in the metropolitan area of Detroit (USA) and Beijing (China), highlighting the Proteobacteria, Actinobacteria and Bacteroides as predominant phyla (Mafiz et al., 2021; Yan et al., 2016). It is well known that some bacteria belonging to Proteobacteria (e.g. *Pseudomonas* spp.) or Actinobacteria phyla can themselves produce antibiotics (such as tetracycline) or antimicrobial molecules, influencing the competition between different bacterial strains (De Simeis and Serra, 2021; Dimkić et al., 2022). Moreover, some antibiotics can act as selective agents, promoting the survival of antibiotic-resistant bacterial strains or facilitating ARGs transfer. However, Proteobacteria or Actinobacteria are not always involved in the transfer of ARGs, and their impact may be altered based on environmental conditions and interactions with other components of the microbiota. Therefore, further studies and investigations into these mechanisms are essential to gain a better understanding of how these bacteria contribute to the spread AR in soils.

Moreover, several studies have shown that the microbiota structure present in the soil plays a key role in spreading ARGs (Forsberg et al., 2014). Therefore, high microbial biodiversity of the soils counteracts the spread of ARGs, acting as a natural barrier, whereas a loss of biodiversity could exacerbate the spread of AR (Chen et al., 2019). Unfortunately, in most highly urbanized environments, there is a constant loss of biodiversity among the soil microbiota (L. Liu et al., 2022a,b), which favors the spread of ARGs. Therefore, by maintaining and improving microbial biodiversity, it would be possible to counteract the ARGs propagation, thus reducing the risk to both human and environmental health.

#### 5. Human and environmental health implications

AR in urban soils represents an important threat to human health and the surrounding ecosystem. The main threat to human health lies in the growing ineffectiveness of the most commonly used antibiotics (e.g., ampicillin, tetracycline, etc.), which makes infections more severe and difficult to treat, thereby increasing the number of serious infections and hospital admissions.

At the same time, the AR also contributes to the increased prevalence of infections, as ARB and ARGs spread and transfer easily across the environment, through different sources, and from person to person. In fact, in recent years, countless deaths caused by infections with ARB have been recorded (Fig. 5), especially in Asian and sub-Saharan African countries (Fig. 6).

Several pathogenic bacteria are distributed in soils, particularly in urban areas. Several studies have noted their concerning ability to resist antimicrobials (Skandalis et al., 2021).

The high antimicrobial resistance of *Staphylococcus aureus*, a very common gram-positive pathogenic bacterium, responsible for severe skin infections or pneumonia, is well known. In particular, Deyno et al. (2017), in a study conducted in Ethiopia on 117 patients, detected for the isolated *S. aureus* a 97% resistance to cloxacillin/methicillin, 91% to amoxicillin, 74.2% to vancomycin and lower resistance values for other drugs such as gentamycin, cephalothin, kanamycin.

However, there is still little information about the presence and diffusion of *S. aureus* strains in soils, even if Gerken et al. (2022) revealed a higher concentration of this bacterium in urban than in native-forest soils, and as this depended by the land provenience or uses.

By contrast, *Escherichia coli* that is a gram-negative microorganism populating animal guts, occurs also in the environment and typically, it transfers to humans by ingesting either contaminated water or raw food. Generally, it is not harmful to humans but in some cases its pathogenic form could cause severe vomiting and diarrhea.

Ingle et al. tested the resistance of some *E. coli* strains to several drugs. Out of the 16 tested drugs, 14 showed resistance to them, and about half of them were resistant to three antimicrobials at least; furthermore, they showed resistances to ampicillin or tetracycline of 65% and 56%, respectively (Ingle et al., 2018).

