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HOSPITAL WASTEWATER PHARMACEUTICAL RESIDUES AND THEIR IMPACT ON COMMUNITY MICROBIAL RESISTANCE: AN EPIDEMIOLOGICAL AND PHARMACEUTICAL SYSTEMATIC REVIEW

Giyantolin[1], Yuli Subiakto[2,3]*, Timbul Partogi Haposan Simorangkir[2], Widyati[2]
[1]Health Information Management Study Program, Faculty of Science & Technology, Universitas Nasional Karangturi, Jl. Raden Patah No.182-192, Rejomulyo, Semarang Timur, Semarang, Central Java 50227, Indonesia
[2]Military Pharmacy Study Program, Faculty of Military Pharmacy, Universitas Pertahanan Republik Indonesia, Kawasan IPSC Sentul, Sukahati, Citeureup, Kabupaten Bogor, West Java 16810, Indonesia
[3]Pharmacy Study Program, Politeknik Kesehatan TNI AU Ciumbuleuit, Jl. Ciumbuleuit No.203, Ciumbuleuit, Cidadap, Bandung, West Java 40142, Indonesia
*y.subiakto09@gmail.com

ABSTRACT
Releases from healthcare facilities account for a large portion of environmental pollution, with wastewater carrying a cocktail of pharmaceutical contaminants, especially antibiotics. These compounds accelerate the accumulation of antimicrobial resistance. The study synthesizes the scientific record on the concentration, fate, and effects of pharmaceutical compounds within hospital wastewater; it foregrounds the links to growing microbial resistance and delineates the threat to public health. The review adhered to the 2020 PRISMA framework. The search strategy applied a combination of keywords ("pharmaceutical residues" OR "antibiotic residues") AND ("hospital wastewater") AND ("antimicrobial resistance") AND ("environmental impact" OR "community"). The search was restricted to titles and abstracts of studies published 2015-2025. The article selection process consisted of title and abstract screening, full-text evaluation, and consensus-based discussion. Of the 405 articles initially identified, 21 met the eligibility criteria and were narratively synthesized. Hospital wastewater was found to contain a variety of antibiotics, particularly β-lactams, fluoroquinolones, tetracyclines, macrolides, and sulfonamides, at concentrations higher than those observed in domestic wastewater. Several ARGs including *blaNDM, blaKPC, blaOXA, sul1, sul2, qnr, tet,* and *mcr* were frequently detected, alongside resistant pathogenic isolates such as *Escherichia coli, Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*. Conventional wastewater treatment processes were shown to be only partially effective, achieving removal efficiencies of 16-50% for pharmaceutical residues and ARGs. Consequently, resistant bacteria and ARGs were still detected in receiving water bodies several kilometers downstream from discharge points. Hospital wastewater serves as a major source of pharmaceutical contamination and plays a critical role in the amplification of microbial resistance in the environment. These findings highlight the urgent need for advanced wastewater treatment technologies, strengthened antibiotic stewardship programs, and the integration of environmental and epidemiological surveillance within the One Health framework to curb the spread of antimicrobial resistance.

Keywords: antimicrobial resistance; epidemiology; hospital waste; one health; pharmaceutical residues

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INTRODUCTION
Out of the many challenges global public health faces, perhaps the most concerning, in today's date, is antimicrobial resistance (AMR). Microbial resistance to antibiotics is increasing at an alarming rate, and this is already undermining effective clinical treatments. In addition, it puts at risk the sustainable developmental goals (SDGs) of the health sector (Friedman et al., 2016). The clinical and agricultural uses of antibiotics has been a long known driver of AMR. But the the pharmaceutical remnants, specifically the antibiotic remnants, discharged via hospital wastes and their trigger on surrounding communities remain under researched.

Hospitals are known to widely utilize and misuse antibiotics, and the chemical and pharmaceutical wastes they produce are contaminated with antibiotics and complex chemicals that are only partly broken down (Bansal, 2019; Craun & Calderon, 2006; Hawkshead, 2008). In many countries, especially those that are categorized as developing or under developed, hospital waste is difficult to manage due to the inadequate and poor treatment infrastructure facilities (Ahmad et al., 2019; Ali et al., 2017; Chisholm et al., 2021; Delmonico et al., 2018; Quttainah & Singh, 2024). Consequently, pharmaceutical compounds, including antibiotics, may contaminate nearby aquatic environments, generating high selective pressure on microorganisms and fostering the emergence of resistant strains even beyond the hospital setting (Bilal et al., 2020; Zhang et al., 2009).

Research conducted over recent years has detected resistant genes and resistant bacteria in the aquatic systems, such as rivers, irrigation canals, and even community wells, that receive hospital wastewater (Al Salah et al., 2020; Aleem et al., 2021; Evoung Chandja et al., 2024; Kalasseril et al., 2020; Zhang et al., 2020). The most disturbing part of these findings is that resistant microorganisms not only move through species, but also cross environmental and geographical boundaries through a food web, human-animal and environmental interactions, as well as the hydrologic cycle. To that end, however, very few comprehensive reviews have incorporated environmental pharmacy and epidemiology, as well as microbial resistance, to assess the impact of exposure to residues of pharmaceuticals in hospital wastewater on the population's microbial resistance.

As a result, this systematic review intends to consolidate the most recent research on the detection of hospital wastewater and its residues of pharmaceuticals in the environment, focusing on community settings, and their contributions to microbial resistance. This work is meant to strengthen the scientific basis for the creation of the One Health-based policies on pharmaceutical waste management, while also reinforcing community and environmental frameworks for controlling antimicrobial resistance.

METHOD

Study Design

This study employed a systematic review design, structured in accordance with the *Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020* guidelines. The review aimed to identify, evaluate, and critically synthesize studies investigating pharmaceutical residues in hospital wastewater and their implications for microbial resistance in surrounding communities.

