ISSN 2055-0286
Advances in Social Sciences Research Journal; Vol. 13 No. 11 (2026) (431-452)
https://doi.org/10.14738/assrj.1311.12734

Bacterial Pathogens: A Review of Transmissibility, Lethality, and Pandemic Potential

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Abstract: Bacterial pathogens remain a major threat to global health despite advances in sanitation, vaccination, antimicrobial therapy, infection prevention, and critical care. Unlike viral threats, bacterial disease burden is further amplified by antimicrobial resistance (AMR), which can render previously treatable infections life-threatening. Among bacterial pathogens, Mycobacterium tuberculosis poses a particularly formidable global threat, combining airborne transmission, prolonged infectiousness, a vast reservoir of latent infection, substantial mortality, and drug resistance. In 2024, tuberculosis caused an estimated 10.7 million cases and 1.23 million deaths worldwide, making it the leading cause of death from a single infectious agent. Other pathogens present distinct epidemiological and clinical threats. *V. cholerae* can cause explosive epidemics through contaminated water, particularly where sanitation and healthcare infrastructure are inadequate. *N. meningitidis*, although less readily transmitted, can cause rapidly progressive, fatal disease, with case fatality rates of approximately 10% to 15% despite appropriate treatment. Meanwhile, antimicrobial-resistant *K. pneumoniae, E. coli, A. baumannii, P. aeruginosa,* and *S. aureus* increasingly compromise the treatment of community-acquired and healthcare-associated infections. Reflecting these concerns, the World Health Organization identifies carbapenem-resistant *A. baumannii*, resistant *Enterobacterales*, and rifampicin-resistant *M. tuberculosis* as critical bacterial threats. This review critically evaluates major bacterial pathogens according to transmissibility, lethality, antimicrobial resistance, epidemic potential, and capacity to sustain widespread disease, highlighting the distinct mechanisms through which they threaten global health security.

Keywords: bacterial pathogens, antimicrobial resistance, tuberculosis, cholera, meningococcal disease, MRSA, Enterobacterales, pandemic preparedness, antibiotic resistance

INTRODUCTION

The advent of antibiotics, combined with advances in vaccination, sanitation, infection prevention, and critical care, transformed bacterial infections from major causes of mortality into increasingly preventable and treatable diseases.[1] However, these achievements have not eliminated the threat of bacterial epidemics and pandemics. Antimicrobial resistance (AMR), persistent reservoirs of infection, global mobility, and vulnerabilities in healthcare and sanitation systems continue to sustain and amplify bacterial disease burdens.[2,3]

Contemporary bacterial threats arise through distinct epidemiological mechanisms. *M. tuberculosis* sustains widespread transmission through airborne dissemination, prolonged infectiousness, and a vast reservoir of latent infection.[4] *V.*

cholerae can precipitate explosive epidemics where water and sanitation systems are compromised.[5] Meanwhile, antimicrobial-resistant Gram-negative bacteria exploit healthcare environments, invasive procedures, antibiotic selection pressure, and vulnerable patient populations, causing infections that are increasingly difficult to treat.[2,3]

The magnitude of a bacterial threat can therefore be conceptualized as a function of transmissibility, virulence, population susceptibility, antimicrobial resistance, ecological opportunity, and the effectiveness of prevention and treatment. Although these determinants also influence viral disease, bacteria present the additional challenge of horizontal gene transfer, which facilitates the dissemination of resistance determinants across bacterial populations and, in some instances, species.[6] Consequently, the next major bacterial crisis may arise not from a novel pathogen but from an established organism that becomes increasingly resistant to effective therapy.

Recognizing this threat, the World Health Organization's 2024 Bacterial Priority Pathogens List identifies 24 antibiotic-resistant pathogens across 15 bacterial families, stratified into critical, high, and medium priority categories to guide research, antimicrobial development, and public health interventions.[3]

Evaluating bacterial pandemic potential therefore requires distinguishing transmissibility, clinical lethality, and the capacity to cause sustained regional or global disease. These characteristics do not necessarily coincide, because highly transmissible organisms may have relatively low case fatality, whereas highly lethal infections may exhibit limited person-to-person transmission. AMR further complicates this relationship by increasing treatment failure and potentially worsening clinical outcomes. This review integrates these dimensions to identify bacterial pathogens posing the greatest contemporary and emerging threats to global health security.

TRANSMISSIBILITY, LETHALITY, AND TREATABILITY

The public health threat posed by a bacterial pathogen depends not only on its intrinsic biological characteristics but also on the epidemiological, environmental, and clinical conditions that govern transmission and disease outcomes. Transmissibility is influenced by the route of infection, infectious dose, environmental persistence, duration of infectiousness, population density, sanitation, vaccination coverage, and host immunity. Similarly, lethality reflects the interaction between pathogen virulence, host susceptibility, disease severity, and access to effective treatment.[7,8]

Cholera illustrates this distinction. Severe untreated infection with Vibrio cholerae can cause fatal dehydration within hours, yet timely fluid and electrolyte replacement can reduce case fatality to below 1%.[7] Thus, the observed lethality of a bacterial infection reflects not only pathogen virulence but also the capacity of healthcare systems to deliver effective treatment.