In this regard, the Global Antimicrobial Resistance and Use Surveillance System (GLASS) Report 2022 from the World Health

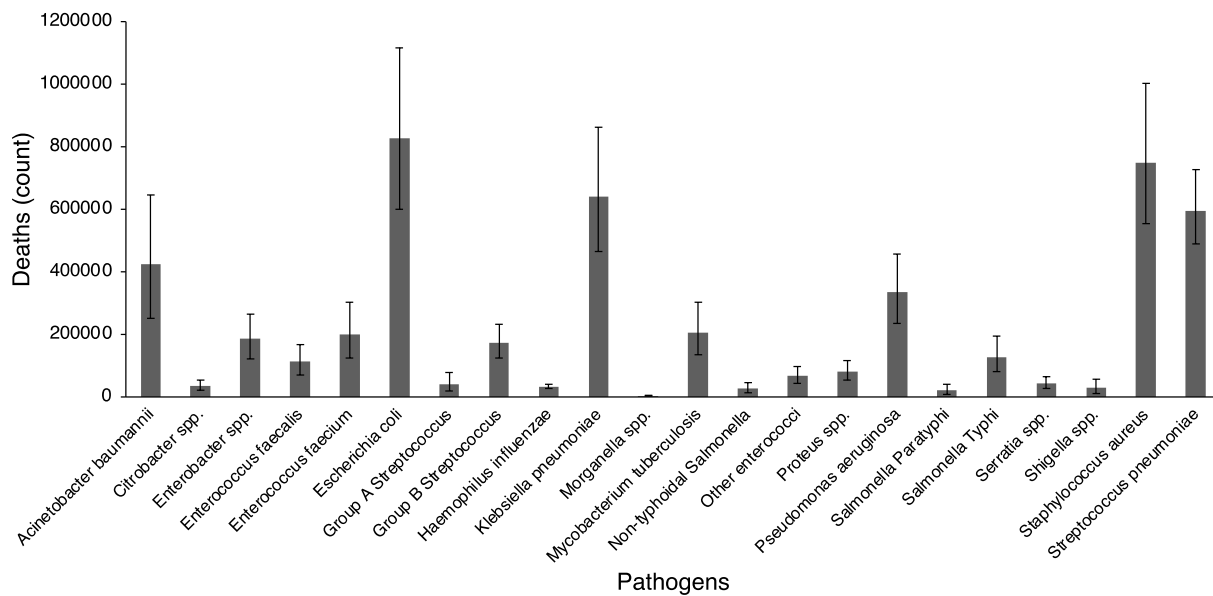


Fig. 5. Global deaths associated to bacterial antimicrobial multiresistance, 2019 (Antimicrobial Resistant Collaborators, 2022).

