

# Antimicrobial Resistance (AMR) to Antibiotic Therapy: An Emerging Healthcare Crisis for Treating Infective Diseases

Ashwini M Bhurre<sup>1\*</sup>, Pratibha Dawaande<sup>2</sup>, Anita Wanjari<sup>3</sup>

<sup>1</sup>Jawaharlal Nehru Medical College, Datta Meghe Institute of Higher Education and Research, deemed to be University, Sawangi (M), Wardha, 442001, India

<sup>2</sup>Datta Meghe Medical College, DMIHER (DU) Wanadongari, Hingna, Nagpur, 441110, India

<sup>3</sup>Mahatma Gandhi Ayurved College Hospital and Research Centre, DMIHER (DU), Salod(H), Wardha, 442001, India

Received: 19<sup>th</sup> Mar, 2025; Revised: 1<sup>st</sup> May, 2025; Accepted: 22<sup>nd</sup> May, 2025; Available Online: 25<sup>th</sup> Jun, 2025

## ABSTRACT

The worldwide healthcare system is facing an increasing danger from antimicrobial resistance (AMR), which is influencing antibiotic treatments and driving up healthcare expenditures. Examining the causes, progression, and mechanisms of resistance, the research highlights the need for innovative treatments, novel antibiotics, infection prevention, stewardship initiatives, and global monitoring. In order to combat AMR and guarantee the efficacy of antibiotics, cooperation between governmental bodies, healthcare providers, and academic institutions is essential.

**Keywords:** antimicrobial resistance, antibiotic therapy, healthcare crisis, antibiotic efficacy.

**How to cite this article:** Ashwini M Bhurre, Pratibha Dawaande, Anita Wanjari. Antimicrobial Resistance (AMR) to Antibiotic Therapy: An Emerging Healthcare Crisis for Treating Infective Diseases. *International Journal of Drug Delivery Technology*. 2025;15(2): 855-66. doi:10.25258/ijddt.15.2.62

**Source of support:** Nil.

**Conflict of interest:** None

## INTRODUCTION

Antibiotic resistance remains a major obstacle to our progress as we approach the dawn of a new age in health and medicine. Public health around the world is seriously threatened by this phenomenon, which is basically when bacteria develop to become resistant to the effects of antibiotics. Once heralded as "miracle medications," antibiotics have revolutionized healthcare since their discovery. They have been essential in the treatment of cancer, operations, and chronic illnesses; they have also reduced once-deadly infections to minor annoyances. The worrying global increase in germs resistant to antibiotics shows the high cost of our over-reliance on antibiotics.<sup>1</sup> Antimicrobial resistance (AMR) can have an actual and potential impact on GDP, healthcare system spending, and population health because there are fewer treatment options. These reasons make AMR a growing threat to world health. According to recent research, the prevalence of illnesses brought on by resistant microorganisms seems to be rising everywhere. In an effort to assess the financial burden of antimicrobial resistance (AMR), policymakers are increasingly basing their evaluation of AMR therapies on precise estimations of the disease's potential economic impact.<sup>2</sup>

Antibiotic resistance has been recognized as a significant public health concern by international organizations like the World Health Assembly; yet, little is known about how common it is in the majority of Southeast Asian nations. Nevertheless, addressing this issue will present significant obstacles for lawmakers and medical experts. Regional antimicrobial resistance plans have been developed by the World Health Organization in an effort to reduce the

amount of antibiotic-resistant diseases. To launch the proper initiatives, it is imperative to evaluate India's existing scenario analysis.<sup>3</sup> Antimicrobial resistance develops when antibiotics are overused, despite the fact that they are essential for treating bacterial infections and averting illnesses in agricultural settings. Food and drink contamination, environmental surfaces, and human-animal contact are all possible routes for the transmission of drug-resistant microorganisms. They are frequently the result of the misuse of antibiotics. Antimicrobial resistance must be monitored in order to identify emerging resistance and to develop and assess mitigation strategies.<sup>4</sup> A person's use of antimicrobials has been found to be influenced by their attitudes, knowledge, and beliefs regarding them throughout time. Their self-medication or asking their general practitioners for antibiotics during consultations are examples of this. Effective communication is essential for controlling the use of antibiotics and stopping the emergence of antimicrobial resistance (AMR).<sup>5</sup>

### *History of Antibiotics*

#### *Pre-Antibiotic Era*

Inadequate knowledge of germs and infectious diseases during this time period resulted in deadly outbreaks like the "Plague." The development of antibiotics dates back to 1676, when discoveries made by Lister, Pasteur, Koch, and van Leeuwenhoek propelled microbiology into the modern era.

#### *Early Antibiotic Era*

In 1893, mycophenolic acid, the first antibiotic, was found. Penicillin, Prontosil, Neosalvarsan, and Salvarsan are some more antibiotics. Gram-positive and Gram-negative bacteria are susceptible to the broad-spectrum antibacterial

action of  $\beta$ -lactam antibiotics, which include ampicillin, carbenicillin, oxacillin, and other derivatives of penicillin. Monobactams, carbapenems, and cephalosporins are some of these antibiotics.

*The Golden Age of Antibiotics*

Tyrothricin was discovered in 1939 by French scientist René Dubos, and this finding paved the way for the discovery of approximately 20 distinct antibiotic

classes. However, because of misuse and a delayed research pipeline brought on by rapid development, there aren't many novel antibiotics in clinical trials (Figure 1).

*Present Situation*

Antibiotic development is decreasing due to financial and regulatory challenges, with only 5 of 20 active pharmaceutical firms. Universities and pharmaceutical corporations are working together to create new groups and

