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RESEARCH PAPER

Progress and gaps in antimicrobial resistance research within One Health sectors in China: a systematic analysis

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Antimicrobial resistance (AMR) presents a multifaceted health threat to humans, animals, plants, food systems, and environments. In response, China initiated extensive research to understand and address AMR. However, there has been a lack of analysis and synthesis of research results at the national level. This study establishes a national AMR knowledge repository through the systematic analysis of over 44,000 scientific publications (2000–2024), employing a machine learning framework that combines transformer-based language models and cluster analysis. Natural language processing (NLP) was used to identify key AMR research topics, subtopics, and AMR detection methods across One Health sectors, including changes over time. Main findings include: (i) China's AMR research in human health aligns with societal disease burdens, yet gaps exist for pathogens like *Clostridium difficile* and Hepatitis B virus, despite their significant risks in China. (ii) While AMR research in probiotics is increasing, potential risks of AMR transmission associated with their use are often underestimated, particularly regarding the post-marketing surveillance and standardization of probiotic products. (iii) Discovery of new antimicrobial agents and alternative therapies is crucial for AMR prevention in China. (iv) Artificial intelligence (AI) methods are promising to guide and accelerate research, including exploration of natural products and plant extracts. Overall, while the AMR research in China aligns with One Health principles, with the plant health sector surpassing global counterparts, food systems require enhanced efforts and cross-sectoral research, particularly in the development of effective AMR detection and surveillance technologies. This work demonstrates a replicable methodological framework for establishing and sustaining country-specific scientific evidence platforms, offering valuable data-driven support for synthesizing findings, decision-making, and developing current and future action plans to manage AMR from a One Health perspective.

antimicrobial resistance | China | One Health | artificial intelligence | evidence integration

INTRODUCTION

The rise of antimicrobial resistance (AMR), specifically bacterial AMR, has positioned it as a pressing public health threat (Murray et al., 2022). In 2021, bacterial AMR was directly associated with an estimated 1.14 million deaths globally (Naghavi et al., 2024). Over 711,000 deaths were associated with AMR, including 160,000 directly attributed to bacterial AMR in China in 2021 (Naghavi et al., 2024).

As the primary global producer and consumer of antibiotics (Zhang et al., 2015; Zhu et al., 2013), China is confronted with escalating AMR, often driven by the excessive and inappropriate use of antibiotics across sectors such as healthcare, agriculture, and animal husbandry (Wang, 2022; Qiao et al., 2018; Van Boeckel et al., 2015). This imprudent usage results in the widespread disposal and transmission of antibiotic residues in ecosystems. For example, in China, an estimated 53,800 tons of 36 commonly used antibiotics were released into the environment by humans and food animals in 2013 (Zhang et al., 2015). It was further estimated that approximately 56% of veterinary antibiotic residues were distributed in soils, 23% in freshwater, and 18% in seawater (Li et al., 2024b). These residues have the

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potential to exert strong selective pressure on bacterial communities in soil and water environments, resulting in the emergence and transmission of resistance (Berendonk et al., 2015). Moreover, the evolution and transmission of drug-resistant bacteria and antibiotic resistance genes (ARGs) often transcend environmental and species boundaries, thereby increasing the potential for AMR to escalate regionally and globally across One Health systems (Arnold et al., 2024; Larsson and Flach, 2022).

The Chinese government introduced its initial National Action Plan (NAP) to address AMR in 2016 (National Health and Family Planning Commission, 2016), followed by the release of the second NAP covering the period from 2022 to 2025 (National Health and Family Planning Commission, 2023). The plans fully embraced the One Health concept and encouraged collaboration among the human, agricultural, and environmental sectors, incorporating measures for managing antibiotic contamination in both agricultural and environmental sectors (Xiao and Li, 2016). However, recent studies have highlighted the necessity of monitoring and evaluating the effectiveness and cost-effectiveness of these policies (Patel et al., 2023). This is crucial for enhancing policy optimization and implementation, considering the disparities in funding allocation, political resilience, and resource constraints (such as the availability of scientific funding resources for developing new antibiotics, vaccines, and diagnostics) (Charani et al., 2023; Laxminarayan et al., 2024; Yang et al., 2024a).

One crucial aspect in addressing existing gaps is to objectively assess activities and advancements in Chinese AMR scientific research. The extensive scientific literature provides substantial evidence to guide future studies and policies, while also serving as a reference to determine whether pressing AMR issues have been adequately addressed or explored in existing research (Anderson et al., 2019; Rogers Van Katwyk et al., 2019). The importance of integrating evidence from scientific research is widely acknowledged for its potential to guide mitigation actions, identify critical surveillance targets for strategic decision-making, and translate AMR NAP objectives into practical and impactful improvements at the national level (The council of the European Union, 2023; The Quadripartite organizations, 2022; World Health Organization, 2016). However, integrating scientific evidence across One Health sectors presents challenges, particularly given the surge in AMR publications in recent years. Between 1999 and 2018, AMR publications increased by 450% (Luz et al., 2022), and in 2022 alone, there were more than twenty thousand AMR publications, with the largest proportion originating from China (Chen et al., 2024). Yet, few studies have systematically assessed AMR research progress among One Health sectors in China, necessitating urgent efforts to explore and leverage available evidence, especially considering the upcoming expiration of China's second NAP on AMR.

Here, we created a comprehensive database of AMR research in China from 2000–2024. The aim was to assess existing data, systematically summarize research progress, identify areas where substantial evidence already exists, and identify knowledge gaps to identify areas that require further research. The goal is to better direct future scientific research on AMR and support the effective implementation of current and future NAPs and policies. A transformer-based language modeling and clustering analysis was first employed to delineate a spectrum of AMR research topics. Secondly, publications across sectors were identified, pinpointing clusters of common research and changes over time between and across topics and sectors. Finally, the analysis was complemented by a detailed extraction of detection methods utilized in Chinese research.

RESULTS

Topic analysis of AMR research in China

The annual numbers of publications fit an exponential growth model (Figure S1 and Table S1) with an R^2 value of 0.96, showing a significant increase in AMR research in China. In 2000, there were only 18 publications related to AMR. By 2024, this number increased by over 390 times, with an annual growth rate of around 12.9%. The most rapid growth occurred between 2015 and 2016, with a remarkable growth rate of 99.4%. The topic modelling and clustering analysis identified eight distinct topics across all 29,159 publications (Figure 1A–C). These topics, arrayed in order from topic 1 to topic 8, include the detection of drug-resistant strains (59.4%), environmental resistome research (19.3%), antibacterials (8.6%), tuberculosis (5.9%), antivirals (2.3%), antifungals (1.9%), phylogenomics (1.4%), and *Helicobacter pylori* (1.3%).