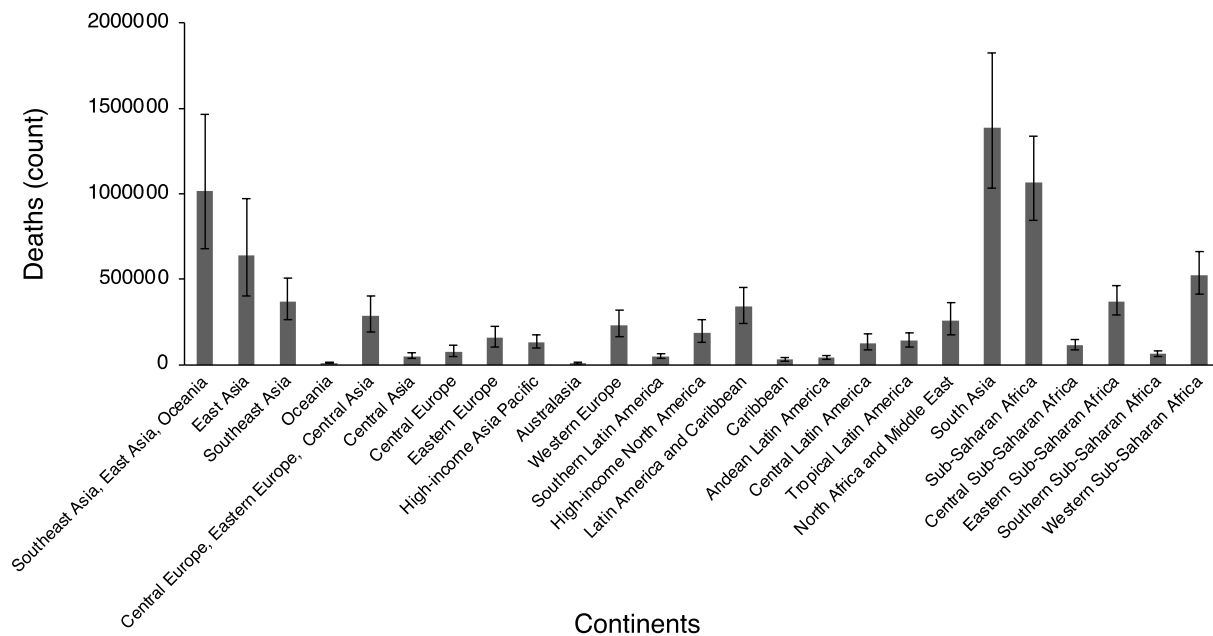


Fig. 6. Global deaths on different continents associated to bacterial antimicrobial multiresistance, 2019 (Antimicrobial Resistant Collaborators, 2022).

Organization, 2022 shows that *E. coli* is the most frequent pathogen resistant to antibiotics. Moreover, other pathogens represent a serious risk to humans and animals such as *Klebsiella pneumoniae*, a bacterial species that can cause pneumonia but also other problematic diseases and infections to both urinary upper respiratory tracts, but also meningitis or bacteremia. Some strains of *K. pneumoniae* are known to be resistant also to carbapenems, one of the last generation antibiotics used to combat this very harmful pathogen. As reported by Church and McKillip (2021) in 2013, approximately 80% of carbapen-resistant *Enterobacteriaceae* infections were caused by *K. pneumoniae*, able to strongly increase the mortality risk in the weakest patients.

Last but not least, AR is certainly more diffused in the poorest countries, where poverty, high population density, limited hygiene and human health services, other than certain agricultural practices, such as the use for crop irrigation of microbial contaminated water contribute to increase this emergence.

However, as a global issue which does not respect borders or barriers, the resolution, or at least its limitation other than management, requires full cooperation among countries and national/international organizations in order to preserve and protect the world community from this serious human and animal problem.

## 6. Mitigation and management strategies

Our review emphasizes the complex nature of antibiotic resistance in urban soils, highlighting the need for a comprehensive approach to address its multifaceted challenges. Acknowledging the interconnectedness between antibiotic use across several civil sectors and the resultant emergence of resistance in urban environments is crucial. Diallo et al. (2020), suggest that regulatory measures are essential, encompassing the oversight of antibiotic use in medical and agricultural sectors, as well as similar to those implemented by countries such as the



European Union, Japan, Switzerland, Canada, etc., enforcement to curb the indiscriminate release of antibiotics into the environment (Schnall et al., 2019).

In particular, European Union's Veterinary Medicinal Products Regulation (EU Regulation, 2019/6) provides frameworks for responsible antibiotic use in livestock farming, aiming to mitigate the development and spread of AR. Additionally, promoting judicious antibiotic prescribing practices in healthcare, such as through antibiotic stewardship programs, are important to minimize unnecessary consumption and subsequent environmental contamination. Furthermore, effective waste management strategies are critical for addressing AR in urban soils. Appropriate disposal of pharmaceuticals and the adoption of advanced wastewater treatment technologies are pivotal steps in mitigating the spread of antibiotic residues in soils and water bodies. Sustainable agricultural practices also play a pivotal role in reducing the reliance on antibiotics in farming while enhancing soil health and biodiversity. The implementation of organic farming methods was discussed by Mondal and Palit (2021), showcasing how agroecological approaches can minimize antibiotic usage and mitigate the environmental impact of agriculture on the spread of either ARB or ARGs. To contrast the pervasive issue of antibiotic and AR contamination in urban soils and restore its quality, innovative remediation techniques such as bio- and phytoremediation are promising avenues.