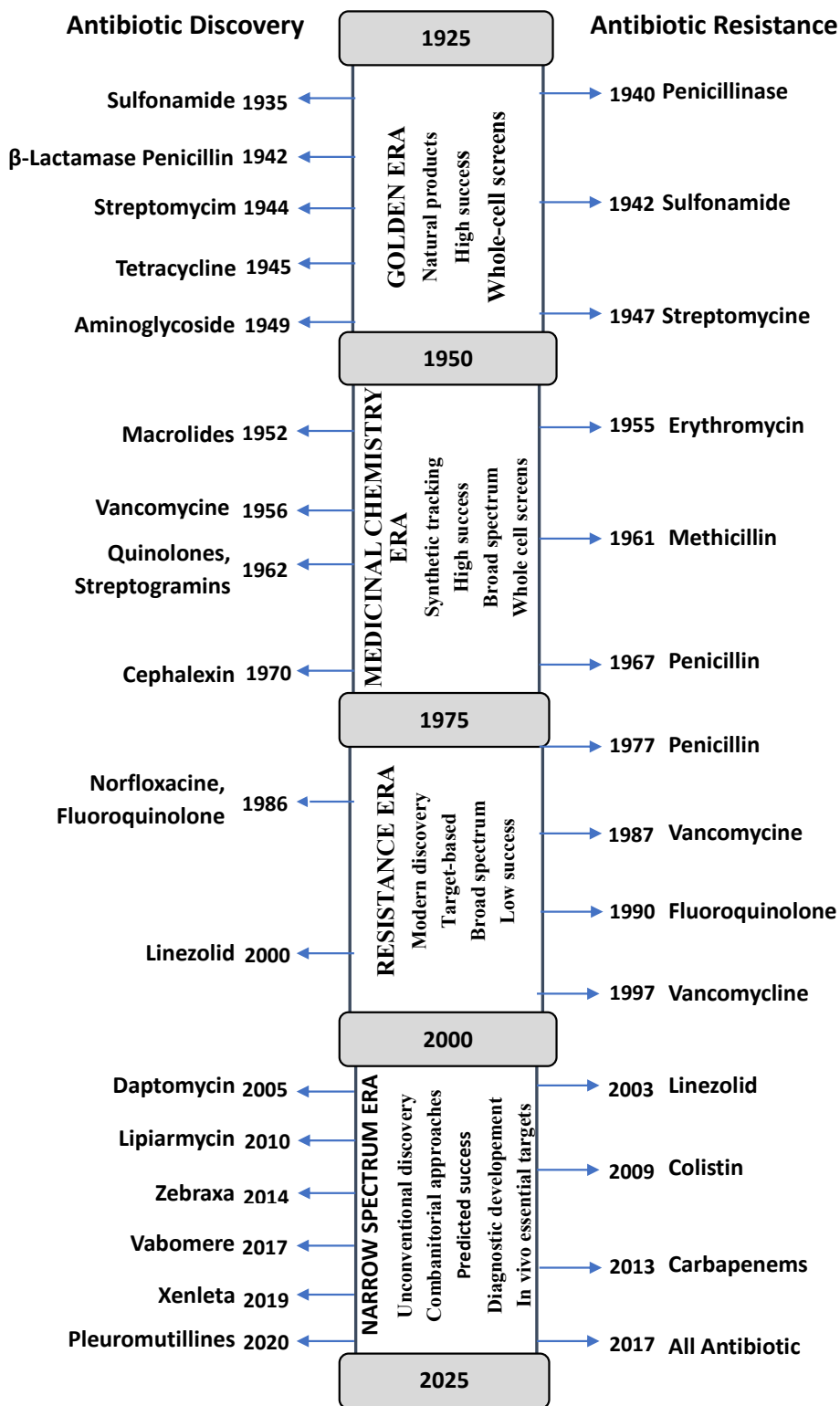


Figure 1: The timeline of important discoveries about antibiotics and antibiotic resistance

investigate alternatives such as bacteriophages and peptides in response to the growing worry over antibiotic resistance.<sup>6</sup>

#### *AMR: Economic and Medical Costs*

The significant clinical and financial costs that AMR places on patients, their families, and the healthcare system are its fault. 12 to 15 AMR claim the lives of at least 700,000 people annually. The economy will be undermined by an estimated \$100 trillion in costs by 2050 if this uncontrollable pattern persists, making it similar to the financial crisis of 2008. AMR also poses a danger to numerous SDGs, or sustainable development goals. Antibiotic resistance might cause up to 33,000 deaths annually, 8 million more hospital days, and up to \$29,000 in total patient expenses in the European Union and European Economic Area by 2050.

#### *Superbugs*

Fungi and bacteria that are resistant to many drugs are examples of superbugs—microorganisms that have shown resistance to antimicrobial medications. The morbidity and mortality rates are increased by superbugs like *Acinetobacter*, *VRE*, *MRSA*, *Pseudomonas aeruginosa*, *CRE*, and others because they are more difficult to treat, necessitate more expensive medical care, and mean longer hospital stays.<sup>7</sup>

## MATERIALS AND METHOD

A survey of the literature was done to identify research done between 2000 and 2024 that looked at how antimicrobial resistance (AMR) affected outcomes linked to *Staphylococcus aureus*, *Salmonella*, malaria, tuberculosis (TB), and hospital-acquired pneumonia. The public health

consequence associated with AMR was found to be the detrimental impact on the enhanced transmission and spread of the prolonged infection; a "clinical outcome" is defined as an unfavorable consequence that includes increased treatment failure, death, and other effects linked to antibiotic resistance<sup>8</sup>. The economic outcome was the unfavorable effect brought on by rising healthcare expenses and declining productivity as a result of antimicrobial resistance (AMR)<sup>9</sup>. The search terms "antimicrobial resistance," "malaria," "tuberculosis," "hospital-acquired pneumonia," "MRSA," "Salmonella," and "outcome impacts" were used to find relevant research in PubMed/Medline. Before the records were included in a full text examination, their titles and abstracts were checked. Subsequently, the complete texts of publications that might be pertinent were scrutinized to verify inclusion according to the eligibility standards<sup>10</sup>.

## RESULTS

An electronic database was used to search for research on the problem of antibiotic resistance. We looked through 85 publications in PubMed, Google Scholar, Web of Science, Scopus, and other databases. Among these were studies on multidrug-resistant malaria, *MRSA*, multidrug-resistant *Salmonella*, multidrug-resistant tuberculosis, and multidrug-resistant hospital-acquired pneumonia (Figure 2).

### *Antimicrobial Resistance Favors the Following Factors*

#### *Overuse of Antibiotics in General*

The main purposes of antibiotics are to stop illness and encourage healthy growth in both humans and animals. 30 to 50% of antibiotics used in people and 40 to 80% in animals are dubious and needless. 24kg of active vancomycin and 24000kg of active avoparcin were utilized as feed additives and human medication, respectively, in Denmark. Human antimicrobial resistance was lowered by avoparcin bans in Germany, Denmark, and the EU.

#### *Medical Professionals Abusing Antibiotics*

Antimicrobial resistance is developed and spreads worldwide as a result of medical professionals misusing antibiotics, especially in intensive care units. Given the scarcity of laboratory testing facilities, developing nations are especially prone to this abuse. Antibiotic-resistant bacteria may gain a competitive edge from overuse of antibiotics, so it's important to apply control measures and sensible antibiotic usage to prevent drug resistance.

#### *Misuse by the Public and Unskilled Practitioners*

Antibiotic underuse and antimicrobial resistance result from medical professionals in underdeveloped nations who are not welltrained in prescribing antibiotics for a range of conditions. Frequently just partially educated, they don't understand the consequences of abuse and don't give a damn about prescriptions that aren't right. Antibiotics are widely accessible, which leads to increased harm, and self-medication is prevalent.

#### *Low-Grade Antibiotics*

The degradation of antibiotics occurs in impoverished countries as a result of severe environments, exposure to temperatures exceeding 25°C, and expired medications. Antibiotics that are counterfeit and contain either little or no

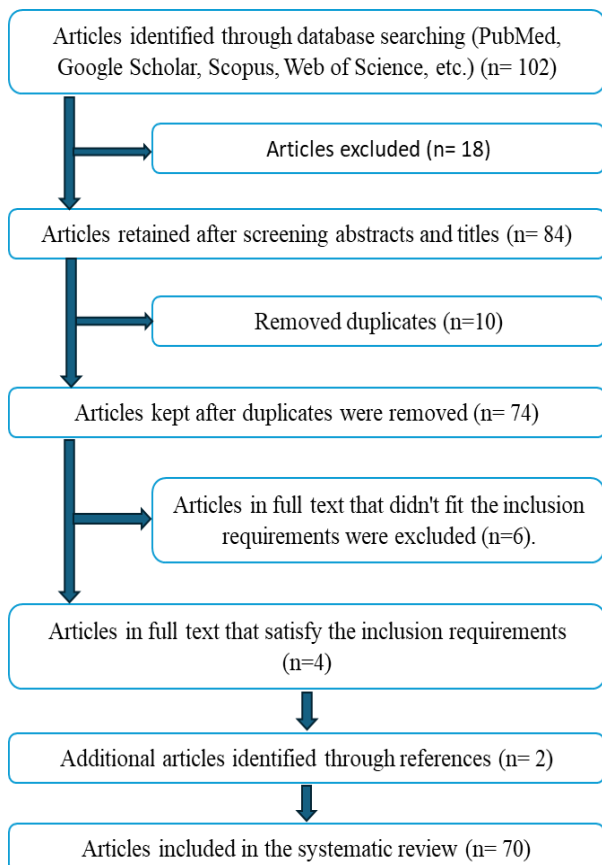


Figure 2: PRISMA Flow Chart

active ingredient have been found in nations across francophone Africa, Nigeria, Indonesia, Brazil, Thailand, Bangladesh, and Malaysia. For added potency, traditional healers combine different antibiotics.