Antimicrobial resistance (AMR) introduces an additional and increasingly consequential determinant of mortality. By limiting therapeutic options, delaying effective treatment, and increasing the risk of treatment failure, AMR can transform otherwise manageable infections into life-threatening diseases. In 2019, bacterial AMR was associated with an estimated 4.95 million deaths globally, including 1.27 million directly attributable to resistance.[2] These findings underscore that the clinical threat posed by a bacterial

pathogen is not static but may increase as effective antimicrobial therapies become unavailable. Accordingly, assessing bacterial pandemic potential requires evaluating not only how efficiently a pathogen spreads and how frequently it causes death under current conditions, but also how its lethality and capacity for sustained transmission may change as antimicrobial resistance increases and healthcare systems become overwhelmed.

TUBERCULOSIS: THE GREATEST EXISTING GLOBAL BACTERIAL THREAT

Among contemporary bacterial pathogens, Mycobacterium tuberculosis represents arguably the most consequential sustained global threat, combining airborne transmission, prolonged infectiousness, a vast reservoir of latent infection, substantial mortality, incomplete vaccine protection, socioeconomic vulnerabilities, and antimicrobial resistance.4

In 2024, an estimated 10.7 million people developed tuberculosis (TB) worldwide, resulting in 1.23 million deaths, including approximately 150,000 among people living with HIV. TB remains the leading cause of death from a single infectious agent, underscoring its exceptional global burden despite the availability of effective preventive and therapeutic interventions.4

Unlike acute epidemic infections, TB can sustain transmission through prolonged, frequently unrecognized infectious disease. Moreover, individuals with latent TB infection harbor viable M. tuberculosis without clinical manifestations or infectiousness but remain at risk of subsequent progression to active disease. This extensive reservoir, compounded by delayed diagnosis, incomplete treatment, socioeconomic disparities, and drug resistance, creates persistent barriers to disease control and elimination.4,9

Multidrug-resistant and rifampicin-resistant tuberculosis (MDR/RR-TB) further intensify this threat by complicating treatment, increasing healthcare demands, and contributing to preventable mortality.[3],[4]

Tuberculosis therefore represents more than a recurring epidemic: it is an enduring global pandemic whose persistence reflects the convergence of efficient airborne transmission, latent infection, antimicrobial resistance, and structural barriers to effective prevention and treatment.

DRUG-RESISTANT TUBERCULOSIS: WHEN TRANSMISSION MEETS ANTIMICROBIAL RESISTANCE

Antimicrobial resistance substantially amplifies the global threat posed by Mycobacterium tuberculosis. Multidrug-resistant tuberculosis (MDR-TB), defined as resistance to at least isoniazid and rifampicin, and rifampicin-resistant tuberculosis (RR-TB) compromise essential first-line treatment regimens, necessitating more complex and resource-intensive therapeutic approaches.[4]

In 2024, approximately 390,000 people developed MDR/RR-TB worldwide, yet only about two in five affected individuals accessed treatment, highlighting persistent deficiencies in diagnosis, therapeutic access, and global disease control.[4]

The epidemiological significance of drug-resistant tuberculosis extends beyond treatment failure. Resistant M. tuberculosis strains can spread directly between individuals,

allowing previously untreated persons to acquire drug-resistant infection through airborne transmission. Consequently, antimicrobial resistance is not merely acquired during treatment but can become an established, transmissible characteristic of circulating bacterial strains.[10]

This convergence of airborne transmission, prolonged infectiousness, substantial mortality, and limited therapeutic options distinguishes MDR/RR-TB from many other antimicrobial-resistant infections. Reflecting its clinical and public health significance, the World Health Organization classifies rifampicin-resistant M. tuberculosis as a critical-priority pathogen in its 2024 Bacterial Priority Pathogens List.[3]

Drug-resistant tuberculosis exemplifies one of the most consequential intersections of transmissibility and antimicrobial resistance: a globally prevalent pathogen capable of transmitting resistance directly to previously uninfected individuals. Together with its extensive reservoir of infection and persistent mortality burden, these characteristics reinforce tuberculosis as arguably the greatest existing global bacterial threat.