Through similarity calculations, it was observed that topic 1 shared the most similarities with topic 2, suggesting potential overlaps in publications related to the detection of drug-resistant strains and environmental resistomes. Further, topic 2 exhibited a higher similarity with topic 7, suggesting connections and overlaps between environmental resistome research and phylogenomics. Topics 3, 4, 5, 6, and 8 were more closely aligned with topic 1, whereas less similar to other topics. These findings are logical, as most AMR-related publications involve the isolation of drug-resistant strains. Additionally, topic 3, centered on antibacterials (primarily antibiotics, see Figure 2), is closely related to topic 1 because resistant bacteria are typically the primary focus of AMR monitoring. This also explains why antifungals and antivirals appear as more isolated topics. Finally, the limited overlap of antifungals and antivirals with phylogenomics suggests the need for increased focus on phylogenetics and phylogenomics within AMR research concerning fungi and viruses.

Sub-topic analysis of AMR research across One Health sectors

The database was further segmented into distinct One Health sectors. Topic modeling and clustering analysis were conducted for each sector. The number of publications is highest in the human health sector, with a diverse range of AMR research topics observed (Figure 3). Many topics have been studied since 2000, although most human health topics exhibited increasing trends in the past five years, except for the topic "hepatitis B virus" (i.e., HBV) (Figure 4).

The animal health sector encompasses the second-highest number of subtopic types, with the topic "*E. coli* and *mcr-1*" representing the largest proportion and showing continuous growth in research activity. However, the environment sector demonstrated the most rapid expansion across most topics. For instance, from 2014 to 2024, the publication number of "drug-resistant isolates in hospitals" increased from 18 to 202, reflecting an annual growth rate of 37.2%. Similarly, the publication number of "antibiotic removal and ARGs in waste-

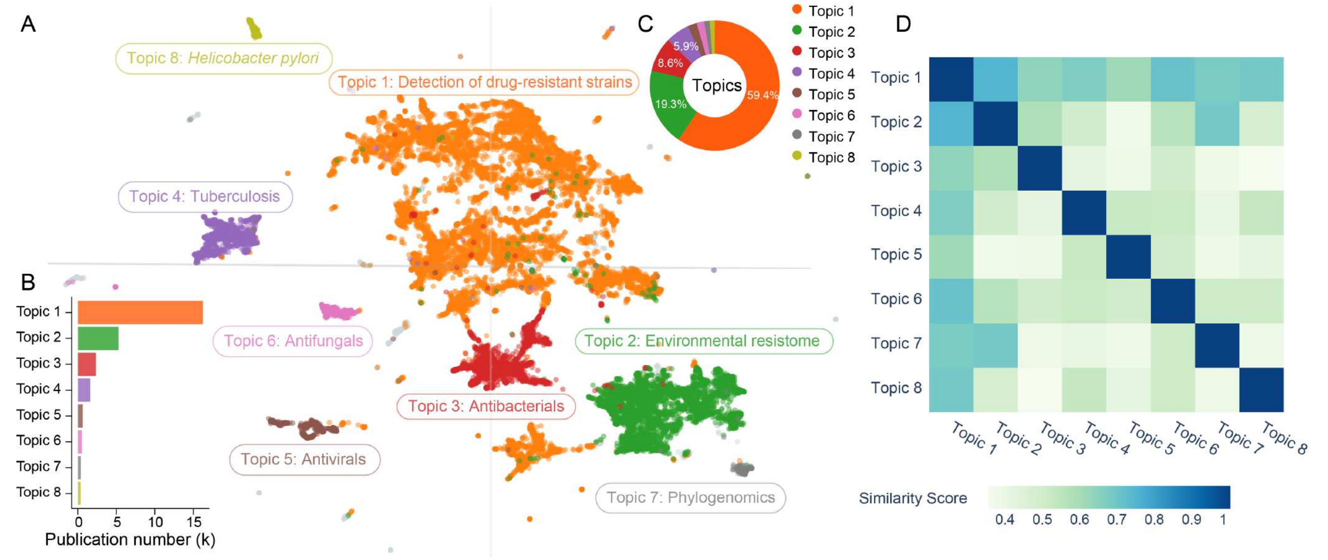


Figure 1. Topic distribution of the literature on AMR in China. A, The topic map, where points represent the positions of publications derived from the dimension reduction of embeddings into a two-dimensional space using UMAP. Different colors indicate the topic to which a publication belongs. B, The total number of publications for each topic and panel. C, The percentage of publications for each topic. D, The similarity matrix of the eight identified topics.

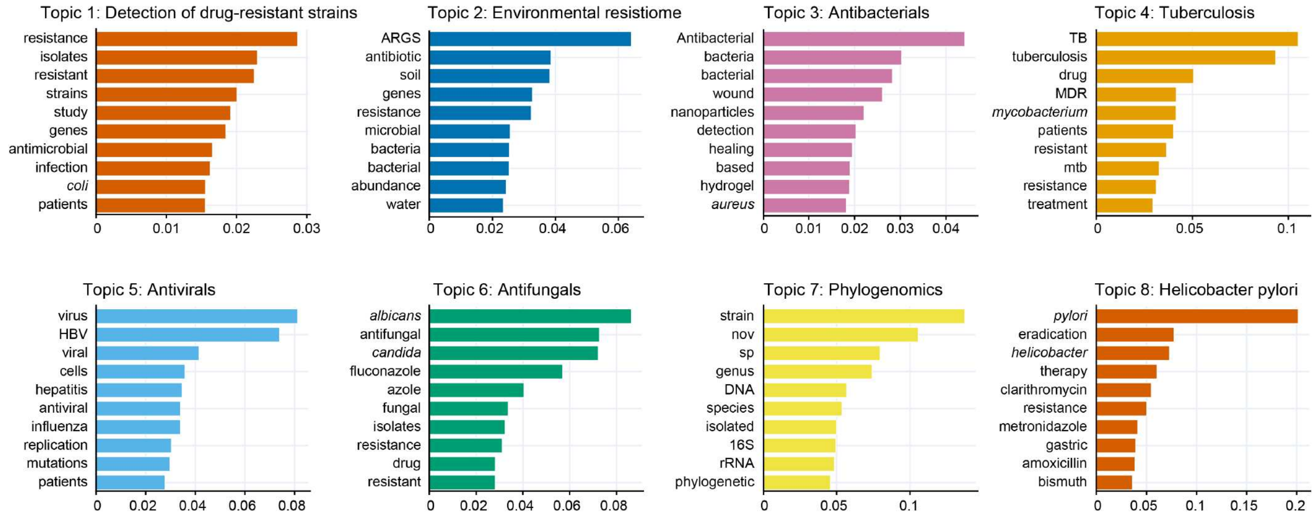


Figure 2. Representative words from the main topic maps. The horizontal axis represents the importance scores calculated using the c-TF-IDF algorithm in BERTopic, while the vertical axis lists the top 10 representative words associated with each cluster. Representative terms and detailed publication numbers of the AMR research topics are detailed in Tables S2 and S3, respectively.

water" rose from 17 to 285 during the same period, with an annual growth rate of 51.3%, indicating sustained attention in this area. In the food system sector, the number of publications was the lowest, although research on the top five subtopics increased in the last five years. Conversely, while the plant health sector encompassed 16 individual topics, a large proportion of publications were focused on "microbial community in rhizosphere". Publications related to plant health remain lower compared with other sectors, with most publications in this sector only exhibiting slight increases in recent years, showing the future research potential in this area. Detailed analysis for each sector is provided in the following sections.