Phytoremediation is a green technology to remove and/or stabilize specific contaminants from polluted soils, sludges, sediments, groundwaters, surfaces, and wastewater through physical-chemical and biological processes. It is considered a green, cost-effective, simple, aesthetically pleasing and environmentally friendly remediation strategy (Gaur et al., 2014). Phytoremediation includes mechanisms such as phyto-extraction, -degradation, -volatilization, -stabilization, -desalination and rhizofiltration of both organic and inorganic pollutants (Ali et al., 2013). Furthermore, phytoremediation is considered an eco-friendly alternative to traditional physical and chemical remediation methods, which may pose higher risks to ecosystems (Stanley et al., 2013). This method is particularly useful for treating hazardous and toxic sites without requiring excavation or transport of contaminated materials, thereby reducing the risk of spreading pollutants. Moreover, phytoremediation is especially useful for large areas with moderate contamination, and it can replace conventional methods while preserving the biological integrity of the reclaimed soil (Jaishankar et al., 2014; Van Ginneken et al., 2007). In addition to being cost-effective, phytoremediation may provide important ecosystem services such as enhancing soil biodiversity and providing biomass that can eventually be converted into bioenergy (Guidi Nissim et al., 2023). Some hyper-accumulating plants, which absorb high levels of metals, can even serve as potential bioenergy crops, and the metal-rich plant residues may be recycled (Jiang et al., 2015). However, phytoremediation also has some limits. Its effectiveness in managing contaminated soil is limited to a few kinds of plants with specific capabilities: they must be fast-growing, have high biomass and a huge root apparatus, be competitive, hardy, and tolerant to pollutants. In addition, these plants that mediate the soil or water cleanup must be located where the pollutant is present and must be able to act on it. The process itself is slow, often taking years or longer to clean a contaminated site and may also be limited by the bioavailability of the pollutants (Parveen et al., 2022). There is also the risk of wildlife consuming contaminated plants, which can lead to bio-accumulation into the food chain (Manisalidis et al., 2020). Additionally, the biomass generated after phytoextraction may be classified as hazardous waste. Maintaining vegetation in heavily contaminated areas presents significant challenges and could further endanger human health since pollutants may enter, as mentioned above, into the food chain. Contaminated soils often lack essential nutrients, which limits plant growth and slows down the remediation process. Furthermore, the microbial communities in these soils tend to be reduced in both diversity and abundance, and those appropriate microorganisms needed for an effective remediation may be absent (Parveen et al., 2022).

Bioremediation involves the use of microorganisms to metabolize or break down contaminants, absorb, detoxify, and accumulate pollutants from environmental matrices (Yaashikaa et al., 2022). Bioremediation works synergistically with phytoremediation in many cases. Both these technologies capitalize on the natural abilities of microbial and plant biodiverse communities to mitigate the presence of antibiotics, thus gradually decreasing their concentrations from the soil matrices (Kaur Sodhi and Singh, 2022). Bioremediation has been shown to be an effective strategy for mitigating antibiotic contamination in soils. A study conducted by Cycoń et al. (2019) showcased the potential of bacterial communities isolated from soil samples to degrade different classes of antibiotics, such as tetracyclines and  $\beta$ -lactams, thereby reducing the concentration in the contaminated soils. Furthermore, research by Ju et al. (2019) showed the effectiveness of bio-augmentation, which involves introducing specialized microbial consortia to enhance the degradation of antibiotics in contaminated soils, thus highlighting the potential for customized bioremediation solutions.