CHOLERA: THE ARCHETYPE OF EXPLOSIVE BACTERIAL EPIDEMIC DISEASE

V. cholerae represents a distinct but equally important model of bacterial epidemic potential. Unlike tuberculosis, which spreads predominantly through airborne transmission, cholera is transmitted through contaminated water and food, enabling rapid, large-scale outbreaks when water, sanitation, and public health infrastructure deteriorate.[7]

The World Health Organization estimates that cholera causes approximately 1.3 to 4 million cases and 21,000 to 143,000 deaths annually worldwide.[7] Outbreaks disproportionately affect populations experiencing unsafe drinking water, inadequate sanitation, armed conflict, displacement, natural disasters, and humanitarian emergencies. These conditions facilitate widespread exposure and can overwhelm already fragile healthcare systems.[7,11]

Cholera is particularly dangerous because of its rapid clinical progression. Severe infection can produce profuse watery diarrhea, profound electrolyte depletion, hypovolemic shock, and death within hours if untreated. Nevertheless, prompt oral or intravenous rehydration can dramatically reduce mortality, with case fatality rates expected to remain below 1% in adequately functioning treatment centers.[7] Thus, cholera demonstrates how epidemic magnitude and observed lethality are profoundly influenced by environmental conditions, healthcare capacity, and timely access to treatment.

Unlike pathogens dependent primarily on sustained person-to-person respiratory transmission, epidemic *V. cholerae* can exploit shared contaminated water sources to expose large populations within a short period. This environmental amplification, combined with rapid disease progression and infrastructure vulnerability, makes cholera particularly capable of generating explosive regional epidemics.[11,12]

Importantly, cholera remains an ongoing pandemic threat rather than a historical disease. The seventh cholera pandemic, which began in 1961, continues to cause outbreaks across multiple continents, demonstrating the persistence of waterborne bacterial transmission despite the availability of effective prevention and treatment.[7,12]

Cholera therefore exemplifies a bacterial threat driven less by intrinsic lethality than by the convergence of rapid environmental transmission, infrastructure failure, and inadequate access to lifesaving treatment.

YERSINIA PESTIS: THE HISTORICAL BENCHMARK FOR BACTERIAL PANDEMIC CATASTROPHE

Y. pestis, the causative agent of plague, remains a defining historical example of bacterial pandemic devastation. The Black Death of the 14th century demonstrated the catastrophic consequences of widespread bacterial transmission in populations lacking effective antimicrobial therapy, surveillance, and coordinated public health interventions.[13]

Plague persists in natural rodent reservoirs and is transmitted to humans primarily through infected fleas or contact with infected animals. Of its principal clinical manifestations, pneumonic plague poses the greatest direct human-to-human transmission risk because respiratory infection permits spread through infectious droplets during close contact. Untreated pneumonic plague can progress rapidly to respiratory failure, sepsis, and death, sometimes within 24 to 48 hours of symptom onset.[14]

Despite its exceptional historical lethality, the contemporary pandemic potential of *Y. pestis* is substantially constrained by effective antibiotics, improved surveillance, vector control, and established outbreak containment measures. Early diagnosis and antimicrobial treatment markedly improve survival, while prompt identification, isolation, contact tracing, and appropriate postexposure prophylaxis can interrupt pneumonic transmission.[14,15] Nevertheless, delayed recognition, inadequate healthcare access, and failures in outbreak response can still permit severe localized epidemics.

Plague therefore illustrates the distinction between historical pandemic devastation and contemporary pandemic risk: although *Y. pestis* retains substantial intrinsic virulence and the capacity for respiratory transmission, effective treatment and public health interventions greatly reduce its potential for sustained global spread.

NEISSERIA MENINGITIDIS: RAPID LETHALITY DESPITE MODERN TREATMENT

N. meningitidis presents a distinct bacterial threat characterized by respiratory transmission, asymptomatic nasopharyngeal carriage, and potentially fulminant invasive disease. Transmission occurs primarily through close or prolonged exposure to respiratory or oropharyngeal secretions, particularly in crowded settings and populations with limited immunity. Although colonization is frequently asymptomatic, invasive infection can develop abruptly and progress to life-threatening meningitis or meningococcemia within hours.[16]

Despite effective antimicrobial therapy, invasive meningococcal disease carries an estimated case fatality rate of 10% to 15%, with particularly high mortality associated with meningococcemia and septic shock. Among survivors, approximately 20% experience long-term complications, including neurological impairment, hearing loss, limb loss, or other permanent disabilities.[16,17] These outcomes underscore the importance of early recognition and immediate treatment, as irreversible injury may develop before definitive microbiological diagnosis.

Unlike tuberculosis or cholera, meningococcal disease generally requires close contact for transmission and does not typically sustain widespread transmission through casual exposure. Nevertheless, outbreaks can occur in congregate settings and susceptible populations, particularly where vaccination coverage is inadequate. Effective vaccines targeting major disease-causing serogroups substantially reduce the risk of invasive disease and associated epidemics, although protection varies by serogroup and vaccine formulation.[16,18]

Meningococcal disease therefore exemplifies a pathogen whose principal threat lies not in exceptional transmissibility but in its capacity to cause rapidly progressive, frequently fatal invasive infection. Its epidemic potential is greatest where susceptible populations, close-contact transmission, and insufficient vaccine-derived immunity converge.