Clustering analysis of human health

The human health sector was divided into 31 topics, comprising 30 distinct topics with representative content, alongside one topic labelled "others", which contained unclustered publications. The top five most abundant publications are related to "tuberculosis" (*n*=919), "ARGs in gut microbiome" (*n*=829), "*mcr-1* and carbapenem-resistant *Enterobacterales* (CRE)" (*n*=703), "carbapenem-resistant hypervirulent *Klebsiella pneumoniae* (CR-hvKP)" (*n*=566), and "methicillin-resistant *Staphylococcus aureus* (MRSA)" (*n*=378). These five topics represent a large portion of all human health-related research, and publication numbers have grown continuously since 2000 (Figure 4A). Among them, the "ARGs in gut microbiome" and "CR-hvKP" showed significant growth in publication numbers ($P<0.01$).

Drug-resistant bacterial pathogens within these topics included *Acinetobacter baumannii*, *Salmonella typhimurium*, carbapenem-resistant *Pseudomonas aeruginosa* (CRPA), as well as fungal

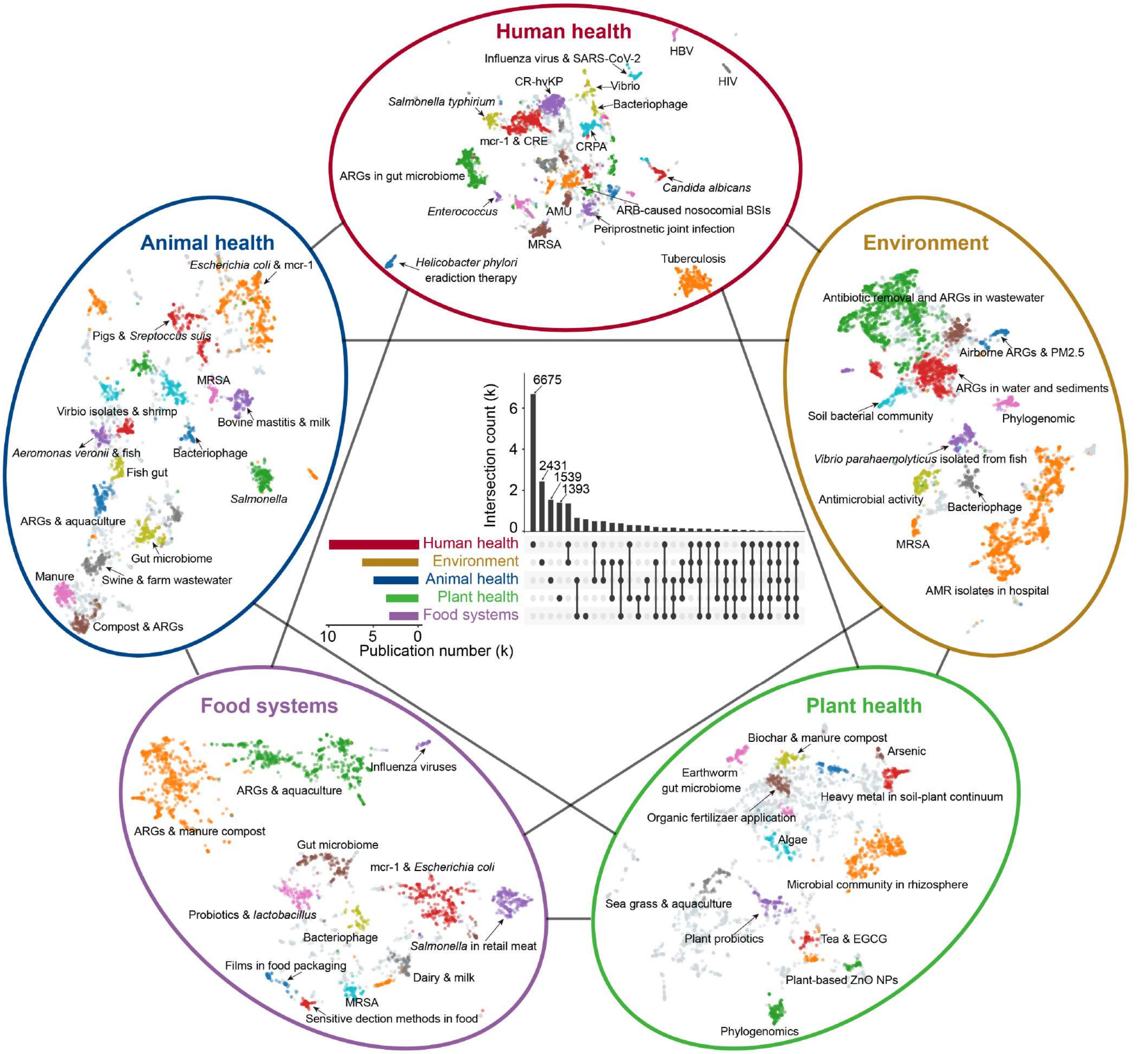


Figure 3. Subtopic distribution of the literature on AMR in China across different One Health sectors. The five panels surrounding the pentagon represent topic maps for various sectors, with points indicating the positions of publications derived from dimension reduction of embeddings into a two-dimensional space using UMAP. Different colors denote the topic to which each publication belongs. The central panel displays an UpSet plot illustrating the publication numbers for individual sectors and across sectors, with dotted lines indicating intersecting research areas. Detailed information on representative terms and publication numbers in each sector is provided in Tables S4–S8, S9–S13, respectively. Data for the UpSet plot is provided in Table S14.

pathogens like *Candida albicans*, and viruses including HBV and human immunodeficiency virus (HIV). Among these, HBV publications appeared relatively early in this research landscape, but displayed a significant decreasing trend in recent years ($P<0.01$). Top topics also covered therapy, diseases, and drug use, reflecting varied research foci related to human health. For example, antimicrobial peptides and bacteriophages (phages) have garnered considerable attention in recent human health research. *Clostridium difficile* infection was also clustered as an individual cluster, and its emergence began after 2013, showing a growing trend in recent years, albeit with a limited number of publications (Figure 4A).

The topic "metagenomics" has gained prominence in human health studies, especially after 2022 (Figure 4A). Representative terms associated with this topic include metagenomics next-generation sequencing (mNGS), pathogens, and diagnostics, indicating the potential utility of metagenomics for the detection and characterization of pathogens in human health contexts.