Sources and Search Strategy

A systematic literature search was conducted across four major scientific databases: PubMed, ScienceDirect, Web of Science, and Springer. The search strategy utilized predefined keyword combinations: ("pharmaceutical residues" OR "antibiotic residues") AND ("hospital wastewater") AND ("antimicrobial resistance") AND ("environmental impact" OR "community"). Searches were limited to titles and abstracts, covering studies published between January 1, 2015, and June 31, 2025. The primary research question guiding this review was: *"What is the relationship between exposure to pharmaceutical residues in hospital wastewater and the occurrence of microbial resistance in community environments?"*

Inclusion and Exclusion Criteria

Eligible studies included original research from environmental laboratory analyses, microbiological surveillance, and community-based epidemiological investigations reporting the presence of pharmaceutical residues particularly antibiotics in hospital wastewater, along with assessments or documentation of microbial resistance in surrounding environments such as soil, surface water, wells, animals, or humans. Only studies published in English between 2015 and 2025 were considered. Studies were excluded if they (i) focused exclusively on hospital-acquired microbial resistance without linking it to wastewater exposure, (ii) addressed wastewater treatment processes without measuring microbial resistance, (iii) involved purely in vivo animal experiments irrelevant to community populations, or (iv) lacked full-text availability.

Study Selection Process

The study selection process was conducted in multiple stages to ensure inclusion of only relevant and eligible articles. Initially, two reviewers independently screened titles and abstracts to assess topic relevance. Articles passing this stage underwent full-text evaluation against predefined inclusion and exclusion criteria. Discrepancies between reviewers were resolved through discussion until consensus was achieved. The entire selection procedure was documented in a PRISMA flow diagram (Figure 1), which illustrates the number of records identified, screened, excluded, and ultimately included for final analysis.

Data Extraction and Synthesis

Data were extracted from all studies meeting the inclusion criteria using a standardized extraction table to ensure consistency. Extracted information included study identifiers (authors, publication year, study location), research objectives, types of pharmaceutical residues detected, wastewater sources, resistance indicators, and key findings with corresponding conclusions. Given the high degree of heterogeneity across studies in terms of populations, types of residues, detection methods, and microbial species, data synthesis was primarily qualitative using a narrative synthesis approach. However, where sufficiently homogenous quantitative data were available, a limited quantitative analysis or descriptive meta-analysis was conducted, for instance, to estimate the prevalence of microbial resistance to specific antibiotic residues.

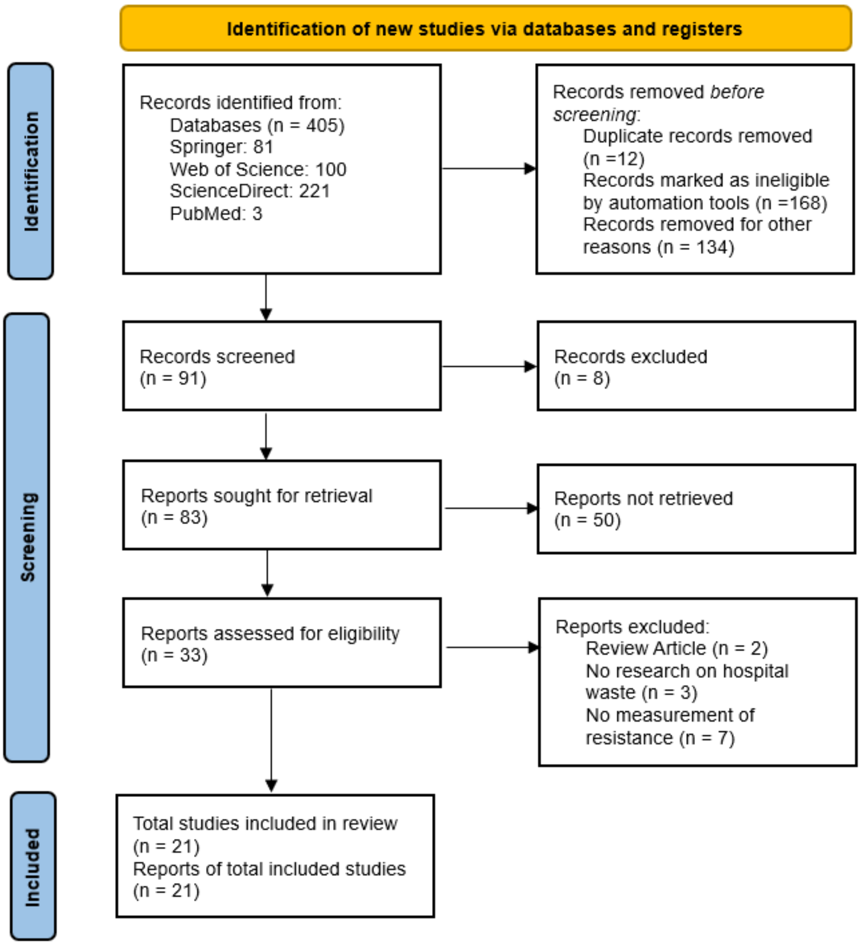

Figure 1. Article Identification Flowchart

RESULT

Study Characteristics

There were 21 articles that met the inclusion criteria (Table 1), published between 2019 and 2024, with an increase in the number of studies observed over the last three years. This indicates a growing global interest in the issue of antimicrobial resistance from hospital waste. Studies were conducted in various countries, with a predominance in Asia (Thailand, Vietnam, India, Pakistan), South America (Brazil), Africa, and several European countries. Most studies used observational field models combined with PCR, qPCR, or metagenomic-based molecular analysis to detect and quantify antibiotic resistance genes (ARGs).

Table 1.
List of articles that meet the criteria and are relevant to the study objectives

No	Autors (Year)	Country	Study Objectives	Key Findings
1	Talat et al., (2025)	India	Examining the filtration efficiency of two different wastewater treatment plants (WWTPs) operating under similar conditions, with a focus on the prevalence and removal of antibiotic resistance genes (ARGs) and	This study identified various clinically important antibiotic resistance genes (ARGs), including those resistant to aminoglycosides, macrolides, lincosamides, sulfonamides (*sul1, sul2*), and β-lactamases (*blaNDM−1*), which remained despite conventional and advanced wastewater treatment. The sul1 and sul2 genes emerge as strong indicators of anthropogenic activity, highlighting the role of humans in the presence of ARGs in the environment. The number of ARGs decreased from 58 in the influent to 46 in conventional wastewater (WWTPC) and 21 in advanced treatment (WWTPA), indicating varying levels of effectiveness. These findings