STAPHYLOCOCCUS AUREUS AND MRSA: THE ADAPTABLE OPPORTUNIST

S. aureus represents a distinct model of bacterial pathogenic success, combining widespread asymptomatic colonization, diverse virulence mechanisms, and the capacity to cause infections ranging from localized skin and soft tissue disease to life-threatening pneumonia, endocarditis, osteomyelitis, bloodstream infection, and sepsis.[19] Its ability to persist in human populations and exploit disruptions in host defenses makes it a major cause of community-acquired and healthcare-associated infections.

The emergence and dissemination of methicillin-resistant *S. aureus* (MRSA) have intensified this threat by limiting conventional ß-lactam treatment options and complicating the management of invasive infections. MRSA spreads through direct contact, contaminated surfaces, and healthcare-associated transmission networks, while asymptomatic carriage provides a persistent reservoir for subsequent infection and dissemination.[19,20] Reflecting its clinical and public health significance, the World Health Organization classifies MRSA among its high-priority antimicrobial-resistant bacterial pathogens.[3]

Unlike pathogens associated with explosive epidemics, MRSA illustrates how sustained colonization, recurrent transmission, and antimicrobial resistance can produce a substantial cumulative disease burden without widespread, simultaneous outbreaks. Its clinical impact is amplified by invasive medical procedures, indwelling devices, immunocompromised hosts, and persistent transmission within healthcare and community settings.[19,20]

MRSA therefore exemplifies a bacterial threat driven primarily by endemic persistence, clinical adaptability, and antimicrobial resistance rather than explosive pandemic transmission. Its significance lies in the capacity to sustain serious infections and preventable mortality across diverse populations despite established infection prevention measures and available therapeutic alternatives.

CARBAPENEM-RESISTANT ENTEROBACTERALES: THE SILENT AMR PANDEMIC

Carbapenem-resistant *Enterobacterales* (CRE), particularly resistant strains of K. pneumoniae and Escherichia coli, represent one of the most consequential emerging threats to global health. These organisms cause urinary tract infections, pneumonia, intra-abdominal infections, bloodstream infections, neonatal sepsis, and other potentially fatal

invasive diseases. Their clinical significance is amplified by resistance to carbapenems, a critically important class of antibiotics used to treat severe infections caused by multidrug-resistant Gram-negative bacteria.[21,22]

The World Health Organization's 2024 Bacterial Priority Pathogens List classifies carbapenem-resistant and third-generation cephalosporin-resistant Enterobacterales as critical-priority pathogens, reflecting their substantial disease burden, resistance prevalence, and therapeutic challenges.[3] Although newer antimicrobial agents have expanded treatment options for certain resistant infections, therapeutic effectiveness remains dependent on the underlying resistance mechanisms, pathogen susceptibility, and access to appropriate treatment.[22]

Unlike classical epidemic pathogens, CRE can disseminate through asymptomatic gastrointestinal colonization, healthcare-associated transmission, contaminated environments, and international movement of colonized or infected individuals. Particularly concerning is the horizontal transfer of mobile genetic elements encoding carbapenemases, including KPC, NDM, and OXA-48-like enzymes, which facilitates the spread of resistance determinants among bacterial strains and species.[21,23] This convergence of persistent colonization, genetic adaptability, and limited therapeutic options enables resistance to propagate across healthcare systems and geographic boundaries, often without conspicuous epidemic outbreaks.

CRE therefore exemplify a global bacterial threat driven not by explosive transmission but by the progressive dissemination of antimicrobial resistance across interconnected human, healthcare, and environmental reservoirs. Their emergence illustrates how common bacterial pathogens can acquire increasingly consequential clinical and epidemiological significance as resistance spreads, potentially undermining the effectiveness of modern antimicrobial therapy.

ACINETOBACTER BAUMANNII: A CRITICAL HEALTHCARE THREAT

Carbapenem-resistant Acinetobacter baumannii (CRAB) represents a major antimicrobial-resistant threat, particularly in hospitals and intensive care units. This opportunistic pathogen causes ventilator-associated pneumonia, bloodstream infections, wound infections, and sepsis, disproportionately affecting critically ill, immunocompromised, and mechanically ventilated patients. Its ability to survive for prolonged periods on environmental surfaces, colonize patients and medical equipment, and persist despite infection control measures facilitates healthcare-associated transmission and recurrent outbreaks.[24,25]

CRAB is particularly concerning because extensive antimicrobial resistance, limited therapeutic options, and severe underlying illness contribute to substantial morbidity and mortality. Although newer treatment strategies have improved management, therapeutic choices remain constrained, particularly for invasive infections caused by highly resistant strains.[22,25] Reflecting these challenges, the World Health Organization classifies CRAB as a critical-priority pathogen in its 2024 Bacterial Priority Pathogens List.[3]

Unlike tuberculosis or cholera, A. baumannii has limited capacity for sustained transmission among healthy community populations. Its epidemiological success instead depends on environmental persistence, transmission through contaminated hands and

equipment, invasive medical interventions, and the concentration of susceptible patients within healthcare facilities.[24,25] Consequently, its greatest threat arises where antimicrobial resistance converges with intensive healthcare exposure and compromised host defenses.