Clustering analysis of the environment

In the environment sector, 15 AMR topics were clustered. The primary clusters in environment research were "AMR isolates in hospital" (n=1,387), and "antibiotic removal and ARGs in wastewater" (n=1,330), followed by "ARGs in water and sediments" (n=556). Specifically, in the topic "antibiotic removal and ARGs in wastewater", the prevalent representative terms

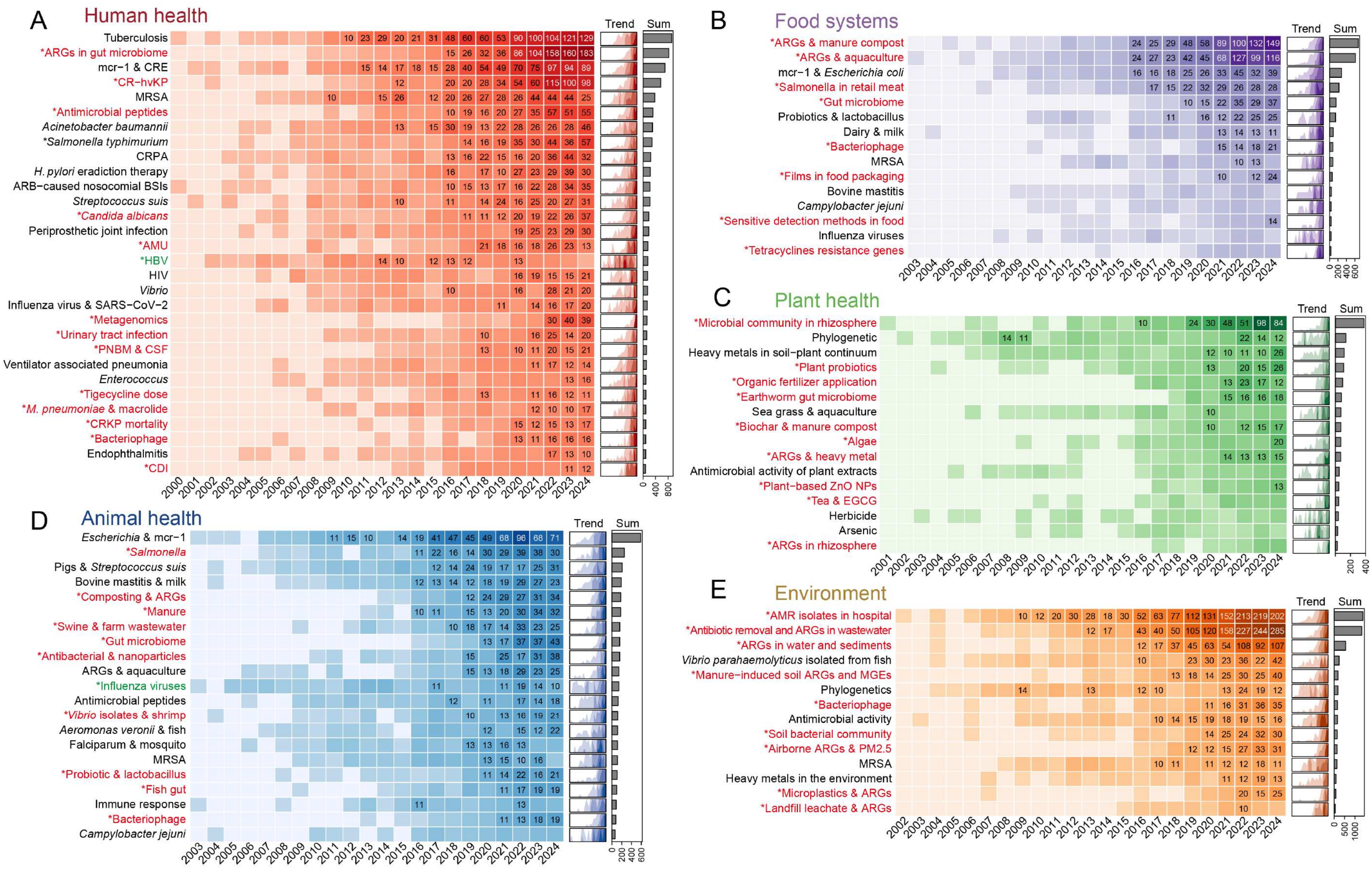


Figure 4. Heatmaps of the annual dynamics of literature on AMR in China across different One Health sectors. A–E, Represent human health, food systems, plant health, animal health, and the environment, respectively. Each panel includes a trend plot that displays overall annual dynamic patterns, while the summary plot presents the total number of publications for each topic. The topic name highlighted in red indicates a significant increase from 2000 to 2024 ($P<0.01$, Mann-Kendall trend test), while the topic name in green shows a significant decrease during the same period ($P<0.01$, Mann-Kendall trend test); topics in black denote no significant change over the years. Additionally, similarity matrices of identified topics for each sector are shown in Figures S7–S11.

include “degradation”, “disinfection”, “UV”, and “anaerobic”, indicating a diverse range of wastewater treatment procedures.

The search results also indicate that while water-related environments and hospital environments are a primary focus, a wide range of other environmental research clusters are apparent, including soil (soil ARGs and mobile genetic elements (MGEs) related to manure, and soil bacterial community), air (airborne ARGs and particulate matter $(PM)_{2.5}$), and the aquaculture environment (e.g., *Vibrio parahaemolyticus* from fish). Bacteriophages were identified as an individual topic, with a significant increase in publication numbers ($P<0.01$). Research on AMR associated with other pollutants, such as heavy metals, microplastics, and landfill leachates, was also clustered and showed a growing trend in recent years. However, research on such “co-exposure” topics remains relatively limited (Figure 4), indicating opportunities in China for future exploration. However, from the One Health perspective, much of the environment sector research is biased to human health considerations, i.e., these two sectors collectively accounted for the largest percentage in bi-sector research (Figure 3). This implies that new research opportunities exist in bi-sectoral research with other sectors, especially within the animal and plant health and food systems quadrants.

Clustering analysis of plant health

The primary AMR research focus in the plant health sector was within the soil-plant continuum. This included research on the rhizosphere (encompassing topics “microbial community in the rhizosphere” and “ARGs in the rhizosphere”, totaling 408 publications), fertilization and other soil amendments (i.e., “organic fertilizer application” and “biochar & manure compost”; n=168 in total), heavy metals in the soil-plant continuum (n=117), and the earthworm gut microbiome (n=81). Additionally, two heavy metals, cadmium (representative term in the topic “Heavy metal in the soil-plant continuum”) and arsenic (clustered as a separate topic), were addressed in the topics, with co-occurring representative terms such as soil and rhizosphere. This highlights the emphasis on the soil-plant continuum in AMR research in the plant health sector.

In addition to the soil-plant continuum, plant health research also has a focus on aquatic plants (i.e., seagrass and algae). The traditional Chinese economic crop tea was also included in the clusters, frequently associated with the term Epigallocatechin gallate (EGCG). Furthermore, the clusters highlight the phylogenomics of strains and plant probiotics from a plant microbiome perspective. Specifically, the representative words in the probiotic cluster are “*Lactobacillus plantarum*” and “fermentation”, predominantly reflecting AMR research related to the silage fermentation process. Of particular significance was the emerging topic of plant-related biosynthesis compounds, encompassing research on the antimicrobial activity of plant extracts and plant-based ZnO nanoparticles (Figure 4). However, publications in the plant health sector were lower than in the other four sectors (Figures 3 and 4). Additionally, cross-sectoral publications at the intersection of plant health and other sectors were also limited.