Phytoremediation, on the other hand, uses the biochemical and physiological processes of plants to clean up contaminated soils. Studies have shown that certain plant species are effective in absorbing antibiotics from soil. A research conducted by Cui et al. (2021) demonstrated the ability of ryegrass (*Lolium multiflorum* Lam) and Indian mustard (*Brassica juncea* L.) to take up antibiotics from soil, thus reducing their concentrations in contaminated environments. Similarly, a study by Bhatt and Gauba (2021) investigated the remediation capability of *Ocimum basilicum* L. on amoxicillin concentrations in soil, highlighting the efficacy of this green technology in reducing antibiotic residues. Overall, bioremediation and phytoremediation represent promising strategies for addressing antibiotics contamination and AR in urban soils, offering environmentally sustainable approaches to restore soil quality and mitigate the risks posed by antibiotic residues. However, the application of phytoremediation plants in urban areas may be limited by the slowness of the remediation process and soil consumption, particularly in densely populated areas.

In particular, some scientific researches have demonstrated the efficacy of bio-phytoremediation processes in reducing AR for the main sources of spread in urban areas (Table 3). According to Gentile et al. (2024), Constructed Wetlands (CWs) with diverse hydraulic configurations have proven successful in rapidly producing high-quality reclaimed wastewater (municipal, industrial or hospital wastewater). This success is attributable to the varied filling media and the use of different plant species, which create a range of habitats conducive to biofilm formation. Additionally, microbiological and molecular analyses have confirmed the presence of ARB and ARGs in the influent, with their significant reduction observed in the effluents, thereby mitigating environmental and health risks.

Moreover, a study conducted by Sousa et al. (2017) showed the effectiveness of ozonation and UV irradiation in reducing the levels of antibiotic-resistant genes in wastewater.

In addition, Spiniello et al. (2023) developed an innovative hybrid phytoremediation system for the removal of pollutants from landfill leachate. The system, known as multiple layer Hybrid Constructed Wetlands (HCW), includes the use of different substrates (such as sand, compost, and carriers) and different plant species (*Phragmites australis* (Cav) Trin. ex Steud., *Arundo donax* L., and *Arundo plinii* Turra). The use of carriers (plastic supports with a specific surface area of  $650 \text{ m}^2 \cdot \text{m}^{-3}$ ) is essential, as they provide an optimal environment for root development and a large colonization surface for microorganisms, significantly improving remediation efficiency. In fact, the authors reported pollutant removal, present in the treated leachates up to 93% in just 10 days. Furthermore, the HCW requires limited space when compared to traditional phytoremediation treatment plants.

However, further research is highly needed to optimize these HCWs for urban contexts, different matrices other than antibiotic classes, as well as to assess their long-term efficacy and potential impacts on soil microbial communities and ecosystem dynamics.

**Table 3**  
Processes for antibiotics and/or ARB/ARGs removal/reduction and their efficiency.

AR source	Antibiotics and/or ARB/ARGs	Removal efficiency	Process	References
Wastewater	<i>tetA, tetB, tetC, tetG, tetL, tetM, tetO, tetQ, tetW, tetX, sul1, sul2, ermB, ermF, ampC, qnrS</i>	97–100%	Activated Sludge (AS)	Yang et al. (2014)
Wastewater	<i>sul1, sul2, sul3, tetG, tetM, tetO, tetX, ermB, ermC, cmlA, floR</i>	63.9–84.0%	Constructed Wetlands (CWs)	Chen et al. (2016)
Wastewater	<i>E. coli, Enterococci, ampC, tetW, ermA, vanA</i>	89–100%	Constructed Wetlands (CWs) combined with UV treatment	Gentile et al. (2024)
Wastewater	Sulfamethoxazole, Tetracycline	99–100%	Constructed Wetlands (CWs) combined with Soil Microbial Fuel Cells (MFCs)	Wen et al. (2020)
Soil	Tetracycline	52–75%	Soil Microbial Fuel Cells (MFCs)	Zhao et al. (2019)
Soil	Antibiotics	4.5–100%	Phytoremediation with <i>Lolium multiflorum</i> L. and <i>Brassica juncea</i> L.	Cui et al. (2021)
Soil	ARGs	11.4–23.2%	Phytoremediation with <i>Lolium multiflorum</i> L. and <i>Brassica juncea</i> L.	Cui et al. (2021)
Soil	Amoxicillin	7.3–29.2%	Phytoremediation with <i>Ocimum basilicum</i>	Bhatt and Gauba (2021)
Soil	ARGs	47–48.1%	Pyroigneous acid for reduction of ARGs and HGT in soil; Electrokinetic treatment of soil for reduction of ARGs	Zheng et al. (2020)
Landfill (solid waste)	<i>sul2, tetM, tetQ, ermB, ermF</i>	25.3–78.6%	Composting process	Tang et al. (2020)
Landfill (solid waste)	Macrolides	67.5–97.6%	Composting process	Tang et al. (2020)
Landfill (leachate)	Penicillin, Chlortetracycline, Sulfamethoxazole,	90.1–97.2%	Anoxic/Oxic membrane bioreactor	Wen et al. (2018)
Landfill (leachate)	<i>sul2, aadA1, sul1, strB, int1</i>	54.3–77.6%	Chlorination	Shi et al. (2022)
	<i>sul2, aadA1, sul1, strB, int1</i>	99%	Fenton oxidation	