CRAB therefore exemplifies a pathogen with comparatively limited community transmissibility but substantial healthcare-associated transmission, extensive antimicrobial resistance, and potentially high mortality in vulnerable patients. Its global significance lies primarily in persistent healthcare-associated outbreaks and the progressive erosion of effective treatment options rather than conventional pandemic spread.

PSEUDOMONAS AERUGINOSA: RESISTANCE IN THE MOST VULNERABLE PATIENTS

P. aeruginosa is a highly adaptable opportunistic pathogen responsible for severe healthcare-associated infections, particularly among critically ill, immunocompromised, mechanically ventilated, and burn patients, as well as individuals with chronic pulmonary disease or invasive medical devices. Its capacity to colonize moist environments, form biofilms, and exploit compromised host defenses contributes to persistent infections, healthcare-associated outbreaks, and substantial morbidity and mortality.[26,27]

The clinical threat posed by *P. aeruginosa* is amplified by intrinsic antimicrobial resistance and its ability to acquire additional resistance through chromosomal mutations and horizontal gene transfer. These mechanisms, including reduced membrane permeability, multidrug efflux systems, ß-lactamase production, and biofilm-associated tolerance, can severely restrict therapeutic options and complicate treatment of invasive infections.[26,27] Recognizing this threat, the World Health Organization classifies carbapenem-resistant *P. aeruginosa* as a high-priority pathogen in its 2024 Bacterial Priority Pathogens List.[3]

Unlike pathogens capable of sustained transmission throughout the general population, *P. aeruginosa* derives much of its clinical significance from its ability to exploit vulnerabilities created by advanced medical care. Intensive care, organ transplantation, chemotherapy, mechanical ventilation, invasive surgery, and implanted devices increase opportunities for infection, particularly when antimicrobial resistance limits effective treatment.[26,27] Thus, the global threat posed by *P. aeruginosa* lies primarily in its ecological adaptability, antimicrobial resistance, and capacity to cause life-threatening infections in medically vulnerable populations rather than explosive community transmission. Its persistence underscores a broader consequence of AMR: the progressive erosion of antimicrobial effectiveness threatens not only the treatment of bacterial infections but also the safety of essential modern medical interventions.

SALMONELLA TYPHI: A PERSISTENT ENTERIC THREAT

Salmonella enterica serovar Typhi, the causative agent of typhoid fever, remains a major enteric bacterial threat, particularly in regions with inadequate sanitation, unsafe drinking water, and limited healthcare access. Transmitted primarily through the fecal-oral route, *S. Typhi* causes systemic infection that can progress to intestinal hemorrhage, perforation, sepsis, and death without timely treatment. Unlike cholera, which primarily causes acute secretory diarrhea, typhoid fever is an invasive systemic disease capable of prolonged illness and serious complications.[28,29]

The emergence of multidrug-resistant and extensively drug-resistant *S. Typhi* has substantially complicated treatment and intensified concerns about international dissemination. Resistance to historically effective antibiotics, including fluoroquinolones and third-generation cephalosporins, can restrict therapeutic options and increase the risk of treatment failure.[29,30] Reflecting this threat, the World Health Organization classifies fluoroquinolone-resistant *S. Typhi* among its high-priority bacterial pathogens.[3]

The epidemiological persistence of typhoid is further supported by asymptomatic chronic carriers, who can shed bacteria and sustain transmission despite the absence of clinical disease. International travel and population movement can facilitate the geographic spread of resistant strains, while inadequate sanitation perpetuates exposure in endemic communities.[28,30] Although improved water and sanitation infrastructure, vaccination, and effective antimicrobial therapy can substantially reduce disease burden, their uneven availability sustains the risk of outbreaks and continued transmission.

Typhoid fever therefore exemplifies the convergence of sanitation-dependent transmission, persistent human reservoirs, and escalating antimicrobial resistance. Its principal global threat lies in sustained endemic transmission and the international dissemination of increasingly resistant strains rather than explosive pandemic spread.