Clustering analysis of animal health

The animal health sector comprised 22 topics, with the largest topic being *Escherichia coli* and *mcr-1* (n=589 publications). The second largest cluster is *Salmonella*, with the representative term being *Salmonella enteritidis*. The cluster related to “pigs and *Streptococcus suis*” included representative terms such as parasuis, pleuropneumonia, and biofilm. Other clusters in animal health addressed issues pertaining to waste from animals, including manure, compost, and wastewater. The compost topic was characterized by the inclusion of ARGs and MGEs as representative terms, while the manure topic focused on terms including soil and fertilization. The wastewater topic was centered around terms including swine and livestock. These distinctions suggest a research emphasis on the management of animal waste in agricultural practices and animal breeding.

The analysis also encompassed a range of animal diseases and pathogens, including influenza viruses, *Vibrio* isolates in shrimp, *Aeromonas veronii* in fish, and *Campylobacter jejuni* in poultry. Interestingly, the topic of influenza viruses exhibited a significant declining trend in recent years ($P<0.01$). Topics related to the gut microbiome emerged as a growing trend in the past five years, consisting of two main clusters. The first cluster is “gut microbiome”, focusing on research objectives such as pigs, metagenomics, and the resistome. The second cluster is “fish gut”, primarily related to the growth and dietary research of fish. In addition, the representative terms in cluster “probiotic and *Lactobacillus*” underscored the relevance to the gut microbiome, including “bile acid”, “intestinal”, and “feces”. Overall, there was a significant emphasis on AMR in the gut microbiome within the animal health sector.

However, the results indicate that while poultry, livestock, and aquacultural animals are extensively researched in China, there is limited research on AMR in companion animals and wild animals, or research that directly intersects with human health, implying that cross-sectoral research on zoonotic diseases presents a major opportunity.

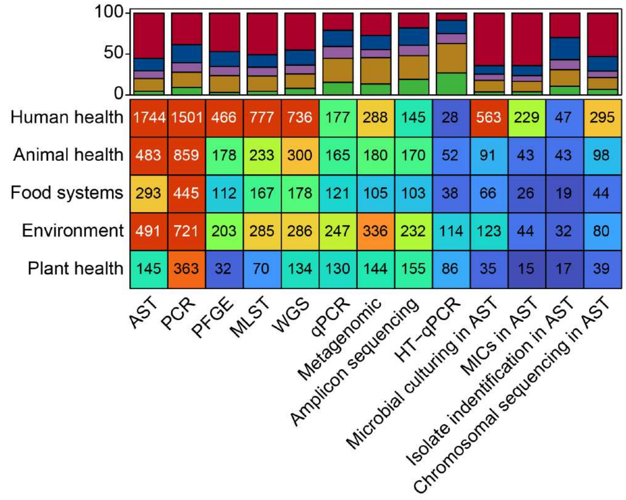
Clustering analysis of food systems

The results revealed that the total number of publications in the food systems sector was the lowest, with a total of 3,177. Research solely focused on the food system sector also ranked last in terms of publication count. The predominant focus of AMR research in food systems was related to ARGs, including topics such as “ARGs and manure compost”, “ARGs and aquaculture”, and “*mcr-1* and *Escherichia coli*”. These topics contained 1,582 publications, representing about half of all publications in this sector, and demonstrated a consistent increase in publication numbers in recent years. Additionally, specific food items were clustered, including retail meat (clustered with *Salmonella*), dairy, and milk. Clusters in food systems also encompass foodborne pathogens such as *Campylobacter jejuni* and diseases associated with food animals like influenza viruses (with representative terms including avian and poultry) and bovine mastitis (with frequently occurring representative terms like MRSA). Biofilms in food packaging were also a trending topic, with a focus on terms including chitosan, nanoparticles, antioxidants, and cellulose. Moreover, the cluster “probiotics and *Lactobacillus*” was also present in the food systems sector, with representative terms such as “Bifidobacterium”, “*Lactobacillus*”, “dairy”, and “fermentation”, indicating AMR research on probiotic supplementation in food-related contexts.

Overall, the results revealed a predominant focus on animal-related research within the food system domain, ranking as the second largest partition of the intersection of research topics (Figure 3). However, in both the food system sector and the human health sector, the publications were the fewest in the bi-sector research. Furthermore, in the food system sector, human health sector, and plant health sector, the publications were the fewest in tri-sector research. This emphasizes the presence of gaps within the One Health framework, encompassing agricultural food and fruits (plant health), contamination in food systems from the environment, and the transmission of AMR from food systems to human health, such as zoonotic diseases.

AMR detection methods across the sectors

A specific search was performed using the advanced search engine in the database to analyze detection methods. The results revealed that the most used methods in AMR research in China were the Antimicrobial Susceptibility Testing (AST) and PCR-based methods. In human health research, AST was more commonly used than other methods (Figure 5). Conversely, in the research across other sectors, PCR-based methods were predominant. In the realm of human health, whole-genome sequencing (WGS)-based methods were most prevalent, followed by the animal health and environmental sectors. It is noteworthy and problematic that a diverse range of detection methods were used in the environmental sector, suggesting a need for greater standardization (Hassoun-Kheir et al., 2021; Yin et al., 2023). Specifically, metagenomic-based methods, amplicon sequencing methods, qPCR-based methods, and high-throughput qPCR methods were most used in environmental health compared with other sectors. However, the use of AST-based methods was notably lower in the food system and plant health sectors compared with other sectors, with the total number of publications in these two sectors being less than that in others.



	AST	PCR	PFGE	MLST	WGS	qPCR	Metagenomic	Amplicon sequencing	HT−qPCR	Microbial culturing in AST	MICs in AST	Isolate indentification in AST	Chromosomal sequencing in AST
Human health	1744	1501	466	777	736	177	288	145	28	563	229	47	295
Animal health	483	859	178	233	300	165	180	170	52	91	43	43	98
Food systems	293	445	112	167	178	121	105	103	38	66	26	19	44
Environment	491	721	203	285	286	247	336	232	114	123	44	32	80
Plant health	145	363	32	70	134	130	144	155	86	35	15	17	39

Figure 5. Heatmaps of the publications containing AMR surveillance methods across different One Health sectors. The stacked histograms above the heatmap display the percentage of each method utilized in the various sectors, with colors corresponding to the One Health sectors indicated in the left legend. PCR, polymerase chain reaction; PFGE, pulsed-field gel electrophoresis; MLST, multi-locus sequence typing; qPCR, quantitative polymerase chain reaction; HT-qPCR, high-throughput quantitative polymerase chain reaction; MICs, minimum inhibitory concentrations.