No	Autors (Year)	Country	Study Objectives	Key Findings
			antibiotic-resistant bacteria (ARBs) in treated water.	emphasize the need for more advanced treatment technologies and a multidisciplinary approach to understand the interactions between ARGs, the microbiome, and mobile genetic elements to optimize resistance control.
2	Hamad & El-Sesy, (2023)	Mesir	Synthesizing copper oxide nanoparticles (CuONPs) and nano-zero-valent iron (NZVi) used as nanoadsorbents to remove levofloxacin and antibiotic resistance genes from water samples.	This study identified levofloxacin as the main contaminant in hospital wastewater contributing to the development of antibiotic resistance genes (ARGs) in pathogenic bacteria such as *Escherichia coli* and *Pseudomonas aeruginosa*. Of the 37 ARGs analyzed, the prevalence of resistance was alarming. The study also showed that CuO nanoparticles (91.4%) and nano-zero-valent iron (95.01%) are effective in adsorbing levofloxacin, offering an environmentally friendly and cost-effective solution to reduce antibiotic contamination in water.
3	Gaşpar et al., (2021)	Rumania	Comparing the level of antibiotic resistance of *Escherichia coli* indicator bacteria in wastewater samples collected from two hospitals and two urban communities.	This study detected antibiotic residues in wastewater using *Escherichia coli* as an indicator, testing ten antibiotics from nine classes according to EUCAST and WHO CIA. The results showed multidrug resistance in 85.11% of hospital isolates and 73.53% of community isolates, with a higher prevalence of carbapenemase producers in the community (76.47%) compared to hospitals (68.09%). These findings confirm the high level of resistance in both sources and the need for monitoring and management of antibiotic use in both healthcare facilities and the community.
4	Lien et al., (2016)	Hanoi, Vietnam	To determine the concentration of various antibiotics in wastewater before and after treatment in rural and urban hospitals in Vietnam, and to explore the relationship between antibiotic concentrations in wastewater and the amount of antibiotics used in rural hospitals during a one-year period in 2013.	This study found high concentrations of various antibiotics in hospital waste, with ciprofloxacin being the highest in rural hospitals, and showed a link between antibiotic use and environmental contamination. Hospital waste has been shown to be a major source of antibiotic residues and resistant bacteria, while different treatment methods in each hospital have not been fully effective. These findings emphasize the need for better waste management strategies to minimize environmental impact.
5	Byrnes et al., (2025)	Wales, UK	Knowledge of wastewater sampling practices, use of limited antibiotics, and sampling from a limited number of hospitals.	This study found more than 40 drug residues in hospital waste, including β-lactams, macrolides, quinolones, sulfonamides, antifungals, antivirals, and metabolites, with clarithromycin, N-desmethyl clarithromycin, fluconazole, and trimethoprim being the most dominant. Antimicrobial concentrations exceeding the PNEC create selective pressure for the emergence of antimicrobial resistance (AMR). Hospital wastewater biofilms also showed higher levels of resistance genes and multidrug-resistant organisms compared to community wastewater biofilms. These findings underscore the need for more effective wastewater management to prevent an increase in AMR risk in the environment.

No	Autors (Year)	Country	Study Objectives	Key Findings
6	Chen et al., (2025)	Shanghai, China	Characterize and assess the risk of antimicrobial resistance and plasmidome levels in hospital waste in major Chinese cities, providing citywide surveillance data and evidence to inform public health interventions.	This study identified 1,237 subtypes of antimicrobial resistance genes (ARGs) from 22 types, mainly beta-lactams, tetracyclines, multidrug, polymyxins, and aminoglycosides, in hospital waste. A total of 97.5% of the 80 metagenome-assembled genomes (MAGs) carried ARGs, including last-line resistance genes such as *blaNDM, blaKPC, blaIMiH*, and *mcr*, as key indicators of resistance. These ARG-carrying pathogenic bacteria pose a serious threat to receiving water environments, emphasizing the importance of advanced wastewater treatment before disposal. This study provides a comprehensive overview of resistance levels and plasmidomes, relevant for public health interventions in Shanghai, China.
7	Ekwanzala et al., (2020)	Gauteng Province, Africa	Investigating the spread of selected antibiotics from hospital wastewater to municipal wastewater and ultimately to receiving water bodies.	This study found antibiotic residues such as azithromycin, ciprofloxacin, clindamycin, doxycycline, and sulfamethoxazole in various matrices, including hospital waste, sludge, and municipal wastewater. Although resistance indicators were not directly described, the presence of these antibiotics has the potential to promote microbial resistance. The highest concentrations were detected in river sediments, while the lowest were found in river water, indicating significant antibiotic release into aquatic environments. These findings emphasize the need for more efficient disposal methods and further research into the sources of antibiotic contamination in river sediments.
8	Sinthuchai et al., (2021)	Bangkok, Thailand	Investigating the occurrence, relative abundance, and fate of eight antibiotics at each treatment stage in four domestic wastewater treatment plants and four hospitals (DWWTP and HWWTP) in Bangkok, Thailand, as well as their bulk loading into the receiving water environment.	This study identified eight major antibiotics, including dicloxacillin, piperacillin, cefazolin, cefaclor, clarithromycin, ciprofloxacin, metronidazole, and sulfamethoxazole, with concentrations significantly higher in hospital wastewater treatment plants (HWWTP) than in domestic wastewater treatment plants (DWWTP). Inlet concentrations at HWWTPs were recorded to be approximately 60 times higher, and effluent concentrations were approximately 10 times higher. Ciprofloxacin was primarily found in the solid phase, while sulfamethoxazole was dominant in the dissolved form, which is more difficult to degrade. This study emphasizes the need to improve wastewater treatment efficiency through the application of advanced technologies to reduce the release of antibiotic residues into aquatic environments.
9	Chiemchaisri et al., (2022)	Thailand	Investigating the efficacy of recent antibiotic residue treatment at practical hospital wastewater treatment plants throughout Thailand.	This study found 19 types of antibiotic residues in hospital waste, including imipenem, ceftriaxone, lincomycin, trimethoprim, ofloxacin, levofloxacin, norfloxacin, meropenem, colistin, ciprofloxacin, tetracycline, ampicillin, amoxicillin, clarithromycin, and others, which are divided into 10 main groups such as penicillin and cephalosporin. High concentrations were particularly observed in amoxicillin, ciprofloxacin, tetracycline, ampicillin, and norfloxacin. Amoxicillin and ampicillin showed high elimination rates (90–99%), while other antibiotics varied (0–93%). The effectiveness of removal is relatively similar across various treatment systems, except for attached growth systems, which tend to be less efficient. This study emphasizes the