*Rise in Foreign Travel*

Global health is at risk due to the international spread of resistant bacteria like *Neisseria gonorrhoea*, which has been brought about by increased travel.<sup>11</sup>

*Characteristics of the Gram-Positive Bacterial Antibiotic Resistance Profile*

*S. pneumoniae* and *S. pyogenes* were identified, as were most of the gram-positive isolates. A high minimum inhibitory concentration of vancomycin was present in 20% of the *S. aureus* strains; nevertheless, the proportion of

bacteria resistant to anti-*Staphylococcal* penicillins (oxycodone, cloxacillin, and methicillin) varied between 35 and 47%. There was also concerning high resistance to TMP/SMX and tetracycline, as well as doxycycline. Azithromycin was shown to be resistant in 28% of *S. pneumoniae* isolates (few isolates examined), ceftriaxone in 10%, and penicillin in 25% of isolates. Penicillin and ceftriaxone resistance in *S. pyogenes* were found to be 24% and 26%, respectively. There was evidence of *S. pyogenes* resistance to tetracycline (42%), TMP/SMX (56%), and amoxicillin/clavulanic acid (32%). Between 8 and 20% of gram-positive bacteria were vancomycin-resistant. Whereas just 8% of *enterococci* were vancomycin-resistant, most *enterococci* species showed resistance to ampicillin.

Table 1: Features of the included research on the effects of AMR on public health<sup>19-68</sup>

Sr. No.	Study organism	Outcome
<b>MULTIDRUG RESISTANT MALARIA</b>		
1.	<i>Plasmodium falciparum</i>	Drug resistance against parasite DV processes is caused by mutations in PfCRT and PfMDR1, but UPR is increased by artemisinin resistance. Reduction of resistance is possible when antithetical drugs are combined.
2.	<i>Plasmodium falciparum</i>	<i>P. falciparum</i> resistance is successfully addressed by new hybrid drugs that are based on antiretroviral therapy, indicating that hybridization may be a viable substitute for more conventional techniques.
3.	<i>Plasmodium falciparum</i>	The malaria resistance genes Pfert 76T and Pfmdr-1 86Y have declined in endemic areas, but policy changes haven't entirely eliminated them, so strong artemisinin medications are still required.
4.	<i>Plasmodium falciparum</i>	Researchers discovered that there is substantial genetic relatedness, minimal genetic variation, and a common origin for KEL1/PLA1 parasites. Since 2016, groupings with strongly correlated crt gene mutations have been identified in Cambodia, Laos, and Vietnam.
5.	<i>Plasmodium falciparum</i>	Drug-resistant forms of <i>P. falciparum</i> are threatening global progress and the usage of drugs such as piperazine and mefloquine by significantly increasing morbidity and mortality in Sub-Saharan Africa. Even though getting rid of these strains is expensive, modern information technology can help with case detection, tracking, and care.
6.	<i>Plasmodium falciparum</i>	Malaria control is seriously threatened by drug-resistant strains of the parasite, especially in Southeast Asia, where artemisinins are the drug of choice. Since mutations in pfmdr1, pfert, and the K13 gene may mediate resistance, it is essential to comprehend molecular markers, component activity, and ACT efficacy.
7.	<i>Plasmodium vivax</i>	Reduced and stopped malaria transmission is a benefit of using local knowledge and experiences learned from the past for managing the disease, particularly in low-transmission or seasonal locations.
8.	<i>Plasmodium vivax</i> , <i>Plasmodium</i> <i>ovale</i> <i>subspecies</i> , <i>Plasmodium knowlesi</i>	The risk of CQ-resistant strains makes antiviral therapy essential for achieving high cure rates and quicker clearing periods in <i>P. vivax</i> -endemic areas. Randomized controlled clinical trials are necessary because there is insufficient information regarding its efficacy in treating <i>P. ovale</i> , <i>P. malariae</i> , and <i>P. knowlesi</i> .
9.	<i>Plasmodium vivax</i>	53% of 58 sites in 129 <i>P. vivax</i> -endemic countries had chloroquine resistance, according to clinical trials, and there was a 100% association between chloroquine sensitivity and 95% of patients' clearance of parasitemia.
10.	<i>Plasmodium falciparum</i>	HIV-positive children and adults can successfully prevent and treat malaria with CTX, an antibiotic that has been used for 50 years in malaria-endemic areas; however, more research is required for non-HIV-positive people.
<b>METHYLENE RESISTANT <i>STYAPHYLOCOCCUS AUREUS</i></b>		
11.	<i>Methicillin-resistant Staphylococcus aureus (MRSA)</i>	In controlling mupirocin resistance in clinical isolates of <i>S. aureus</i> and <i>MRSA</i> , the current study highlights the importance of surveillance, carrier identification, antibiotic stewardship measures, infection control protocols, monitoring, and accurate diagnostic tests.

Table 1: Features of the included research on the effects of AMR on public health<sup>19-68</sup>

Sr. No.	Study organism	Outcome
12.	<i>Methicillin-resistant Staphylococcus aureus (MRSA)</i>	Antibiotic-resistant <i>S. aureus</i> has raised concerns about mortality worldwide, particularly in community settings. Careful screening and typing are necessary to develop resistant strains, but there is no guarantee of clinical success. People may be momentarily protected by current drugs, but healthcare systems may fail soon after.
13.	<i>Methicillin-resistant Staphylococcus aureus (MRSA)</i>	Health concerns associated with CA-MRSA transmission exist in the Asia-Pacific area, necessitating multilayer management through community action plans, antibiotic treatment, and priority control through cleanliness measures.
14.	<i>Methicillin-resistant Staphylococcus aureus (MRSA)</i>	Particularly in residential locations and pet-friendly places, MRSA is a persistent and hazardous disease. Decolonizing agents are still difficult to detect, despite the study's goal of identifying pathogenic factors. Combating this superbug will require research and development.
15.	<i>Methicillin-resistant Staphylococcus aureus (MRSA)</i>	The global proliferation of CA-MRSA, especially in densely populated, homeless-prone areas, calls for balancing antibiotic stewardship protocols with MRSA associated with purulent SSTIs.
16.	<i>Methicillin-resistant Staphylococcus aureus (MRSA)</i>	Three main lineages make up HA-MRSA, with CC88 being found in Africa. Clonal forms of CA-MRSA differ throughout continents, whereas mecC-MRSA is a sporadic strain and LA-MRSA is a very small fraction of human MRSA.
17.	<i>Methicillin-resistant Staphylococcus aureus (MRSA)</i>	Molecular epidemiology research and surveillance are needed since the CC5 subset of pandemic MRSA clones is the most common in Africa. In addition to combining MSSA genotyping with population-based surveillance, collaboration between physicians and microbiologists is advised in MRSA surveillance.
18.	<i>Methicillin-resistant Staphylococcus aureus (MRSA)</i>	Effective antibiotic control is required due to the rise in MRSA infections in different areas, which calls for increased awareness and strain monitoring due to contact with food, animals, and the environment.
19.	<i>Methicillin-resistant Staphylococcus aureus (MRSA)</i>	Vancomycin is still the best option for treating MRSA infections because of its availability, safety risks, and clinical efficacy. However, linezolid and daptomycin are other popular options. Promising new antibacterial potential is provided by experimental medications.
20.	<i>Methicillin-resistant Staphylococcus aureus (MRSA)</i> and <i>Vancomycin-resistant Enterococcus (VRE)</i>	A slow decline in the amount of time required for MRSA and VRE colonization to vanish is found in this systematic review. Inconsistent infection control policies are suggested by the data, notwithstanding uncertainties. According to the study, screening recommendations for people who are no longer colonized should be updated, and sampling bias needs to be addressed.
<b>MULTIDRUG RESISTANT SALMONELLA</b>		
21.	<i>Salmonella enterica</i>	<i>Salmonella typhoidalis</i> is the most common kind of clinical ciprofloxacin resistance caused by CyrA mutations. Finding invasive germs that are resistant to fluoroquinolones will require more investigation.
22.	<i>Salmonella enterica, S. typhi</i> and <i>S. paratyphi A</i>	Intestinal microbial resistance in <i>S. typhi</i> and <i>S. paratyphi A</i> is rising as a result of antibiotic use. This necessitates improved water and sanitation standards, GAVI guidelines, evidence-based treatment recommendations, and surveillance.
23.	<i>Non-typhoidal Salmonella (NTS)</i>	Invasive NTS infections are associated with MDR, C3G resistance, and FQNS in sub-Saharan Africa; standardized monitoring data and evidence-based treatment recommendations are necessary.
24.	<i>Salmonella enterica</i>	Global outbreaks of <i>Salmonellosis</i> have been associated with NTS, specifically with serovars <i>Typhimurium</i> , <i>Enteritidis</i> , Heidelberg, and Newport. These pathogens infiltrate hosts, elude medications, and raise hospitalization, treatment failure, and fatality rates.
25.	<i>Salmonella enterica</i>	Conjugate typhoid vaccine research is being prompted by the expectation that antimicrobial resistance in <i>S. typhi</i> will continue, resulting in treatment failure, policy changes, and greater resistance in endemic areas.
26.	<i>S. Typhi, S. Typhimurium</i> and <i>S. Enteritidis</i>	The majority of clinical ciprofloxacin resistance is caused by CyrA mutations, with typhoidal <i>Salmonella</i> being the most prevalent kind. To find invasive bacteria resistant to fluoroquinolones, more investigation is required.
27.	<i>Salmonella Typhi</i> and <i>Salmonella Paratyphi A</i>	A major global health issue is invasive <i>Salmonella</i> illness, which is brought on by typhoidal and nontyphoidal serovars. African transmission knowledge and