DISCUSSION

The overall pattern of AMR research in China was assessed using transformer-based language models, revealing eight primary topics. Results indicated that while AMR research in China did not exhibit strong divisions among various One Health sectors, environmental resistomes and associations with human health emerged as a prominent theme. The environment sector also demonstrated a higher overlap with phylogenomics. This indicates associations between environmental resistome research and sequencing-based methods, suggesting advancements in genomic surveillance for AMR at the One Health interfaces (Muloi et al., 2023; Wheeler et al., 2023). In a broader context, AMR research in China encompassed various AMR components (antivirals, antifungals, and antibacterials) and demonstrated a clear trend towards pathogen/disease focus at the national level. Specifically, TB and *Helicobacter pylori* were the main topics in AMR research in China.

As background, TB is one of the top causes of death globally, resulting in over a million deaths annually, and it is also the primary cause of death due to drug-resistant infection (Floyd et al., 2018). In 2016, there were approximately 10.4 million cases of TB worldwide, with a substantial proportion of infectious cases resistant to rifampicin. China accounted for a significant percentage of these infection cases, ranking behind only India and Indonesia (Floyd et al., 2018). China has raised concerns regarding the control of TB and has developed a series of national tuberculosis control plans (Central Committee of the Communist Party and the State Council, 2016). Our observed clustered research showing consistent annual growth on tuberculosis-related AMR, with the representative terms in the tuberculosis topic including multidrug resistance (Figure 2), serves as evidence of the ongoing focus in this area (the annual growth of publication numbers of topics is detailed in Table S3). However, according to the WHO Global Tuberculosis Report 2024 (World Health Organization, 2024), China still faces a high burden of TB, HIV-associated TB, as well as multidrug-resistant or rifampicin-resistant TB. This underscores the importance of ongoing research on TB, aligning with the global research agenda for AMR in human health (World Health Organization, 2023). One of the top five urgent research priorities is drug-resistant TB, encompassing the study of effective preventive TB vaccines, optimal TB diagnostics, treatments, and prevention strategies.

H. pylori has been classified by the International Agency for Research on Cancer as a Group 1 carcinogen and is one of the leading causes of gastric cancer, which is the fifth most commonly diagnosed cancer and the second leading cause of cancer-related mortality worldwide (Li et al., 2023; Wang et al., 2024; Yang et al., 2021). The estimated incidence of *H. pylori* in China is 56.2%, with antibiotic-resistant *H. pylori* infections posing a considerable burden on healthcare in the country (Wang et al., 2023). However, despite being clustered in the entire database, the publication number of *H. pylori* remains relatively limited compared with other topics. Importantly, despite the fecal-oral and oral-oral transmission route for *H. pylori*, studies have demonstrated that water can serve as a reservoir for *H. pylori* transmission (Aziz et al., 2015). Consequently, infection rates may increase when individuals are exposed to contaminated water and unsanitary conditions (including the risk of contamination even in bottled mineral water (Ranjbar et al., 2016). Further, irrigated water contaminated with *H. pylori* also poses a potential risk of transmission through the food chain (Mashak et al., 2020; Yahaghi et al., 2014). These findings warrant the need for new research to understand the transmission routes and control of *H. pylori* in the environment. However, our results show a lack of research in China focusing on AMR of *H. pylori*, especially in food and environmental systems (Figure 1D).

Secondly, machine-learning-based methods were used to further characterize AMR research patterns across different One Health sectors. In our analysis, we identified several emerging topics that warrant further exploration in future AMR research. For instance, in the human health sector, ESKAPE pathogens and related resistance were widely identified. In addition to these, *Clostridium difficile*, recognized as the primary pathogen responsible for antibiotic-associated diarrhea and infectious diarrhea in healthcare facilities, emerged as a trending topic but with relatively limited publication numbers (Leffler and Lamont, 2015). The infection of *C. difficile* is acknowledged as a high-risk epidemic pathogen in the United States (Guh et al., 2020) and Europe (European Centre for Disease Prevention and Control, 2023). AMR plays a pivotal role in the evolution and epidemiological shifts of *C. difficile*, with multidrug resistance widely prevalent among the majority of epidemic strains (Putsathit et al., 2021). *C. difficile* with AMR has been classified as an urgent threat by the US Centers for Disease Control and Prevention (US Centers for Disease Control and Prevention, 2019). However, in China, the epidemiology of *C. difficile* remains underexplored. Most studies on *C. difficile* in China have been limited to regional and genotypic investigations, lacking large-scale and comprehensive studies including the analysis of drug resistance patterns (Wu et al., 2022; Zhou et al., 2019). Given the evolving epidemiological landscape and limited AMR research in *C. difficile*, additional research and surveillance are essential.

This work highlights a growing focus in China on mNGS-based methods in human health research. mNGS enables the unbiased amplification and enrichment of nucleic acids from samples, facilitating comprehensive analysis of microbial and host nucleic acids in patient samples (Chiu and Miller, 2019). One promising application of this method in AMR research is the effective detection of microorganisms and resistance genes, or mutations from microbial DNA (Gu et al., 2019; Wilson et al., 2019). It has been shown that improved mNGS-based testing will be crucial for monitoring and tracking new disease outbreaks (Chiu and Miller, 2019; Duan et al., 2025). Combining mNGS with isolation-based methods for AMR research could provide a valuable platform for detecting AMR pathogens in One Health research across different scenarios.

While much of the research in the human health sector has shown a strong correlation with societal needs, particularly in areas such as the top five subtopics of predominant and high-risk pathogens and drug-resistant pathogens, there are still several topics with limited research coverage. For instance, results showed a significant declining trend in HBV-related research (Figure 4A). Despite China's progress in meeting WHO targets for preventing new infections—illustrated by the decrease in HBsAg prevalence in the general population from 9.72% in 1992 to 5.86% in 2020, and from 9.67% to 0.30% among 1–4 year-olds (Hui et al., 2024)—an estimated 296 million people worldwide were living with hepatitis B in 2019, with approximately one-third of these cases in China (Cui et al., 2023). The large group of HBV-carrying population indicates that, beyond effectively controlling perinatal and childhood HBV infection, continuous efforts should focus on enhancing clinical treatments for individuals with HBV to reduce the risks of cirrhosis, liver cancer, and HBV-related mortality. However, recent studies reported an increase in antiviral drug resistance across HBV genotypes in different regions of China (Guo et al., 2018; He et al., 2024), which directly drives treatment failure and accelerates disease progression. This underscores the need for large-scale, genotype-specific surveillance and mechanistic studies on HBV drug resistance to guide regionally tailored treatment strategies.

The Chinese AMR research environmental sector covers a wide array of compartments, including soil, water, and air, with topics focusing on emerging pollutants, reflecting diverse research objectives in the environmental dimension. However, the results suggest that future environmental AMR work needs more cross-sectoral research involving food systems and plant health. A previous study evaluating AMR policy documents throughout China reveals that the environment sector has received less attention compared with the human and animal sectors (Yang et al., 2024b). When combining the findings from our study, it becomes evident that China not only needs to enhance the role of the environment sector in action plans but also should advocate for more One Health-based research from a policy guidance perspective. This, in turn, would offer robust scientific evidence to inform policymaking. Key evidence from our study indicates that within AMR research in China, common sites are investigated not only in the environmental sector but also in plant health, animal health, and food systems. These areas are recognized as potential sites for AMR transmission, involving wastewater and other waste from livestock farms, fertilized soils, and aquaculture farms. This emphasizes the opportunity and capacity to establish surveillance and sampling systems, particularly focusing on high-risk environmental settings under a One-Health perspective.