SHIGELLA: HIGH TRANSMISSIBILITY AT A LOW INFECTIOUS DOSE

Shigella species represent an important enteric bacterial threat distinguished by an exceptionally low infectious dose, with as few as 10 to 100 organisms potentially sufficient to establish infection. This characteristic facilitates efficient fecal-oral transmission through direct person-to-person contact, contaminated food or water, and sexual contact, particularly in crowded settings and populations with inadequate sanitation.[31,32]

Shigellosis typically causes acute inflammatory diarrhea, often accompanied by fever, abdominal cramping, and dysentery. Although most infections are self-limited or respond to appropriate treatment, severe disease can cause dehydration, systemic complications, and death, particularly among young children, malnourished individuals, and immunocompromised patients.[31]

The emergence of multidrug-resistant and extensively drug-resistant Shigella has intensified its clinical and epidemiological significance. Resistance to commonly prescribed antibiotics, including fluoroquinolones, azithromycin, and third-generation cephalosporins, can complicate treatment and prolong bacterial shedding, potentially facilitating further transmission.[32,33] Reflecting these concerns, the World Health Organization classifies fluoroquinolone-resistant Shigella among its high-priority bacterial pathogens.[3] Unlike pathogens requiring substantial environmental exposure or prolonged respiratory contact, Shigella can spread efficiently through relatively limited fecal contamination. Its low infectious dose, asymptomatic or minimally symptomatic shedding, international mobility, and expanding antimicrobial resistance create opportunities for recurrent outbreaks across community and institutional settings.

Shigella therefore exemplifies a bacterial threat in which a low infectious dose, efficient person-to-person transmission, and increasing antimicrobial resistance converge to sustain outbreaks and complicate disease control. Although its overall lethality is generally

lower than that of several invasive bacterial pathogens, its transmission efficiency and evolving resistance profile make it an important global public health concern.

NEISSERIA GONORRHOEAE: THE THREAT OF AN INCREASINGLY UNTREATABLE COMMON INFECTION

N. gonorrhoeae represents a distinct global bacterial threat characterized less by acute lethality than by widespread transmission, frequent asymptomatic infection, and an exceptional capacity to develop antimicrobial resistance. The organism has progressively acquired resistance to multiple antibiotic classes, including penicillins, tetracyclines, fluoroquinolones, and macrolides, while emerging resistance to extended-spectrum cephalosporins threatens the reliability of established treatment regimens.[34,35] Reflecting these concerns, the World Health Organization classifies third-generation cephalosporin-resistant and/or fluoroquinolone-resistant *N. gonorrhoeae* among its high-priority bacterial pathogens.[3]

Gonorrhea spreads primarily through sexual contact, with asymptomatic pharyngeal, rectal, and urogenital infections facilitating unrecognized transmission. Although rarely fatal, untreated infection can cause pelvic inflammatory disease, tubal infertility, ectopic pregnancy, epididymitis, and disseminated gonococcal infection, while perinatal transmission can result in neonatal conjunctivitis and potentially severe ocular complications.[34,36] These outcomes demonstrate that bacterial disease burden cannot be assessed solely through case fatality or pandemic potential.

The emergence of strains with reduced susceptibility or resistance to recommended therapies presents a particularly consequential challenge. Continued transmission, frequent reinfection, limited vaccine availability, and the organism's genetic adaptability create conditions in which resistance can spread through sexual networks and across international borders.[34,35] The principal global threat posed by N. gonorrhoeae is therefore not a highly lethal pandemic but the progressive loss of reliable treatment for a common, transmissible infection with substantial reproductive and neonatal consequences. Its evolution illustrates how antimicrobial resistance can transform an established, generally curable bacterial disease into an increasingly difficult public health challenge.

STREPTOCOCCUS PNEUMONIAE: HIGH BURDEN HIDDEN BY FAMILIARITY

S. pneumoniae exemplifies how a common bacterial pathogen can impose a substantial global disease burden through widespread transmission, frequent asymptomatic nasopharyngeal carriage, and the capacity to cause both localized and invasive infections. Pneumococcus is a leading bacterial cause of community-acquired pneumonia and an important cause of meningitis, bacteremia, sepsis, and otitis media, with the greatest risk of severe disease occurring among young children, older adults, immunocompromised individuals, and populations with limited healthcare access.[37,38]

Transmission occurs primarily through respiratory secretions, while asymptomatic colonization provides a persistent reservoir for bacterial dissemination. Although pneumococcal conjugate vaccines have substantially reduced invasive disease caused by vaccine-covered serotypes, the continued circulation of nonvaccine serotypes, incomplete vaccination coverage, and antimicrobial resistance sustain a considerable global burden.[37,39]

Resistance to commonly used antibiotics, particularly penicillins and macrolides, further complicates treatment and disease control. Reflecting these concerns, the World Health Organization classifies macrolide-resistant *S. pneumoniae* among its medium-priority bacterial pathogens in the 2024 Bacterial Priority Pathogens List.[3] Nevertheless, effective vaccines and antimicrobial therapies remain central to reducing pneumococcal morbidity and mortality.

Pneumococcal disease therefore illustrates that global bacterial threat is determined not solely by exceptional virulence or pandemic potential, but also by the cumulative consequences of widespread carriage, recurrent transmission, invasive disease, and antimicrobial resistance. Its enduring public health significance demonstrates how familiar, vaccine-preventable pathogens can generate a greater aggregate disease burden than rare organisms with substantially higher individual case fatality.