Table 1: Features of the included research on the effects of AMR on public health<sup>19-68</sup>

Sr. No.	Study organism	Outcome
28.	<i>Salmonella</i>	diagnostic methods impede control efforts. Use of antibiotics, hygiene, and immunizations as advised by the WHO are crucial. Antibiotic use, MDR strains, and genetic adaptation make <i>Salmonella</i> infection a global public health concern. Given the scarcity of <i>S. paratyphi</i> vaccines and enteric fever vaccines, more research is necessary.
29.	<i>Salmonella</i>	<i>Salmonella</i> strains in Ethiopia have been resistant to multiple drugs since the 1970s; ciprofloxacin may be useful in this regard, but third-generation cephalosporins are not; therefore, more research is necessary.
30.	<i>Salmonella enterica Typhi</i>	The study shows that clinical bacterial isolates have a significant incidence of antimicrobial resistance (AMR), underscoring the need for enhanced surveillance techniques to support empirical therapy in SA.
<b>MULTIDRUG RESISTANT TUBERCULOSIS</b>		
31.	Multidrug-resistant (MDR-TB)	TB MDR-TB is increasing in HIV/AIDS patients, necessitating balanced resource allocation in Asia, Europe, and Africa to prevent primary and secondary MDR-TB, especially in the elderly population.
32.	Multidrug-resistant tuberculosis (MDR-TB)	MDR-TB is a serious public health issue in Ethiopia that is more common in people who have had previous treatment. It calls for early detection, suitable therapy, and side effect prevention.
33.	Multidrug-resistant tuberculosis (MDR-TB)	Improving adherence in all patient populations—including migrants—is imperative because it is critical for lowering health outcomes and limiting the transmission of MDR-TB. However, many patients stop therapy early.
34.	Multidrug-resistant (MDR-TB)	TB The study emphasizes that bi-directional screening and co-management are necessary to prevent TB-DM co-morbidity, that strict TB treatment and follow-up are necessary for patients with diabetes mellitus (DM), and that early identification and treatment are crucial for policymakers.
35.	Multidrug-resistant (MDR-TB)	TB The prevalence of MDR-TB in Ethiopia has not changed in the last ten years, which emphasizes the necessity of implementing the DOTS program and infection control protocols effectively.
36.	Multidrug-resistant tuberculosis (MDR-TB)	MDR-TB treatment has increased dramatically during the last seven years, but methodological problems and inadequate reporting have hampered advancements. Collaboration and strong research designs are suggested for safer, more potent medications.
37.	Multidrug-resistant tuberculosis (MDR-TB)	Multidrug-resistant tuberculosis (MDR-TB) is still a serious public health concern in Ethiopia, and antituberculosis drugs constitute a key risk factor for this disease. Control may be enhanced by improving the efficacy of follow-up programs and primary TB therapy.
38.	Multidrug-resistant (MDR) tuberculosis (TB)	According to a meta-analysis, LTBI stops MDR-TB from progressing, yet few trials fit the inclusion criteria. The majority of affordable MDR-LTBI regimens involve one or two medications, and significant PZA-containing treatment dropout rates imply cost-effectiveness.
39.	Multidrug-resistant (MDR)	MDR/XDR Linezolid treats tuberculosis (TB), a global health concern, but side effects must be watched out for. Further study and particular TB recommendations are needed to achieve accessibility and cost savings.
40.	Multidrug-resistant tuberculosis (MDR-TB)	The meta-analysis indicates that MDR-TB patients have superior responses to chemotherapy and surgery; nevertheless, better design and reporting are required because of low-quality data resulting from observational design, insufficient reporting, and confounding adjustment.
<b>MULTIDRUG RESISTANT HOSPITAL ACQUIRED PNEUMONIA</b>		
41.	<i>Escherichia coli</i> , <i>Pseudomonas aeruginosa</i> , <i>Klebsiella pneumoniae</i> , and <i>Acinetobacter baumannii</i>	In acute care and hospitals, gram-negative bacteria resistance raises mortality rates and healthcare expenses. In order to address this, evidence-based antibiotic stewardship programs, effective treatment, and infection prevention are needed. Improved care can result from knowledge of local resistance patterns.
42.	<i>Methicillin susceptible S. aureus</i> , <i>Streptococcus pneumoniae</i> and <i>Haemophilus influenzae</i>	Long-term antibiotic therapy for VAP may not be beneficial due to compromised immune systems or circumstances requiring extended treatment, as shorter courses minimize antibiotic exposure and prevent relapses.