No	Autors (Year)	Country	Study Objectives	Key Findings
				importance of improving treatment technology and continuous monitoring to more effectively control antibiotic contamination.
10	Buelow et al., (2020)	Haute-Savoie, Prancis	Characterizing the resistome, microbiota, and eco-exposome signatures of separately treated and then mixed hospital and urban wastewater samples to evaluate the impact of their combined treatment on the spread of antimicrobial resistance to the environment.	This study shows that hospital wastewater (HWW) contains higher levels of micro-pollutants and antimicrobial resistance (AMR) markers than urban wastewater (UWW). Interestingly, the streptogramin resistance gene VatB and the transposase gene ISS1N are more abundant in UWW, potentially serving as specific indicators for that source. After treatment, the cumulative abundance of various classes of resistance genes decreased significantly, with differences ranging from 3 to 78 times lower compared to untreated samples. These findings emphasize the importance of monitoring and management strategies for both HWW and UWW, with a focus on specific gene classes and taxa for more effective assessment of AMR spread risks.
11	Cahill et al., (2019)	Irlandia	Testing hospital waste and municipal wastewater in urban areas in Ireland for the presence of carbapenemase-producing Enterobacterales (CPE), which pose a significant health threat due to their resistance to almost all available antibiotics.	This study identified drug residues associated with carbapenemase-producing Enterobacterales (CPE) in hospital waste and municipal wastewater. Resistance genes such as bla OXA-48, bla VIM, and bla IMP were detected in clinical samples, while KPC producers were only found in hospital waste, indicating potential transmission from humans to the environment. All CPE isolates exhibited multidrug resistance profiles, with non-susceptibility to at least 9 of 15 antimicrobial agents, and four isolates were resistant to all agents tested, signifying a serious threat to public health. These findings confirm that hospital wastewater serves as the primary source of CPE in municipal wastewater streams, underscoring the importance of monitoring hospital wastewater as an early warning system for the spread of resistance. This study advocates for the implementation of specialized wastewater treatment facilities in hospitals to reduce the release of harmful contaminants, although it still faces cost and operational challenges.
12	Silvester et al., (2025)	Wales, UK	Performing metagenomic sequencing on wastewater from hospitals across Wales to screen for antimicrobial resistance genes (ARGs) and opportunistic pathogens, highlighting the emergence and spread of antimicrobial resistance in healthcare settings.	This study identified various drug residues with a focus on antimicrobial resistance genes (ARGs) in hospital wastewater across Wales. The most dominant resistance was found against aminoglycosides, beta-lactams, and macrolide-lincosamide-streptogramins, with OXA-type beta-lactamases as the most prominent ARGs. Resistance indicators included spatial variability of the “big five” carbapenemases (KPC, IMP, VIM, NDM, OXA-48-like), *mcr* genes, and the presence of WHO priority pathogens such as pathogenic fungi and the ESKAPEE group, including Enterococcus faecium and Staphylococcus aureus. These findings indicate significant differences in the abundance and diversity of ARGs between hospitals, emphasizing the need for tailored mitigation strategies. The study concludes that the implementation of pre-treatment of hospital waste is an important step in limiting the release of micro-pollutants, ARGs, and harmful pathogens into the environment.

No	Autors (Year)	Country	Study Objectives	Key Findings
13	Zhang et al., (2021)	Jaipur, India	Characterization of ARG and biocide/metal resistance genes (BMRG) in four wastewater treatment plants (WWTPs) in Jaipur, India.	This study highlights the enrichment of antibiotic resistance genes (ARGs) in municipal wastewater, indicating significant resistance indicators. Bacterial resistance is influenced by various chemicals in wastewater, exerting selective pressure on bacterial survival. Hospital wastewater contains more pharmaceutical compounds, contributing to higher ARG abundance compared to municipal sources. The presence of biocides and heavy metals in wastewater may co-select for antibiotic resistance.
14	Petrovich et al., (2020)	Tel Alive, Israel	Characterizing the composition and persistence of antibiotic resistance genes (ARGs), dsDNA viruses, and bacteria from influent to effluent in a pilot-scale hospital wastewater treatment system in Israel using shotgun metagenomics, addressing knowledge gaps regarding the fate and relationships between these elements in hospital wastewater systems.	This study identified various antibiotic resistance genes (ARGs) in hospital wastewater, including *AAdA, blaTEM-1, blaNDM-1, blaOXA-2, blaOXA-35, bla OXA-10, MeFa, mel, TetX*, and *sul1,* which were detected in most samples. The efficiency of ARG removal was only around 16%, indicating the high persistence of these genes despite the treatment process. The most common ARGs confer resistance to aminoglycosides, cephalosporins, macrolides, penams, and tetracyclines, with most associated with plasmid genes. These findings highlight the potential public health threat posed by the spread of ARGs through wastewater, particularly when reused for irrigation, and emphasize the need for more effective wastewater treatment strategies to reduce the risk of antibiotic resistance.
15	Fabiyi et al., (2025)	Benin, West Africa	Characterizing Gram-negative bacteria isolated from various sources around Lake Nokoué in southern Benin, highlighting the spread of antimicrobial-resistant bacteria in natural and human-impacted environments and the need for urgent public health interventions.	This study identified the presence of various antibiotic resistance genes in water samples from Lake Nokoué, including *aac(6')-Ib-Cr, qnRb*, and *blaVIM*. The *blaVIM* gene was found in *Pseudomonas putida* from animal feed, indicating serious carbapenem resistance. Other resistance indicators include the aac(6′)-Ib-Cr gene in *Klebsiella pneumoniae,* which confers resistance to aminoglycosides and fluoroquinolones, and the qnrB gene in *Escherichia coli* and K. *pneumoniae*, consistent with previous reports. These findings confirm that Lake Nokoué serves as a reservoir for bacteria carrying clinically important resistance genes, necessitating immediate environmental and public health interventions to reduce the risk of resistance spread.