Education and awareness campaigns play a pivotal role in driving behavioral changes. These initiatives are powerful tools to engage professionals and the public, fostering a deeper understanding of the complexities surrounding antibiotic use and resistance (Huttner et al., 2010). By disseminating accurate information and evidence-based guidelines, education campaigns empower healthcare providers to adopt judicious antibiotic prescribing practices (Costelloe et al., 2010), minimizing unnecessary antibiotic use and curbing the selective pressure driving resistance development. Simultaneously, these campaigns target the broader community, raising awareness about the far-reaching consequences of antibiotic misuse and the urgent need for collective action. Through various mediums such as public service announcements, workshops, and educational materials, these initiatives emphasize the importance of responsible antibiotic use in safeguarding both individual and public health.

However, addressing AR in urban soils requires collaborative efforts across multiple stakeholders, including policymakers, researchers, healthcare professionals, and the community. By fostering partnerships and knowledge-sharing platforms, stakeholders can leverage their collective expertise to develop and implement effective strategies tailored to local contexts. Ultimately, by adopting a comprehensive approach that integrates regulatory measures, sustainable practices, remediation techniques, and educational initiatives, we can effectively manage AR in urban soils, safeguarding public health and environmental integrity for present and future human generations.

## 7. Conclusions

In conclusion, the presence and persistence of AR in urban soils pose significant concerns due to potential implications for both human and animal health as well as the environment. This review aims to highlight the complex interplay of several and different factors contributing to the presence and spread of AR in urban and peri-urban soils, including anthropogenic activities such as agriculture, wastewater discharge, and improper pharmaceutical disposal. The accumulation of ARB and ARGs in urban soils underscores the urgent need for enhanced surveillance, management, and mitigation strategies.

Moving forward, integrated approaches that combine environmental

monitoring, microbial ecology, and molecular biology techniques will be crucial in better understanding the dynamics of AR in urban soil ecosystems. Furthermore, there is a pressing need for policy interventions and public/medical awareness campaigns to promote responsible antibiotic use and waste management practices. By addressing these challenges collaboratively, we can work towards safeguarding urban soils and mitigating the risks associated with AR for both current and future generations.

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## CRedit authorship contribution statement

**Annamaria Gentile:** Writing – original draft, Formal analysis, Data curation, Conceptualization. **Luca Di Stasio:** Writing – original draft, Data curation, Conceptualization. **Gianmaria Oliva:** Writing – original draft, Formal analysis, Data curation, Conceptualization. **Giovanni Vigliotta:** Writing – review & editing. **Angela Cicatelli:** Writing – review & editing. **Francesco Guarino:** Writing – review & editing. **Walter Guidi Nissim:** Writing – review & editing. **Massimo Labra:** Supervision, Resources, Funding acquisition. **Stefano Castiglione:** Writing – review & editing, Supervision, Resources, Funding acquisition.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Data availability

No data was used for the research described in the article.

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