Table 1: Features of the included research on the effects of AMR on public health<sup>19-68</sup>

Sr. No.	Study organism	Outcome
43.	<i>P aeruginosa</i> and <i>ESBL+</i> , <i>MRSA</i>	According to the study, <i>MRSA</i> is the most frequent kind of pneumonia among community patients, with a low prevalence of MDR pneumonia. Risk ratings help medical providers better regulate the use of antibiotics and infection therapy.
44.	<i>S. pneumoniae</i> , <i>Haemophilus influenzae</i> , <i>Klebsiella pneumoniae</i> , <i>S. pneumoniae</i> , <i>MRSA</i> , <i>methicillin-susceptible S.</i> <i>aureus</i> , <i>P. aeruginosa</i>	The study discovered that patients with CAP and HCAP shared comparable risk indicators for CAPDRPs, and it suggested a novel guideline for drug resistance prediction based on risk factors.
45.	<i>Acinetobacter spp.</i> , <i>P. aeruginosa</i> , <i>S. aureus</i> , and <i>K. pneumoniae</i> .	In Asian adults with HAP or VAP, the incidence of <i>Acinetobacter spp.</i> , <i>P. aeruginosa</i> , <i>S. aureus</i> , and <i>K. pneumoniae</i> contributes to antibiotic resistance and rising pneumonia death rates.
46.	<i>P. aeruginosa</i> , <i>Klebsiella pneumoniae</i>	The study emphasizes the variety of HCAP patients and promotes individual assessment and tailored antibiotic therapy, treating the majority of them in a manner akin to that of CAP patients.
47.	<i>Enterobacteriaceae</i> , <i>Haemophilus influenzae</i> , <i>Staphylococcus aureus</i> , <i>Streptococcus pneumoniae</i> , <i>Candida spp.</i>	The study emphasizes the growing connection between drug-resistant disorders caused by metallo-β-lactamases, AmpC βlactamases, and ESBL and VAP. It suggests doing multicenter studies, treating MDR infections with piperacillin-tazobactam and colonistin, and treating late-onset VAP with appropriate antibiotics.
48.	<i>A. baumannii</i> , <i>P. aeruginosa</i> , <i>K. pneumoniae</i> , and <i>S. aureus</i>	Nosocomial pneumonia is a serious problem at Siriraj Hospital. It mainly affects older patients who have co-morbidities and prolonged hospital stays, which frequently leads to inadequate antimicrobial therapy.
49.	<i>Acinetobacter spp.</i> , <i>Pseudomonas aeruginosa</i>	The study, which includes rotating antibiotic therapy and educational initiatives, emphasizes the significance of quantitative ETA culture for early VAP diagnosis and MDR organism detection in critical illness units.
50.	<i>Pseudomonas aeruginosa</i> , <i>Escherichia coli</i> , <i>Klebsiella pneumoniae</i>	The research shows that longer ICU stays are associated with higher rates of high-admission acute pain (HAP), especially VAP, and antibiotic resistance-related mortality is on the rise, especially in the 26–50 age range.

#### Characteristics of the Gram-Negative Bacterial Antibiotic Resistance Profile

*P. aeruginosa*, *K. pneumoniae*, and *E. coli* are among the gram-negative bacteria that are most commonly responsible for urinary tract infections (UTIs). These bacteria frequently show resistance to antimicrobial medications, with over half of them being resistant to ceftazidime, clavulanic acid, and amoxicillin.

The Ethiopian standard treatment guideline (STG) for UTI states that most common pathogenic bacteria have a somewhat high level of resistance. It has been shown that *Shigella*, *Campylobacter*, and *Salmonella* are frequently responsible for hemorrhagic diarrhea. Penicillin G, amoxicillin, ceftriaxone, and other antibiotics are the top five medicines that cause community-acquired pneumonia. Ocular infections were primarily caused by five causal agents: *S. aureus*, *E. coli*, *S. pyogenes*, *S. pneumoniae*, and *coagulase-negative staphylococci (CONS)*. The five most common bacteria that cause middle ear infections are *Proteus spp.*, *Klebsiella spp.*, *E. coli*, *S. aureus*, and *P. aeruginosa*. Amoxicillin is the recommended antibacterial drug for treating middle ear infections, despite a 74% resistance rate.<sup>12</sup>

#### Multidrug-Resistant Microbes and their Resistant Drugs

##### Multidrug-Resistant Malaria

The management of drug-resistant malaria has emerged as a significant issue. With the exception of artemisinin and its derivatives, resistance in vivo has been documented to nearly all antimalarial medications. It has been established that *P. falciparum* and *P. vivax* are resistant to antimalarial drugs. *P. falciparum* demonstrates widespread resistance to all currently known antimalarial drugs in addition to chloroquine.<sup>13</sup> All antimalarial medications used to treat *Plasmodium falciparum* over the past 50 years have been rendered ineffective against it, including piperazine, mefloquine, quinine, sulphadoxine, pyrimethamine, and chloroquine.<sup>14</sup>

##### Multidrug-Resistant MRSA

More stable penicillins have replaced methicillin-resistant *S. aureus* since it was first described in England in 1961 (*MRSA*). It has caused *MRSA* connected to animals, hospital epidemics, and *MRSA* linked to the community. Although it was first utilized in medical settings, it has since been linked to exposure to livestock and other health problems.<sup>15</sup>

##### Multidrug-Resistant Salmonella

*Salmonella enterica* and *S. bongori* are the two main species in the genus; the former is vital to the health of both humans and animals. Both humans and animals can be harmed by specific serotypes of the intracellular pathogen *Salmonella* species. The two main serotypes of *Salmonella* that cause disease are typhoidal and nontyphoidal. Typhoidal serotypes are most often associated with typhoid fever and paratyphoid fever. Nontyphoidal serotypes are typically associated with food-borne infections such as salmonellosis. Chloramphenicol, trimethoprim, ampicillin, and other drug-resistant strains of *Salmonella* can also be resistant to other drugs.<sup>16</sup>

#### *Multidrug-Resistant Tuberculosis*

Rifampicin and isoniazid are the two cornerstones of the traditional first-line therapy for tuberculosis. Isoniazid and rifampicin are not effective against the illness referred to as "multidrug-resistant tuberculosis." The significance of this classification lies in the fact that patients in this category have much inferior treatment outcomes compared to those with tuberculosis that is either less or completely drug-resistant. Widespread resistance to tuberculosis refers to the disease's resistance to numerous medications, including any fluoroquinolone (ofloxacin or moxifloxacin), kanamycin, amikacin, and capreomycin, the three second-line injectable medications.<sup>17</sup>

#### *Multidrug Resistant Hospital Acquired Pneumonia*

In critical care units (ICUs), hospital-acquired pneumonia (HAP) is the most prevalent infection. This includes pneumonia brought on by artificial ventilation as well as severe pneumonia obtained in a hospital. Patients who have been hospitalized for at least 48 hours are more likely to experience this syndrome after 48 hours of artificial ventilation. Pathogens include *Pseudomonas aeruginosa*, *Enterobacteriaceae*, *Acinetobacter baumannii*, and *Staphylococcus aureus*.<sup>18</sup> The Features of the included research on the effects of AMR on public health are mentioned in Table 1.

## DISCUSSION

The main objective of this research was to determine which perspectives and corresponding methods have been used in recent literature to estimate the burden of AMR and what impact they have had on the burden estimates themselves. A total of 102 articles were looked up using a computer-based search engine. Specifically, PubMed, Google Scholar, Web of Science, Scopus, and other resources were searched for multidrug resistance to certain species. Following the screening process, 70 articles that met the requirements were chosen. The broad range of estimates that fit into these categories is discussed in this paper, along with the methods employed to get them. A quality assessment of the health evidence, the healthcare system, and the financial implications were also included in this exploratory study. The quality and quantity of studies on economic costs were not as good as those on health and the healthcare system. Determined that worldwide public health is seriously threatened by antibiotic resistance, which has an impact on patient outcomes, medical expenses, and death rates. Its spread is facilitated by elements such as improper use, overprescription, abuse in agriculture, and