No	Autors (Year)	Country	Study Objectives	Key Findings
16	Yao et al., (2021)	East China	Investigating the characteristics and removal of antibiotics and antibiotic resistance genes (ARGs) in independent hospital treatment processes of different scales (primary, secondary, and tertiary hospitals) and understanding the occurrence of these pollutants in hospital wastewater.	This study identified antibiotic residues in hospital wastewater, with cefradine (first-generation cephalosporin) concentrations of 2.38 µg/L in the primary hospital (H1) and cefepime (fourth-generation cephalosporin) concentrations of up to 540.39 µg/L in the tertiary hospital (H3). The detected resistance indicators included the bla GES-1, qnrA, and InTi1 genes, with the highest relative abundance in treated wastewater. The efficiency of ofloxacin removal varied, with 44.2% at H1, 51.5% at H2, and 81.6% at H3, indicating differences in effectiveness between treatment processes. These findings confirm the coexistence of antibiotics, resistance genes, and resistant pathogens in hospital wastewater, highlighting the need to improve treatment system efficiency to limit the spread of harmful contaminants into the environment.
17	Nasri et al., (2024)	Tunisia, Africa	Investigating the occurrence and risk of pharmaceuticals and personal care products (PPCPs) in wastewater from seven hospitals in Tunisia, assessing their potential ecotoxicological effects on aquatic organisms.	This study identified various drug residues in hospital wastewater in Tunisia, including benzotriazoles (BZT), benzophenone 3 (BP3), and drugs such as ofloxacin, trimethoprim, acetaminophen, carbamazepine, and caffeine, with BZT and BP3 being the most frequently detected. Resistance indicators were shown through hazard quotients (HQ), revealing that marbofloxacin, enrofloxacin, and BZT pose significant risks to aquatic organisms and may contribute to resistance. The findings highlight the environmental risks of high concentrations of acetaminophen and ofloxacin in some hospitals and emphasize the need for improved monitoring and management of PPCPs in hospital wastewater to minimize impacts on aquatic ecosystems.
18	Bakon et al., (2023)	Selangor Malaysia	Determining the prevalence of antibiotic-resistant pathogenic bacteria and antibiotic residue levels in hospital waste in Selangor, Malaysia.	This study focuses on the prevalence of antibiotic-resistant pathogenic bacteria and antibiotic residue levels in hospital waste in Selangor, Malaysia, with particular attention to the ESKAPE group. Preliminary results indicate differences in resistance patterns between hospitals: E. faecium isolates from Hospital A showed 80% resistance to vancomycin and 10% to ciprofloxacin, while isolates from Hospital B showed 100% resistance to vancomycin but remained sensitive to ciprofloxacin. This study also screened for antibiotic resistance genes (ARGs) via multiplex PCR to identify resistance mechanisms in ESKAPE isolates. Further analysis of wastewater samples is expected to reveal more types of antibiotic residues present, thereby enriching our understanding of the impact of hospital wastewater on antimicrobial resistance. These findings will contribute to the literature through scientific publications and conferences, while also providing a basis for resistance control strategies in hospital settings.

No	Autors (Year)	Country	Study Objectives	Key Findings
19	Rahim et al., (2024)	Punjab, Pakistan	Investigating the prevalence of antibiotic-resistant bacteria (ARB) and antibiotic resistance genes (ARG) in wastewater from the Sutlej River, highlighting the need for improved wastewater treatment and monitoring practices to protect public health and environmental integrity.	This study found various antibiotic residues in wastewater with high levels of resistance in *Escherichia coli* (90%), *Klebsiella pneumoniae* (58%), *Pseudomonas aeruginosa* (55%), and *Salmonella* spp. (53%). The main resistance genes detected included aminoglycosides (AAdA, 41%), sulfonamides (Sul1, Sul3; 35%), and tetracyclines (TetA/B/D; 29–12%). The findings indicate the limitations of wastewater treatment in eliminating ARB and ARG, necessitating stricter antibiotic use policies, more effective treatment technologies, as well as routine monitoring and surveillance programs to curb the spread of antibiotic resistance.
20	Marathe et al., (2019)	Mumbai, India	Investigating the microbiota and antibiotic resistome of hospital waste collected from the city of Mumbai, India, with a particular focus on identifying novel carbapenemases and other resistance genes not yet described in clinical strains.	This study identified 112 different antibiotic resistance genes in hospital wastewater, particularly clinically important beta-lactamases such as NDM, VIM, IMP, KPC, and OXA-48, as well as sulfonamide genes (sul1 and sul4) as key indicators of resistance. The findings confirm that hospital wastewater microbiota serve as a reservoir for new resistance genes that could potentially spread to human pathogens, underscoring the urgent need for exploration and characterization of environmental ARGs to prevent the risk of resistance transfer.
21	Krul et al., (2025)	Brazil	Investigating the presence and spread of antimicrobial resistance genes, particularly in the ESKAPEE group, through hospital waste, highlighting the public health risks associated with these microorganisms in pediatric hospital environments in southern Brazil.	This study identified carbapenem resistance genes bla KPC-2, bla GES-5, and bla NDM-1 in bacterial isolates, with sequence type (ST) variation as an indicator in *Enterobacter cloacae*, including ST520, which was also found in Spain. The findings indicate the co-production of carbapenemases in E. *kobei*, as well as the polyclonal nature of K. *pneumoniae* and E. *cloacae*, while E. *coli* exhibits a clonal nature. These results highlight the serious risk of ESKAPEE group spread through hospital waste, underscoring the need for strict monitoring and control to protect public health and food safety.

Types of Pharmaceutical Residues in Hospital Wastewater

Analysis of 21 reviewed articles revealed a wide spectrum of pharmaceutical residues, predominantly derived from antibiotic classes. These residues include β-lactams (penicillins, cephalosporins, carbapenems), macrolides (clarithromycin, azithromycin), fluoroquinolones (ciprofloxacin, levofloxacin, ofloxacin), tetracyclines (doxycycline, oxytetracycline), sulfonamides (sulfamethoxazole, sul1, sul2), aminoglycosides, and other antimicrobial agents such as antifungals (fluconazole), antivirals, analgesics (acetaminophen), as well as personal care compounds including benzotriazoles. The majority of studies reported that antibiotic residues in hospital wastewater are present at higher concentrations compared to domestic or general environmental effluents, frequently exceeding the predicted no effect concentration

(PNEC). These findings underscore hospital effluents as a major point source of antibiotic exposure in the environment.

Detected Indicators of Resistance

The most frequently reported indicators of antimicrobial resistance were antimicrobial resistance genes (ARGs) and antibiotic-resistant bacteria (ARB). Dominant ARGs included *blaNDM, blaKPC, blaOXA, blaVIM, sul1, sul2, qnr, tet,* and the *mcr* gene associated with colistin resistance. In addition to ARGs, several studies identified pathogenic bacterial isolates of high clinical relevance, such as *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*, including members of the ESKAPEE group, which exhibited high levels of multidrug resistance. Some studies documented that more than 70% of isolates displayed resistance to multiple antibiotic classes, with reports of complete resistance against up to 15 antimicrobial agents. Plasmid mobilization and integrons were also highlighted as key drivers accelerating horizontal gene transfer in environmental settings.