COMPARATIVE THREAT MATRIX

The major bacterial pathogens differ substantially in transmission dynamics, clinical severity, antimicrobial resistance (AMR), and capacity for epidemic or sustained global spread. Table 1 integrates these characteristics to distinguish pathogens responsible for widespread endemic disease, explosive epidemics, and healthcare-associated antimicrobial resistance.[3,4,7,16,19,21,31,34,37]

Table 1: Comparative Epidemiological and Clinical Characteristics of Major Bacterial Pathogens

Pathogen	Principal transmission	Clinical lethality	AMR concern	Epidemic or pandemic potential	Dominant threat
M. tuberculosis	Airborne	Substantial, particularly untreated	High	Sustained global transmission	Persistent global mortality and latent infection reservoir
MDR/RR-TB	Airborne	Substantial; treatment-dependent	Critical	Sustained international transmission	Direct transmission of resistant strains
V. cholerae	Contaminated water and food	High if untreated	Variable	Very high epidemic potential	Explosive waterborne outbreaks
Y. pestis	Fleas; respiratory droplets in pneumonic plague	Very high untreated	Relatively limited	Historically catastrophic; currently limited	Rapidly fatal pneumonic disease
N. meningitidis	Close respiratory contact	10% to 15% in invasive disease despite treatment	Relatively limited	Regional outbreaks	Fulminant meningitis and septicemia
MRSA	Direct contact and colonization	Potentially high in invasive disease	High priority	Widespread endemic transmission	Persistent healthcare and community infections
Carbapenem-resistant *Enterobacterales*	Contact, endogenous flora, healthcare networks	Potentially high in invasive disease	Critical priority	Extensive global dissemination	Severe infections with limited treatment options
CRAB	Healthcare contact and contaminated environments	Potentially high in critically ill patients	Critical priority	Healthcare-associated outbreaks	Persistent ICU transmission and difficult-to-treat infections
Carbapenem-resistant *P. aeruginosa*	Environmental and healthcare exposure	Potentially high in vulnerable patients	High priority	Primarily healthcare associated	Resistant invasive infections
S. Typhi	Fecal-oral	Potentially severe untreated	High priority for fluoroquinolone resistance	Regional epidemics and international spread	Enteric transmission and drug resistance
Shigella spp.	Fecal-oral; direct contact	Generally low with treatment;	High priority for fluoroquinolone resistance	High outbreak potential	Low infectious dose and efficient transmission

		higher in vulnerable populations			
N. gonorrhoeae	Sexual and perinatal	Low mortality; substantial morbidity	High priority for specified resistance phenotypes	Sustained global endemic transmission	Progressive loss of effective therapy
S. pneumoniae	Respiratory secretions	Variable; substantial in invasive disease	Medium priority for macrolide resistance	High endemic burden and localized outbreaks	Pneumonia, meningitis, and invasive disease

Abbreviations: AMR, antimicrobial resistance; CRAB, carbapenem-resistant Acinetobacter baumannii; ICU, intensive care unit; MDR/RR-TB, multidrug-resistant or rifampicin-resistant tuberculosis; MRSA, methicillin-resistant Staphylococcus aureus.

Interpretation. This matrix is a qualitative comparison rather than a numerical ranking. Lethality depends on the clinical syndrome, host susceptibility, resistance phenotype, and availability of timely treatment. Likewise, widespread endemic transmission, explosive epidemic potential, and international dissemination of resistant strains represent distinct epidemiological phenomena and should not be treated as equivalent measures of pandemic risk. WHO priority classifications reflect antimicrobial resistance concerns and research priorities, not direct rankings of transmissibility, lethality, or pandemic potential. Collectively, these comparisons demonstrate that bacterial threats cannot be assessed along a single dimension: tuberculosis exemplifies sustained global transmission and mortality; cholera, explosive epidemic potential; and resistant opportunistic pathogens, the progressive erosion of effective antimicrobial treatment.

RANKING BY TRANSMISSIBILITY

Bacterial transmissibility cannot be meaningfully ranked without accounting for transmission route, infectious dose, duration of infectiousness, environmental conditions, host susceptibility, and opportunities for exposure. Unlike pathogens sharing a common transmission mechanism, airborne, waterborne, fecal-oral, and healthcare-associated bacteria exhibit fundamentally different patterns of dissemination.[8]

M. tuberculosis represents the most consequential sustained airborne bacterial threat, capable of transmission through shared air during prolonged, frequently unrecognized infectious disease.[4] In contrast, *V. cholerae* can generate explosive epidemics when contaminated water supplies expose large populations simultaneously, producing rapid increases in cases without requiring direct person-to-person contact.[7] Shigella species exhibit particularly efficient fecal-oral transmission because of their exceptionally low infectious dose, facilitating outbreaks even with limited contamination.[31]