inadequate sanitation. A comprehensive approach that incorporates education, infection control, evidence-based treatments, surveillance, and supportive legislation is required<sup>69</sup>. The One Health philosophy and international cooperation are crucial. In order to tackle antibiotic resistance, invest in healthcare infrastructure, and promote infection prevention, policymakers, healthcare professionals, and the general public must collaborate. Study concluded that antimicrobial resistance (AMR)-related increases in treatment failures, issues, and costs represent a global health concern. Strong political impetus and a concerted worldwide effort are required to prevent AMR. Developing antimicrobial stewardship, enforcing stringent antibiotic policies, enhancing microbiology procedures, surveillance, and monitoring, reducing the use of over-the-counter antibiotics, expanding access to high-quality medications and vaccines, and enforcing the law are some strategies. The various interventions in this review demonstrate that no intervention's long-term effects are assessed. As most medications have an immediate effect on knowledge gained, attitudes about more education regarding the use of antibiotics and antimicrobial resistance (AMR) have not changed much. The pandemic social media initiatives can provide insights about engagement strategy and its importance for long-term retention in subsequent interventions. Medical practice is severely challenged by antimicrobial resistance (AMR), particularly in Ethiopia, where the healthcare system primarily relies on empirical treatment. Common bacterial isolates and other antimicrobial agents are highly resistant to commonly used antibiotics. Developing guidelines for the appropriate use of antibiotics, raising community awareness of research findings, promoting rational use, updating national antimicrobial standard treatment guidelines, upgrading laboratory infrastructure, and enhancing antimicrobial stewardship programs are some of the recommendations made to address this. The development and dissemination of AMR should be the primary focus of future research. The Sustainable Development Goals (SDGs) are impacted by antibiotic resistance (AMR), a significant problem in human medicine. To monitor the effects of AMR and track interventions, a specific metric is needed. Universal health care could attract more people to sustainable development. Since government stakeholders are aware of the connection between resistance and the SDGs, they should place a high priority on combating AMR on national agendas. Antimicrobial resistance (AMR) must be prevented and mitigated, and responsible antibiotic use must be encouraged, through AMS policies and initiatives. To save medical expenses and spot resistance tendencies, healthcare professionals should take the lead in developing vaccination schedules, evidence-based policies, and public awareness campaigns. Research on the transmission of HIV, TB, and malaria has shown negative effects on clinical, public health, and economic results; therefore, investigations on *gonorrhoea* are warranted. The study emphasizes the need for more research to enhance the quality of data about the secondary effects of antibiotic resistance on healthcare, the economy, and public health. It also emphasizes the role of perspective in calculating the burden of an acute myocardial

infarction. The multiagency program NARMS offers data on enteric bacteria's resistance to antibiotics. It assists in identifying and classifying new risks to food, animals used as food, and humans. Policy, regulatory, and educational initiatives are developed using data from NARMS. Because it allows for data comparisons and hypothesis testing, the One Health approach is essential for addressing antimicrobial resistance. Acquiring comprehensive information about farm management practices facilitates the identification of focused interventions. The selective use of antibiotics combined with bacterial evolution has led to a growing public health concern: antimicrobial resistance. Since it's present in species that haven't been exposed, resistance mechanisms may be involved. Research using genomics can shed light on the biology of *enterococci* and *E. coli* and help develop novel therapeutic strategies. Studies conducted in hospitals demonstrate a wide range of antibiotic resistance, whereas community-based research is scarce. Improvements in factor determination and quantification are needed in the public healthcare delivery system. It is imperative that national strategies, standard treatment recommendations, and antimicrobial policies be strengthened. It is best to conduct research on public health issues and information and education communication at the same time<sup>70</sup>.

## CONCLUSION

Antibiotic resistance imperils public health worldwide and casts doubt on the efficacy of these "wonder drugs" that transformed contemporary medicine. The advent and dissemination of resistant bacteria is the main cause of its growth, which is attributed to misuse in both people and animals. Treatment of infections may become more difficult as a result, driving up healthcare expenses and possibly jeopardizing necessary medical treatments. Due to the urgency of the situation, several strategies, such as the following, must be used to address this complicated issue: *Encouraging Appropriate use of Antibiotics* boosting public awareness, enforcing stricter prescription guidelines, and fighting misuse in the areas of animal and human health.

*Increasing Research and Monitoring* tracking the development of new medicines and other treatments, spotting new dangers, and keeping an eye on increases in resistance.

*Improving Prevention of Infections*

In order to stop the development of resistant germs, strong hygiene measures should be implemented in communities and hospital settings.

*Encouragement of Worldwide Cooperation*

encouraging international cooperation in the battle against antibiotic resistance by exchanging knowledge, resources, and strategies.

The impact of antibiotic resistance may be lessened, and the efficacy of these vital, life-saving drugs may be maintained, if we address these problems completely and cooperatively.

## REFERENCES

1. Nabi IG, Khan M, Mubeen H. Antimicrobial Resistance: Challenges and Innovative Solutions. New

- Emirates Medical Journal. 2025 Feb 3:e02506882352704.
2. Naylor NR, Atun R, Zhu N, Kulasabanathan K, Silva S, Chatterjee A, Knight GM, Robotham JV. Estimating the burden of antimicrobial resistance: a systematic literature review. *Antimicrobial Resistance & Infection Control*. 2018 Dec;7:1-7.
3. Kumar SG, Adithan C, Harish BN, Sujatha S, Roy G, Malini A. Antimicrobial resistance in India: A review. *Journal of natural science, biology, and medicine*. 2013 Jul;4(2):286.
4. Karp BE, Tate H, Plumblee JR, Dessai U, Whichard JM, Thacker EL, Hale KR, Wilson W, Friedman CR, Griffin PM, McDermott PF. National antimicrobial resistance monitoring system: two decades of advancing public health through integrated surveillance of antimicrobial resistance. *Foodborne pathogens and disease*. 2017 Oct 1;14(10):545-57.
5. Parveen S, Garzon-Orjuela N, Amin D, McHugh P, Vellinga A. Public health interventions to improve antimicrobial resistance awareness and behavioural change associated with antimicrobial use: a systematic review exploring the use of social media. *Antibiotics*. 2022 May 16;11(5):669.
6. Uddin TM, Chakraborty AJ, Khusro A, Zidan BR, Mitra S, Emran TB, Dhama K, Ripon MK, Gajdacs M, Sahibzada MU, Hossain MJ. Antibiotic resistance in microbes: History, mechanisms, therapeutic strategies and future prospects. *Journal of infection and public health*. 2021 Dec 1;14(12):1750-66.
7. Salam MA, Al-Amin MY, Salam MT, Pawar JS, Akhter N, Rabaan AA, Alqumber MA. Antimicrobial resistance: a growing serious threat for global public health. *InHealthcare* 2023 Jul 5 (Vol. 11, No. 13, p. 1946). MDPI.
8. Helmy YA, Taha-Abdelaziz K, Hawwas HA, Ghosh S, AlKafaas SS, Moawad MM, Saied EM, Kassem II, Mawad AM. Antimicrobial Resistance and Recent Alternatives to Antibiotics for the Control of Bacterial Pathogens with an Emphasis on Foodborne Pathogens. *Antibiotics*. 2023 Jan 30;12(2):274.
9. Brown ED, Wright GD. Antibacterial drug discovery in the resistance era. *Nature*. 2016 Jan 21;529(7586):336-43.
10. Jiang T, Chen XS. Outcome impacts due to pathogen-specific antimicrobial resistance: A narrative review of published literature. *International Journal of Environmental Research and Public Health*. 2020 Feb;17(4):1395.
11. Komolafe OO. Antibiotic resistance in bacteria-an emerging public health problem. *Malawi medical journal*. 2003;15(2):63-7.
12. Berhe DF, Beyene GT, Seyoum B, Gebre M, Haile K, Tsegaye M, Boltena MT, Tesema E, Kibret TC, Biru M, Siraj DS. Prevalence of antimicrobial resistance and its clinical implications in Ethiopia: a systematic review. *Antimicrobial Resistance & Infection Control*. 2021 Dec;10:1-4.
13. Farooq U, Mahajan RC. Drug resistance in malaria. *Journal of vector borne diseases*. 2004 Dec;41(3/4):45.