Findings and Public Health Implications

Cross-study analysis demonstrated that conventional hospital wastewater treatment processes are insufficient to effectively reduce pharmaceutical residues and ARG contamination, with reported removal efficiencies ranging only between 16-50% in several facilities. Both ARGs and ARB were consistently detected in receiving water bodies (rivers, lakes, or groundwater) several kilometers downstream from discharge points, indicating a substantial risk of dissemination into ecosystems and human populations. A positive correlation was observed between antibiotic concentrations and ARG abundance, alongside seasonal variations influencing the accumulation of pharmaceutical residues and resistance determinants. Overall, these findings identify hospitals as critical hotspots in the transmission chain of antimicrobial resistance. This underscores the urgent need for advanced wastewater treatment technologies, routine surveillance, and antibiotic stewardship policies under the One Health framework to mitigate public health risks.

DISCUSSION

Based on the articles selected through inclusion and exclusion criteria, nearly all studies emphasized that hospitals are the primary sources of pharmaceutical residues released into the environment. Reported concentrations of antibiotics in hospital effluents were consistently higher than those observed in domestic or industrial sources. The predominant residues detected included fluoroquinolones, β-lactams, tetracyclines, macrolides, and sulfonamides, reflecting clinical prescription patterns in healthcare facilities (Byrnes et al., 2025; Chen et al., 2025; Chiemchaisri et al., 2022; Petrovich et al., 2020; Rahim et al., 2024; Yao et al., 2021). Several studies identified ciprofloxacin and levofloxacin at concentrations exceeding environmental safety thresholds, thereby exerting selective pressure on environmental bacteria (Bakon et al., 2023; Chiemchaisri et al., 2022; Ekwanzala et al., 2020; Lien et al., 2016; Sinthuchai et al., 2021). Furthermore, the persistence of residues within wastewater treatment systems demonstrates that hospital wastewater treatment plants (WWTPs) are not fully effective in removing pharmaceutical compounds, allowing residues to remain detectable in final effluents discharged into natural water bodies. From an epidemiological perspective, this highlights a continuous exposure pathway from hospitals to surrounding communities.

Hospital wastewater also revealed a strong correlation between the presence of antibiotic residues and the increased prevalence of antimicrobial resistance genes (ARGs) and antibiotic-resistant bacteria (ARB). The most frequently detected resistance genes included *blaNDM*, *blaKPC*, *blaOXA*, *sul1*, *sul2*, *qnr*, *tet*, and *mcr* (Aleem et al., 2021; Bakon et al., 2023; Chen et al., 2025; Kalasseril et al., 2020; Krul et al., 2025; Silvester et al., 2025; Talat et al., 2025; Yao et al., 2021). These genetic markers were often associated with the isolation of *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*, exhibiting multidrug resistance profiles (Aleem et al., 2021; Bakon et al., 2023; Chen et al., 2025; Gaşpar et al., 2021; Hamad & El-Sesy, 2023; Kalasseril et al., 2020; Krul et al., 2025; Rahim et al., 2024; Ruhnke et al., 2014; Silvester et al., 2025; Yao et al., 2021). Metagenomic studies further demonstrated a positive association between antibiotic residue concentrations and ARG abundance, particularly *sul1* and *tetA* (Chen et al., 2025; Petrovich et al., 2020; Silvester et al., 2025; Talat et al., 2025; D. Zhang et al., 2021). From a pharmaceutical perspective, these findings underscore the role of pharmaceutical residues as critical "drivers" of resistance, facilitating horizontal gene transfer through plasmids, integrons, and transposons. Epidemiologically, this indicates that antimicrobial resistance not only originates in clinical settings but is also maintained and propagated within environmental compartments.

Another critical finding is that pharmaceutical residues and ARGs in hospital wastewater extend beyond treatment systems into the surrounding environment. Several studies documented ARG persistence in recipient rivers up to several kilometers downstream from discharge points. This poses a direct risk to communities relying on these water sources for domestic use, agricultural irrigation, or direct contact. Moreover, the detection of resistance genes against last-resort antibiotics, such as *mcr-1* associated with colistin resistance, signals a severe public health threat (Bakon et al., 2023). From an epidemiological standpoint, this highlights the flow of resistance determinants from hospitals to communities, amplifying the risk of difficult-to-treat infections. These findings are further corroborated by reports of high prevalence of multidrug-resistant bacterial isolates in community environments adjacent to hospitals, suggesting both direct and indirect transmission from hospital effluents (Aleem et al., 2021; Ariza-Heredia & Chemaly, 2018; Evoung Chandja et al., 2024).

The results of this review carry significant implications for both pharmaceutical and epidemiological domains. From a pharmaceutical standpoint, the evidence reinforces the necessity for prudent antibiotic management in hospitals, including the implementation of antimicrobial stewardship programs, stricter control of drug distribution, and the adoption of advanced wastewater treatment technologies capable of substantially reducing pharmaceutical residues and ARGs (Ariza-Heredia & Chemaly, 2018; Byrnes et al., 2025). From an epidemiological perspective, comprehensive environmental surveillance systems are required to monitor the distribution of pharmaceutical residues and resistance determinants in the community, with integration of environmental data into clinical surveillance frameworks (Byrnes et al., 2025). The integration of these two approaches aligns with the One Health concept, emphasizing the interconnectedness of human, animal, and environmental health. Evidence-based policies that account for local contexts, such as seasonal variations in antibiotic use and the capacity of wastewater treatment infrastructure, should be prioritized to prevent further dissemination of antimicrobial resistance.

CONCLUSION

Hospital wastewater is a primary source of pharmaceutical residues, particularly antibiotics, which are detected at high concentrations and act as key drivers of microbial resistance in the environment. Evidence synthesized from 21 studies demonstrates a strong association between the presence of antibiotic residues and the increased prevalence of antimicrobial resistance genes (ARGs), as well as the emergence of multidrug-resistant bacteria capable of disseminating into surrounding communities through receiving water bodies and other environmental media. This phenomenon poses serious public health implications, as antimicrobial resistance can compromise the effectiveness of antibiotic therapies and heighten the risk of hard-to-treat infections. Thus, a key tactic to slow the spread of antibiotic resistance within the One Health framework is to combine epidemiological viewpoints through environmental and community-based resistance surveillance with pharmaceutical approaches through sensible antibiotic management and the creation of more efficient wastewater treatment technologies.