The results show that "probiotics" are clustered in the plant health, food system, and animal health sectors, primarily focusing on the terms "lactic" and "*Lactobacillus*". These elements represent AMR research on lactic acid bacteria. *Lactobacillus*, the largest genus within the group of lactic acid bacteria, is considered a major probiotic organism extensively utilized in agricultural practices and food industries (Giraffa et al., 2010). The lactic acid bacteria group could serve as starter and adjunct cultures for producing fermented products and contribute to agricultural systems by promoting plant health as biological insecticides and biocontrol agents. Moreover, they can be used as health supplements in livestock to enhance gut health and facilitate animal growth (Filannino et al., 2018). Nevertheless, ARGs have been detected in commercial probiotic products, including lactic acid bacteria, and the genomes of commonly used probiotic supplement species. As a result, probiotics may serve as a channel for the transmission of ARGs to opportunistic and other bacterial pathogens from animals and humans through the food chain (Imperial and Ibana, 2016; Mathur and Singh, 2005). The European Food Safety Authority (EFSA) emphasizes the need to assess the potential AMR transmission risk of probiotics used as feed additives or in production organisms. It recommends utilizing whole-genome sequencing to detect the genomic resistance profile in probiotic products (Rychen et al., 2018).

While we have observed a broad spectrum and an increasing number of studies focusing on probiotics related to AMR in China, there is only one general standard for probiotics in food established by the Chinese Institute of Food Science and

Technology (Chinese Institute of Food Science and Technology, 2022). Formal policy documents or national standards regarding the assessment and control of AMR in commercial probiotics remain limited. Furthermore, from a human health perspective, a recent study has shown that probiotics can exacerbate the expansion of the resistome in the gastrointestinal tract (Montassier et al., 2021). Therefore, it is essential to further investigate the impact on the resistome in gut health when probiotics are consumed for health purposes or in combination with antibiotic treatments.

The current strategy to address the AMR crisis entails a worldwide effort to innovate and broaden novel antimicrobial agents and more alternative therapies (Ghosh et al., 2019; Xuan et al., 2023). Antimicrobial peptides (AMPs), bacteriophages, and nanotechnologies are emerging as effective alternatives in combating AMR in bacterial pathogens (Ghosh et al., 2019). The above technologies are extensively clustered as subtopics across all five sectors in China, with the recently increasing publication numbers. Interestingly, search results show that plant extracts and AMR form a distinct cluster within the plant health sector. The utilization of extracts from various plants to synthesize nanoparticles with antibacterial activity is an emerging trend in green chemistry (Venkat Kumar and Rajeshkumar, 2018). These plant-based sources of antimicrobial agents are considered natural, nutritionally safe, and easily degradable (Li et al., 2024a). Particularly, Chinese commercial plant tea with the tea extract, EGCG, is also highlighted in a separate cluster. Research has demonstrated that EGCG is a promising treatment for multidrug-resistant pathogens (Siriphap et al., 2022), suggesting a growing interest in utilizing natural plant extracts for AMR research.

Recent advancements in artificial intelligence (AI) and machine learning have led to breakthroughs in mining the sequencing data, biomolecular properties, and structure data for designing and developing antimicrobial agents, particularly AMPs (Ma et al., 2022; Santos-Júnior et al., 2024; Wan et al., 2024). In addition to AMPs, there are studies using deep learning to effectively mine bioinformatic data to identify antibacterial phage lysins (Zhang et al., 2024b), as well as studies employing machine learning to predict the antibacterial efficacy of nanoparticles (Mirzaei et al., 2021). In the future, there will be a critical need to utilize AI for the development of antimicrobial agents in China, including harnessing more local natural extracts. While AI demonstrates transformative potential for addressing AMR, its application requires critical ethical consideration. Models trained on geographically or taxonomically biased datasets risk prioritizing pathogens prevalent in well-surveilled regions, potentially overlooking those disproportionately burdening resource-limited settings. Additionally, equitable access to novel AMR therapies remains a challenge, necessitating policy and infrastructural interventions.

Overall, the subtopic analysis offers a comprehensive overview of research trends in AMR research in China across various sectors. Each sector exhibits distinct trends regarding specific pathogens. For instance, in the animal health sector, pathogens such as *Streptococcus suis* and *Salmonella Enteritidis* from pigs (Li et al., 2021), as well as *Vibrio parahaemolyticus* isolated from fish (You et al., 2021), are clearly clustered. In the food system sector, foodborne pathogens like *Campylobacter jejuni* are clustered (Lopes et al., 2021). This underscores the importance of increased focus on emerging pathogens at the national level, but also expanded surveillance for them and associated research across different sectors. In contrast to our previous work on global AMR research patterns, which indicated that plant health had the least AMR surveillance with limited research methods (Chen et al., 2024), this study reveals that in China, AMR research in plant health is relatively substantive. This is evidenced by the utilization of a wide range of research methods, including culture-based and sequencing-based methods. For instance, the results indicated that the HT-qPCR methods were widely utilized in the environment and plant health sector, primarily in conjunction with HT-qPCR arrays developed with a wide range of primer sets targeting ARGs (Zhu et al., 2013; Zhu et al., 2017). Meanwhile, there is future potential for AMR research in the plant health sector, given that most topics are still in a growth stage (Figure 4C).

However, further development of surveillance is needed for AMR research in food systems. This is crucial considering that food production and the food commercial system serve as a primary conduit for human exposure to AMR organisms and ARGs, and the food chain also acts as a transmission pathway for the dissemination of resistance across animal and environmental domains (Shay et al., 2023). The cluster "sensitive detection methods in food" in the AMR research of the food system sector highlights this trend. On the other hand, metagenomics-based methods were predominantly clustered in the human health sector (Figure 4A) and frequently employed in human health and environment research activities (Figure 5) (Wu et al., 2024; Zhang et al., 2024a); while HT-qPCR methods demonstrated potential applicability in food systems. These results highlight the utility of detecting microorganisms and resistance genes in food health contexts.

For cross-sectoral research, our analysis (Figure 3) indicates that while human-environment and animal-food system research are prevalent in integrated studies, collaborations between human and food systems are notably lacking, particularly in tri-sectoral research (e.g., human-food-plant health). To address these gaps, we propose the following evidence-driven recommendations to advance integrated One Health research: (i) prioritize research at underrepresented cross-sectoral interfaces: allocate targeted funding to incentivize research that bridges multiple sectors, such as human health and food systems. (ii) Develop standardized protocols for cross-sectoral AMR surveillance and research: integrate various detection methods (culture-based and sequencing-based) into cohesive frameworks for monitoring AMR across sectors. This entails harmonizing sampling strategies for high-risk nodes (e.g., aquaculture farms, retail meat supply chains) to trace AMR transmission from environments, plants, food systems, to human and animal populations. (iii) Strengthen policy-research synergies and promote interdisciplinary training and collaboration: align national AMR action plans with research priorities, such as mandating AMR risk assessments for probiotic products (currently lacking in China); enhance cross-sectoral data sharing and establish platforms for collaborative initiatives across disciplines.