14. Thu AM, Phyo AP, Landier J, Parker DM, Nosten FH. Combating multidrug-resistant *Plasmodium falciparum* malaria. *FEBS J.* 2017 Aug;284(16):2569-2578. doi: 10.1111/febs.14127. Epub 2017 Jun 30. PMID: 28580606; PMCID: PMC5575457.
15. Lee AS, De Lencastre H, Garau J, Kluytmans J, Malhotra-Kumar S, Peschel A, Harbarth S. Methicillin-resistant *Staphylococcus aureus*. *Nature reviews Disease primers.* 2018 May 31;4(1):1-23.
16. Rowe B, Ward LR, Threlfall EJ. Multidrug-resistant *Salmonella typhi*: a worldwide epidemic. *Clin Infect Dis.* 1997 Jan;24(Suppl 1):S106-9. doi: 10.1093/clinids/24.supplement\_1.s106. PMID: 8994789.
17. Millard J, Ugarte-Gil C, Moore DA. Multidrug resistant tuberculosis. *Bmj.* 2015 Feb 26;350.
18. Leone M, Bouadma L, Bouhemad B, Brissaud O, Dager S, Gibot S, Hraiech S, Jung B, Kipnis E, Launey Y, Luyt CE. Hospital-acquired pneumonia in ICU. *Anaesthesia Critical Care & Pain Medicine.* 2018 Feb 1;37(1):83-98.
19. Thu AM, Phyo AP, Landier J, Parker DM, Nosten FH. Combating multidrug-resistant *Plasmodium falciparum* malaria. *The FEBS journal.* 2017 Aug;284(16):2569-78.
20. Ocan M, Akena D, Nsohya S, Kanya MR, Senono R, Kinengyere AA, Obuku EA. Persistence of chloroquine resistance alleles in malaria endemic countries: a systematic review of burden and risk factors. *Malaria journal.* 2019 Dec;18(1):1-5.
21. Cui L, Mharakurwa S, Ndiaye D, Rathod PK, Rosenthal PJ. Antimalarial drug resistance: literature review and activities and findings of the ICEMR network. *The American journal of tropical medicine and hygiene.* 2015 Sep 9;93(3 Suppl):57.
22. Çapcı A, Lorion MM, Wang H, Simon N, Leidenberger M, Borges Silva MC, Moreira DR, Zhu Y, Meng Y, Chen JY, Lee YM. Artemisinin-(Iso) quinoline Hybrids by C- H Activation and Click Chemistry: Combating Multidrug-Resistant Malaria. *Angewandte Chemie International Edition.* 2019 Sep 9;58(37):13066-79.
23. Price RN, Von Seidlein L, Valecha N, Nosten F, Baird JK, White NJ. Global extent of chloroquine-resistant *Plasmodium vivax*: a systematic review and meta-analysis. *The Lancet infectious diseases.* 2014 Oct 1;14(10):982-91.
24. Hamilton WL, Amato R, van der Pluijm RW, Jacob CG, Quang HH, Thuy-Nhien NT, Hien TT, Hongvanthong B, Chindavongsa K, Mayxay M, Huy R. Evolution and expansion of multidrug-resistant malaria in southeast Asia: a genomic epidemiology study. *The Lancet Infectious Diseases.* 2019 Sep 1;19(9):943-51.
25. Newby G, Hwang J, Koita K, Chen I, Greenwood B, Von Seidlein L, Shanks GD, Slutsker L, Kachur SP, Wegbreit J, Ippolito MM. Review of mass drug administration for malaria and its operational challenges. *The American journal of tropical medicine and hygiene.* 2015 Jul 7;93(1):125.
26. Manyando C, Njunju EM, D'Alessandro U, Van Geertruyden JP. Safety and efficacy of co-trimoxazole for treatment and prevention of *Plasmodium falciparum* malaria: a systematic review. *PLoS one.* 2013 Feb 22;8(2):e56916.
27. Wicht KJ, Mok S, Fidock DA. Molecular mechanisms of drug resistance in *Plasmodium falciparum* malaria. *Annual review of microbiology.* 2020 Sep 8;74:431-54.
28. Visser BJ, Wieten RW, Kroon D, Nagel IM, Bèlard S, van Vugt M, Grobusch MP. Efficacy and safety of artemisinin combination therapy (ACT) for non-falciparum malaria: a systematic review. *Malaria journal.* 2014 Dec;13(1):1-8.
29. Dadashi M, Hajikhani B, Darban-Sarokhalil D, van Belkum A, Goudarzi M. Mupirocin resistance in *Staphylococcus aureus*: A systematic review and meta-analysis. *Journal of global antimicrobial resistance.* 2020 Mar 1;20:238-47.
30. Rodvold KA, McConeghy KW. Methicillin-resistant *Staphylococcus aureus* therapy: past, present, and future. *Clinical infectious diseases.* 2014 Jan 1;58(suppl\_1):S20-7.
31. Gajdács M. The continuing threat of methicillin-resistant *Staphylococcus aureus*. *Antibiotics.* 2019 May 2;8(2):52.
32. Abdulgader SM, Shittu AO, Nicol MP, Kaba M. Molecular epidemiology of Methicillin-resistant *Staphylococcus aureus* in Africa: a systematic review. *Frontiers in microbiology.* 2015 Apr 30;6:348.
33. Lakhundi S, Zhang K. Methicillin-resistant *Staphylococcus aureus*: molecular characterization, evolution, and epidemiology. *Clinical microbiology reviews.* 2018 Oct;31(4):10-128.
34. Grema HA, Geidam YA, Gadzama GB, Ameh JA, Suleiman A. Methicillin resistant *Staphylococcus aureus* (MRSA): a review. *Adv Anim Vet Sci.* 2015;3(2):79-98.
35. Aires-de-Sousa M. Methicillin-resistant *Staphylococcus aureus* among animals: current overview. *Clinical Microbiology and Infection.* 2017 Jun 1;23(6):373-80.
36. Loewen K, Schreiber Y, Kirlow M, Bocking N, Kelly L. Community-associated methicillin-resistant *Staphylococcus aureus* infection: Literature review and clinical update. *Canadian Family Physician.* 2017 Jul 1;63(7):512-20.
37. Shenoy ES, Paras ML, Noubary F, Walensky RP, Hooper DC. Natural history of colonization with methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE): a systematic review. *BMC infectious diseases.* 2014 Dec;14(1):1-3.
38. Wong JW, Ip M, Tang A, Wei VW, Wong SY, Riley S, Read JM, Kwok KO. Prevalence and risk factors of community-associated methicillin-resistant *Staphylococcus aureus* carriage in Asia-Pacific region from 2000 to 2016: a systematic review and meta-analysis. *Clinical Epidemiology.* 2018 Oct 12;12:1489-501.
39. Tack B, Vanaenrode J, Verbakel JY, Toelen J, Jacobs J. Invasive non-typhoidal *Salmonella* infections in sub-Saharan Africa: a systematic review on antimicrobial resistance and treatment. *BMC medicine.* 2020 Dec;18:1-22.