REFERENCES

Ahmad, R., Liu, G., Santagata, R., Casazza, M., Xue, J., Khan, K., Nawab, J., Ulgiati, S., & Lega, M. (2019). LCA of hospital solid waste treatment alternatives in a developing country: The case of District Swat, Pakistan. *Sustainability (Switzerland)*, *11*(13). https://doi.org/10.3390/su11133501

Al Salah, D. M. M., Ngweme, G. N., Laffite, A., Otamonga, J. P., Mulaji, C., & Poté, J. (2020). Hospital wastewaters: A reservoir and source of clinically relevant bacteria and antibiotic resistant genes dissemination in urban river under tropical conditions. *Ecotoxicology and Environmental Safety*, *200*(November 2019). https://doi.org/10.1016/j.ecoenv.2020.110767

Aleem, M., Azeem, A. R., Rahmatullah, S., Vohra, S., Nasir, S., & Andleeb, S. (2021). Prevalence of Bacteria and Antimicrobial Resistance Genes in Hospital Water and Surfaces. *Cureus*, *13*(10). https://doi.org/10.7759/cureus.18738

Ali, M., Wang, W., Chaudhry, N., & Geng, Y. (2017). Hospital waste management in developing countries: A mini review. *Waste Management and Research*, *35*(6), 581–592. https://doi.org/10.1177/0734242X17691344

Ariza-Heredia, E. J., & Chemaly, R. F. (2018). Update on infection control practices in cancer hospitals. *CA: A Cancer Journal for Clinicians*, *68*(5), 340–355. https://doi.org/10.3322/caac.21462

Bakon, S. K., Mohamad, Z. A., Jamilan, M. A., Hashim, H., Kuman, M. Y., Shaharudin, R., Ahmad, N., & Muhamad, N. A. (2023). Prevalence of Antibiotic-Resistant Pathogenic Bacteria and Level of Antibiotic Residues in Hospital Effluents in Selangor, Malaysia: Protocol for a Cross-sectional Study. *JMIR Research Protocols*, *12*(July 2022), 1–12. https://doi.org/10.2196/39022

Bansal, O. P. (2019). Antibiotics in hospital effluents and their impact on the antibiotics resistant bacteria and remediation of the antibiotics: A review. *Network Pharmacology*, *4*(4), 6–30. www.iaees.orgArticle

Bilal, M., Mehmood, S., Rasheed, T., & Iqbal, H. M. N. (2020). Antibiotics traces in the aquatic environment: persistence and adverse environmental impact. *Current Opinion in Environmental Science and Health*, *13*, 68–74. https://doi.org/10.1016/j.coesh.2019.11.005

Byrnes, N. A., Silvester, R., Cross, G., Weightman, A. J., Jones, D. L., & Kasprzyk-Hordern, B. (2025). Assessing the risk of antimicrobial resistance and potential environmental harm through national-scale surveillance of antimicrobials in hospital and community wastewater. *Environment International*, *202*(February), 109606. https://doi.org/10.1016/j.envint.2025.109606

Chen, M., Liu, Y., Zhou, Y., Pei, Y., Qu, M., Lv, P., Zhang, J., Xu, X., Hu, Y., & Wang, Y. (2025). Deciphering antibiotic resistance genes and plasmids in pathogenic bacteria from 166 hospital effluents in Shanghai, China. *Journal of Hazardous Materials*, *483*(November 2024). https://doi.org/10.1016/j.jhazmat.2024.136641

Chiemchaisri, W., Chiemchaisri, C., Hamjinda, N. S., Jeensalute, C., Buranapakdee, P., &

Thamlikitkul, V. (2022). Field investigation of antibiotic removal efficacies in different hospital wastewater treatment processes in Thailand. *Emerging Contaminants*, *8*, 329–339. https://doi.org/10.1016/j.emcon.2022.07.002

Chisholm, J. M., Zamani, R., Negm, A. M., Said, N., Abdel daiem, M. M., Dibaj, M., & Akrami, M. (2021). Sustainable waste management of medical waste in African developing countries: A narrative review. *Waste Management and Research*, *39*(9), 1149–1163. https://doi.org/10.1177/0734242X211029175

Craun, G. F., & Calderon, R. L. (2006). Workshop summary: Estimating waterborne disease risks in the United States. *Journal of Water and Health*, *4*(SUPPL. 2), 241–254. https://doi.org/10.2166/wh.2006.025

Delmonico, D. V. d. G., Santos, H. H. do., Pinheiro, M. A. P., de Castro, R., & de Souza, R. M. (2018). Waste management barriers in developing country hospitals: Case study and AHP analysis. *Waste Management and Research*, *36*(1), 48–58. https://doi.org/10.1177/0734242x17739972

Ekwanzala, M. D., Lehutso, R. F., Kasonga, T. K., Dewar, J. B., & Momba, M. N. B. (2020). Environmental dissemination of selected antibiotics from hospital wastewater to the aquatic environment. *Antibiotics*, *9*(7), 1–16. https://doi.org/10.3390/antibiotics9070431

Evoung Chandja, W. B., Onanga, R., Mbehang Nguema, P. P., Lendamba, R. W., Mouanga-Ndzime, Y., Mavoungou, J. F., & Godreuil, S. (2024). Emergence of Antibiotic Residues and Antibiotic-Resistant Bacteria in Hospital Wastewater: A Potential Route of Spread to African Streams and Rivers, a Review. *Water (Switzerland)*, *16*(22). https://doi.org/10.3390/w16223179

Friedman, N. D., Temkin, E., & Carmeli, Y. (2016). The negative impact of antibiotic resistance. *Clinical Microbiology and Infection*, *22*(5), 416–422. https://doi.org/10.1016/j.cmi.2015.12.002

Gaşpar, C. M., Cziszter, L. T., Lăzărescu, C. F., Ţibru, I., Pentea, M., & Butnariu, M. (2021). Antibiotic resistance among escherichia coli isolates from hospital wastewater compared to community wastewater. *Water (Switzerland)*, *13*(23), 1–11. https://doi.org/10.3390/w13233449

Hamad, M. T. M. H., & El-Sesy, M. E. (2023). Adsorptive removal of levofloxacin and antibiotic resistance genes from hospital wastewater by nano-zero-valent iron and nano-copper using kinetic studies and response surface methodology. *Bioresources and Bioprocessing*, *10*(1), 1–29. https://doi.org/10.1186/s40643-022-00616-1

Hawkshead, J. J. (2008). Hospital wastewater containing pharmaceutically active compounds and drug- resistant organisms: A source of environmental toxicity and increased antibiotic resistance. *Journal of Residuals Science & Technology*, *5*(2), 51–60.