However, several limitations need to be acknowledged. First, all publications included in this analysis are in English, which may introduce language bias. This bias stems from the fact that primary international databases predominantly index English-language journals in the field of AMR research. In future updates, we plan to incorporate multilingual searches and ensure the translation capacity for accurate interpretation of technical terminology in Chinese as we integrate the multilingual publications. Secondly, the scientific evidence was integrated at the national level, necessitating the need for future research on more specific geographic regions or provinces across China. Additionally, an important next phase of evidence integration will involve a comprehensive evaluation of the funding, policies, and practical implementations related to AMR, ensuring the effective allocation of resources to maximize cost-effectiveness.

CONCLUSION

This study offers a comprehensive view of AMR research in China from a One Health perspective. Systematic clustering and integrated analysis rooted in transformer-based language models were utilized to address the challenge of extensive literature at the national level. Several key findings are apparent. First, from the human health perspective, most of the research aligns with the disease burden in society, particularly concerning predominant topics related to high-risk AMR pathogens. However, research on AMR related to *C. difficile* and HBV remains limited in China and disproportionately low compared with their disease burden and potential AMR risks in the country. Second, while research on AMR in probiotics is increasing across One Health sectors, the potential risk of AMR transmission associated with probiotics is not known and may be underestimated, particularly in terms of formal standardization. Therefore, work here suggests that there is an urgent need to more deeply explore the AMR risks of probiotics and establish related monitoring standards for the surveillance of probiotic products. Third, empowering the use of AI in antimicrobial agent and alternative therapy discovery is essential to address AMR in China, especially in the huge potential of natural and plant extracts.

Overall, the AMR research in China emphasizes One Health principles, with the plant health sector being more extensively researched than in many other countries. However, increased efforts and cross-sectoral research are needed in the food system sector, particularly in the development of more comprehensive and sensitive AMR detection and surveillance technologies. Further, greater research needs to be explicitly designed and integrated across sectors a priori, such as simultaneously assessing AMR in human and animal health in tandem with characterizing environmental and food supply factors that might impact health. Regardless of priorities, the analysis here demonstrates a platform potentially useful for other countries and regions to gather and synthesize scientific literature and translate it into evidence for practical application. This can better guide policymaking tailored to local research needs.

MATERIALS AND METHODS

Database construction, preprocessing, and screening

A comprehensive search string was first developed (Supporting Information) from the Scopus website to query the AMR research database, including titles, abstracts, keywords, and author and journal information. The search was restricted to publications from 2000 to 2024 and those published in English, and from sources with clear and known levels of peer review, including journal articles, reviews, and conference papers. The initial database was then filtered to include publications with corresponding author/authors' addresses only belonging to China. After removing duplicates and literature lacking necessary information, data from 44,606 publications were retained. Next, we used a machine-learning model that was trained on a human-labelled document dataset from our previous work (Chen et al., 2024) to determine the relevance to AMR with corresponding One Health sectors. Upon expert evaluation of representative terms (detailed in Topic extraction and clustering analysis) and full-text sampling, we discovered that two irrelevant topics had been mistakenly included in the dataset. One topic involved gene editing of plants to confer resistance to plant diseases (deemed irrelevant to AMR as it did not pertain to antimicrobial resistance but rather focused on enhancing plant disease resistance without antimicrobial use). The other topic was related to cancer drug resistance. After removing these publications, the final dataset contained 29,159 publications for the subsequent analysis.

Topic extraction and clustering analysis

The BERTopic method was employed to analyze the combination of title, abstract, and keywords. BERTopic is a topic modeling framework that can extract latent topics from texts, which enhances traditional topic modeling by leveraging state-of-the-art language models to capture the semantic structure of texts (Grootendorst, 2022). The core algorithm uses pre-trained transformer-based language models to create text embeddings, which are then used to generate topic representations through dimensionality reduction and clustering of these embeddings. A series of Natural Language Processing (NLP)-based methods were then applied to analyze the clusters and identify the topic representations.

Specifically, the text data was first transformed into embeddings using the sentence transformer model all-MiniLM-L6-v2 (Aarsen, 2021). After training the transformer-based model, we obtained 29,159 text embeddings, each consisting of 384 dimensions. Subsequently, the embeddings were dimensionality-reduced using the UMAP algorithm (McInnes and Healy, 2018) and then clustered using the HDBSCAN clustering algorithm integrated into BERTopic (McInnes et al., 2017). A range of NLP methods were used here, including employing the tokenization method, CountTokenizer v0.21 from scikit-learn (Pedregosa et al., 2011), to segment the texts into words. Additionally, the spaCy package was used to lemmatize the words (Ines Montani et al., 2020), converting them to their root forms. All lemmatized nouns were extracted from the text segments using spaCy's part-of-speech tagging functionality (Ines Montani et al., 2020). Subsequently, the c-TF-IDF algorithm in BERTopic was applied to calculate scores in terms of importance for each word in a cluster, identifying a set of representative words for the cluster. Human validation was then conducted to choose the hyperparameter of the topic representations for the topics. Three AMR domain experts independently evaluated the representativeness of topic labels generated with varying "top_n_words" values (10, 15, 20, 25) and collectively determined "top_n_words"=20 as the optimal parameter to balance topic coverage and specificity. Subsequently, they annotated the top 10 terms for each topic as "core", "peripheral", or "irrelevant" based on their semantic alignment with the inferred themes. Terms flagged as "irrelevant" by at least two experts were systematically replaced with the next highest-ranked c-TF-IDF terms from the same topic cluster, ensuring terminological precision. The finalized list of top 10 terms per topic was then

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derived from these validated rankings. This validated framework was first applied to the full corpus of AMR documents, then was stratified by five One Health sectors, and the same analytical workflow (embedding, clustering, c-TF-IDF term extraction, and expert validation) was iteratively applied to each sector to identify domain-specific sub-topic thematic patterns.

Statistical analysis

Following the generation of topic embeddings, pairwise similarities between topics were calculated using cosine similarity, which assesses the angular alignment between topic embedding vectors in the 384-dimensional semantic space. Descriptive analyses were then performed on publication numbers and annual trends in topics and AMR detection method occurrence. To evaluate the temporal trends in publication volume across the identified topics from 2000 to 2024, we utilized the Mann-Kendall (MK) trend test, a non-parametric statistical method, by employing the mk.test function within the R "trend" package. The MK test was used to assess the presence of a monotonic trend in annual publication numbers. The resulting test statistic (z-value) indicated the direction and magnitude of the trend: a positive z-value indicated an increasing trend, while a negative z-value indicated a decreasing trend. All analyses were conducted using Python (version 3.11) or R (version 4.1).

Compliance and ethics

The authors declare that they have no conflict of interest.

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Supporting information

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