40. Britto CD, Wong VK, Dougan G, Pollard AJ. A systematic review of antimicrobial resistance in *Salmonella enterica* serovar Typhi, the etiological agent of typhoid. *PLoS neglected tropical diseases*. 2018 Oct 11;12(10):e0006779.
41. Eng SK, Pusparajah P, Ab Mutalib NS, Ser HL, Chan KG, Lee LH. *Salmonella*: a review on pathogenesis, epidemiology and antibiotic resistance. *Frontiers in Life Science*. 2015 Jul 3;8(3):284-93.
42. Jajere SM. A review of *Salmonella enterica* with particular focus on the pathogenicity and virulence factors, host specificity and antimicrobial resistance including multidrug resistance. *Veterinary world*. 2019;12(4):504.
43. Tadesse G, Tessema TS, Beyene G, Aseffa A. Molecular epidemiology of fluoroquinolone resistant *Salmonella* in Africa: A systematic review and meta-analysis. *PLoS One*. 2018 Feb 12;13(2):e0192575.
44. Akinyemi KO, Ajoseh SO, Fakorede CO. A systemic review of literatures on human *Salmonella enterica* serovars in Nigeria (1999-2018). *The Journal of Infection in Developing Countries*. 2021 Sep 30;15(09):1222-35.
45. Browne AJ, Kashef Hamadani BH, Kumaran EA, Rao P, Longbottom J, Harriss E, Moore CE, Dunachie S, Basnyat B, Baker S, Lopez AD. Drug-resistant enteric fever worldwide, 1990 to 2018: a systematic review and meta-analysis. *BMC medicine*. 2020 Dec;18:1-22.
46. Kariuki S, Gordon MA, Feasey N, Parry CM. Antimicrobial resistance and management of invasive *Salmonella* disease. *Vaccine*. 2015 Jun 19;33:C21-9.
47. Leopold SJ, van Leth F, Tarekegn H, Schultsz C. Antimicrobial drug resistance among clinically relevant bacterial isolates in sub-Saharan Africa: a systematic review. *Journal of Antimicrobial Chemotherapy*. 2014 Sep 1;69(9):2337-53.
48. Tadesse G. A meta-analysis of the proportion of antimicrobial resistant human *Salmonella* isolates in Ethiopia. *BMC Pharmacology and Toxicology*. 2014 Dec;15(1):1-9.
49. Bastos ML, Lan Z, Menzies D. An updated systematic review and meta-analysis for treatment of multidrug-resistant tuberculosis. *European Respiratory Journal*. 2017 Mar 1;49(3).
50. Sultana ZZ, Hoque FU, Beyene J, Akhlak-UI-Islam M, Khan MH, Ahmed S, Hawlader DH, Hossain A. HIV infection and multidrug resistant tuberculosis: a systematic review and meta-analysis. *BMC infectious diseases*. 2021 Dec;21(1):1-3.
51. Marks SM, Mase SR, Morris SB. Systematic review, meta-analysis, and cost-effectiveness of treatment of latent tuberculosis to reduce progression to multidrug-resistant tuberculosis. *Clinical Infectious Diseases*. 2017 Jun 15;64(12):1670-7.
52. Girum T, Muktar E, Lentiro K, Wondiye H, Shewangizaw M. Epidemiology of multidrug-resistant tuberculosis (MDR-TB) in Ethiopia: a systematic review and meta-analysis of the prevalence, determinants and treatment outcome. *Tropical diseases, travel medicine and vaccines*. 2018 Dec;4:1-2.
53. Asgedom SW, Teweldemedhin M, Gebreyesus H. Prevalence of multidrug-resistant tuberculosis and associated factors in Ethiopia: a systematic review. *Journal of pathogens*. 2018 Apr 3;2018.
54. Eshetie S, Gizachew M, Dagne M, Kumera G, Woldie H, Ambaw F, Tessema B, Moges F. Multidrug resistant tuberculosis in Ethiopian settings and its association with previous history of anti-tuberculosis treatment: a systematic review and meta-analysis. *BMC infectious diseases*. 2017 Dec;17:1-2.
55. Tegegne BS, Mengesha MM, Teferra AA, Awoke MA, Habtewold TD. Association between diabetes mellitus and multi-drug-resistant tuberculosis: evidence from a systematic review and meta-analysis. *Systematic reviews*. 2018 Dec;7:1-3.
56. Agyeman AA, Ofori-Asenso R. Efficacy and safety profile of linezolid in the treatment of multidrug-resistant (MDR) and extensively drug-resistant (XDR) tuberculosis: a systematic review and meta-analysis. *Annals of clinical microbiology and antimicrobials*. 2016 Dec;15:1-7.
57. Nellums LB, Rustage K, Hargreaves S, Friedland JS. Multidrug-resistant tuberculosis treatment adherence in migrants: a systematic review and meta-analysis. *BMC medicine*. 2018 Dec;16(1):1-1.
58. Harris RC, Khan MS, Martin LJ, Allen V, Moore DA, Fielding K, Grandjean L. The effect of surgery on the outcome of treatment for multidrug-resistant tuberculosis: a systematic review and meta-analysis. *BMC infectious diseases*. 2016 Dec;16(1):1-5.
59. Chung DR, Song JH, Kim SH, Thamlikitkul V, Huang SG, Wang H, So TM, Yasin RM, Hsueh PR, Carlos CC, Hsu LY. High prevalence of multidrug-resistant nonfermenters in hospital-acquired pneumonia in Asia. *American journal of respiratory and critical care medicine*. 2011 Dec 15;184(12):1409-17.
60. Mukhopadhyay C, Bhargava A, Ayyagari A. Role of mechanical ventilation & development of multidrug resistant organisms in hospital acquired pneumonia. *Indian Journal of Medical Research*. 2003 Dec 1;118:229-35.
61. Garcia-Vidal C, Viasus D, Roset A, Adamuz J, Verdaguer R, Dorca J, Gudiol F, Carratala J. Low incidence of multidrug-resistant organisms in patients with healthcare-associated pneumonia requiring hospitalization. *Clinical microbiology and infection*. 2011 Nov 1;17(11):1659-65.
62. Aliberti S, Cilloniz C, Chalmers JD, Zanaboni AM, Cosentini R, Tarsia P, Pesci A, Blasi F, Torres A. Multidrug-resistant pathogens in hospitalised patients coming from the community with pneumonia: a European perspective. *Thorax*. 2013 Nov 1;68(11):997-9.
63. Werarak P, Kiratisin P, Thamlikitkul V. Hospital-acquired pneumonia and ventilator-associated pneumonia in adults at Siriraj Hospital: etiology, clinical outcomes, and impact of antimicrobial resistance. *J Med Assoc Thai*. 2010 Jan 1;93(Suppl 1):S126-38.
64. Joseph NM, Sistla S, Dutta TK, Badhe AS, Rasitha D, Parija SC. Ventilator-associated pneumonia in a tertiary

- care hospital in India: role of multi-drug resistant pathogens. *The Journal of Infection in Developing Countries*. 2010 Jan 18;4(04):218-25.
65. Shindo Y, Ito R, Kobayashi D, Ando M, Ichikawa M, Shiraki A, Goto Y, Fukui Y, Iwaki M, Okumura J, Yamaguchi I. Risk factors for drug-resistant pathogens in community-acquired and healthcare-associated pneumonia. *American journal of respiratory and critical care medicine*. 2013 Oct 15;188(8):985-95.
66. Dey A, Bairy I. Incidence of multidrug-resistant organisms causing ventilator-associated pneumonia in a tertiary care hospital: A nine months' prospective study. *Annals of thoracic medicine*. 2007 Apr 1;2(2):52-7.
67. Morris S, Cerceo E. Trends, epidemiology, and management of multi-drug resistant gram-negative bacterial infections in the hospitalized setting. *Antibiotics*. 2020 Apr 20;9(4):196.
68. Majumder MA, Rahman S, Cohall D, Bharatha A, Singh K, Haque M, Gittens-St Hilaire M. Antimicrobial stewardship: Fighting antimicrobial resistance and protecting global public health. *Infection and drug resistance*. 2020 Dec 29:4713-38.
69. Gajdács M, Urbán E, Stájer A, Baráth Z. Antimicrobial resistance in the context of the sustainable development goals: A brief review. *European Journal of Investigation in Health, Psychology and Education*. 2021 Jan 19;11(1):71-82.
70. Radhouani H, Silva N, Poeta P, Torres C, Correia S, Igrejas G. Potential impact of antimicrobial resistance in wildlife, environment and human health. *Frontiers in microbiology*. 2014 Feb 5;5:23.