Kalasseril, S. G., Krishnan, R., Vattiringal, R. K., Paul, R., Mathew, P., & Pillai, D. (2020). Detection of New Delhi Metallo-β-lactamase 1 and Cephalosporin Resistance Genes Among Carbapenem-Resistant Enterobacteriaceae in Water Bodies Adjacent to Hospitals in India. *Current Microbiology*, *77*(10), 2886–2895. https://doi.org/10.1007/s00284-020-02107-y

Krul, D., Negoseki, B. R. da S., Siqueira, A. C., Tomaz, A. P. de O., dos Santos, É. M., de Sousa, I., Vasconcelos, T. M., Marinho, I. C. R., Arend, L. N. V. S., Mesa, D., Conte, D., & Dalla-Costa, L. M. (2025). Spread of antimicrobial-resistant clones of the ESKAPEE group: From the clinical setting to hospital effluent. *Science of the Total*

Environment, *973*(November 2024). https://doi.org/10.1016/j.scitotenv.2025.179124

Lien, L. T. Q., Hoa, N. Q., Chuc, N. T. K., Thoa, N. T. M., Phuc, H. D., Diwan, V., Dat, N. T., Tamhankar, A. J., & Lundborg, C. S. (2016). Antibiotics in wastewater of a rural and an urban hospital before and after wastewater treatment, and the relationship with antibiotic use-a one year study from Vietnam. *International Journal of Environmental Research and Public Health*, *13*(6), 1–13. https://doi.org/10.3390/ijerph13060588

Petrovich, M. L., Zilberman, A., Kaplan, A., Eliraz, G. R., Wang, Y., Langenfeld, K., Duhaime, M., Wigginton, K., Poretsky, R., Avisar, D., & Wells, G. F. (2020). Microbial and Viral Communities and Their Antibiotic Resistance Genes Throughout a Hospital Wastewater Treatment System. *Frontiers in Microbiology*, *11*(February), 1–13. https://doi.org/10.3389/fmicb.2020.00153

Quttainah, M. A., & Singh, P. (2024). Barriers to Sustainable Healthcare Waste Management: A Grey Method Approach for Barrier Ranking. *Sustainability (Switzerland)*, *16*(24), 1–19. https://doi.org/10.3390/su162411285

Rahim, K., Nawaz, M. N., Almehmadi, M., Alsuwat, M. A., Liu, L., Yu, C., & Khan, S. S. (2024). Public health implications of antibiotic resistance in sewage water: an epidemiological perspective. *Bioresources and Bioprocessing*, *11*(1). https://doi.org/10.1186/s40643-024-00807-y

Ruhnke, M., Arnold, R., & Gastmeier, P. (2014). Infection control issues in patients with haematological malignancies in the era of multidrug-resistant bacteria. *The Lancet Oncology*, *15*(13), e606–e619. https://doi.org/10.1016/S1470-2045(14)70344-4

Silvester, R., Perry, W. B., Webster, G., Rushton, L., Baldwin, A., Pass, D. A., Byrnes, N. A., Farkas, K., Heginbothom, M., Craine, N., Cross, G., Kille, P., Kasprzyk-Hordern, B., Weightman, A. J., & Jones, D. L. (2025). Metagenomic profiling of hospital wastewater: A comprehensive national scale analysis of antimicrobial resistance genes and opportunistic pathogens. *Journal of Infection*, *90*(6), 106503. https://doi.org/10.1016/j.jinf.2025.106503

Sinthuchai, D., Boontanon, S. K., Piyaviriyakul, P., Boontanon, N., Jindal, R., & Polprasert, C. (2021). Fate and mass loading of antibiotics in hospital and domestic wastewater treatment plants in Bangkok, Thailand. *Journal of Water Sanitation and Hygiene for Development*, *11*(6), 959–971. https://doi.org/10.2166/washdev.2021.092

Talat, A., Bashir, Y., Khalil, N., Brown, C. L., Gupta, D., & Khan, A. U. (2025). Antimicrobial resistance transmission in the environmental settings through traditional and UV-enabled advanced wastewater treatment plants: a metagenomic insight. *Environmental Microbiome*, *20*(1). https://doi.org/10.1186/s40793-024-00658-2

Yao, S., Ye, J., Yang, Q., Hu, Y., Zhang, T., Jiang, L., Munezero, S., Lin, K., & Cui, C. (2021). Occurrence and removal of antibiotics, antibiotic resistance genes, and bacterial communities in hospital wastewater. *Environmental Science and Pollution Research*, *28*(40), 57321–57333. https://doi.org/10.1007/s11356-021-14735-3

Zhang, D., Peng, Y., Chan, C. L., On, H., Wai, H. K. F., Shekhawat, S. S., Gupta, A. B., Varshney, A. K., Chuanchuen, R., Zhou, X., Xia, Y., Liang, S., Fukuda, K., Medicherla, K. M., & Tun, H. M. (2021). Metagenomic Survey Reveals More Diverse and Abundant Antibiotic Resistance Genes in Municipal Wastewater Than Hospital Wastewater. *Frontiers in Microbiology*, *12*(August). https://doi.org/10.3389/fmicb.2021.712843

Zhang, X. X., Zhang, T., & Fang, H. H. P. (2009). Antibiotic resistance genes in water environment. *Applied Microbiology and Biotechnology*, *82*(3), 397–414. https://doi.org/10.1007/s00253-008-1829-z

Zhang, X., Yan, S., Chen, J., Tyagi, R. D., & Li, J. (2020). Physical, chemical, and biological impact (hazard) of hospital wastewater on environment: presence of pharmaceuticals, pathogens, and antibiotic-resistance genes. *Current Developments in Biotechnology and Bioengineering Analgesics*, *21*(1), 1–9. https://www.golder.com/insights/block-caving-a-viable-alternative/