N. meningitidis and *S. pneumoniae* spread through respiratory secretions, with asymptomatic nasopharyngeal carriage sustaining transmission. However, their epidemiological patterns differ from tuberculosis because invasive disease occurs in only a subset of colonized individuals and transmission dynamics are strongly influenced by population immunity and close-contact exposure.[16,37]

Healthcare-associated pathogens, particularly carbapenem-resistant *A. baumannii* and *Enterobacterales*, demonstrate substantial transmission potential within hospitals and intensive care units, where susceptible patients, invasive devices, contaminated environments, and antimicrobial selection pressures facilitate dissemination. Their capacity

for sustained transmission among healthy community populations is generally more limited, although resistant *Enterobacterales* can also circulate outside healthcare settings.[21,24]

Bacterial transmissibility is therefore best understood as an ecological and epidemiological characteristic rather than a fixed property of the organism. Tuberculosis predominates as a sustained airborne global threat; cholera exemplifies explosive common-source epidemic transmission; Shigella demonstrates efficient transmission at a low infectious dose; and resistant opportunistic pathogens exploit healthcare environments. These distinct mechanisms preclude a universal ranking based on contagiousness alone.

RANKING BY LETHALITY

Bacterial lethality varies substantially according to pathogen virulence, clinical manifestation, host susceptibility, antimicrobial resistance, and access to timely treatment. Consequently, comparisons must distinguish mortality in untreated disease from outcomes achieved with modern medical care, while recognizing that case fatality rates are not directly comparable across different clinical syndromes.[14,16,22]

Untreated pneumonic plague ranks among the most rapidly fatal bacterial infections, potentially progressing to respiratory failure, sepsis, and death within days.[14] Invasive meningococcal disease also carries substantial lethality despite appropriate treatment, with an estimated case fatality rate of 10% to 15%, rising considerably in severe meningococcemia and septic shock.[14] Similarly, invasive infections caused by carbapenem-resistant Enterobacterales, Acinetobacter baumannii, and Pseudomonas aeruginosa can produce high mortality, particularly among critically ill patients with limited therapeutic options.[21,24,26]

Tuberculosis differs in its typically slower clinical progression but remains a major cause of preventable mortality, particularly when diagnosis is delayed, treatment is unavailable, or drug resistance compromises therapeutic effectiveness.[4] Cholera illustrates the opposite temporal pattern: severe infection can cause fatal hypovolemic shock within hours, yet prompt rehydration can reduce case fatality to below 1%.[7]

The lethality of bacterial infection is therefore not determined by pathogen virulence alone but by the interaction of disease severity, host vulnerability, and treatment effectiveness. Antimicrobial resistance is especially consequential because it can increase mortality by delaying or eliminating effective therapy, potentially reversing decades of progress in the management of previously treatable bacterial infections.[2]

Accordingly, the greatest bacterial threat is not necessarily the pathogen with the highest untreated case fatality, but one capable of combining substantial mortality with widespread transmission, persistent reservoirs, and diminishing treatment effectiveness.

THE ANTIMICROBIAL RESISTANCE MULTIPLIER

Antimicrobial resistance (AMR) is a defining feature of the contemporary bacterial threat because it can transform previously treatable infections into severe, potentially fatal diseases. Unlike intrinsic virulence or transmissibility, resistance can evolve under antimicrobial selection pressure and disseminate through both clonal transmission and horizontal gene transfer, progressively undermining established therapeutic strategies.[2,6]

The interaction of major determinants of bacterial threat can be represented conceptually as: **Bacterial Threat ∝ T × L × R × E**

where **T** represents transmissibility, **L** denotes clinical lethality, **R** reflects resistance to effective antimicrobial treatment, and **E** represents ecological opportunities for transmission and persistence. Although this relationship is conceptual rather than a validated quantitative model, it illustrates how antimicrobial resistance can amplify the consequences of transmission and disease severity. A highly transmissible pathogen with relatively low case fatality may generate substantial cumulative mortality, whereas a highly lethal organism with limited transmission may cause severe but geographically restricted outbreaks. More concerning is a pathogen capable of sustained dissemination that progressively acquires resistance to multiple effective therapies, increasing the risk of treatment failure and preventable death.

This interaction helps explain why the World Health Organization's 2024 Bacterial Priority Pathogens List emphasizes antimicrobial resistance alongside disease burden and other public health considerations rather than ranking organisms solely by intrinsic lethality. The WHO identifies carbapenem-resistant *A. baumannii*, carbapenem-resistant and third-generation cephalosporin-resistant Enterobacterales, and rifampicin-resistant *M. tuberculosis* as *critical-priority pathogens*, reflecting their substantial clinical impact and the urgent need for effective interventions.[3] AMR therefore acts as a multiplier of bacterial threat by weakening the therapeutic defenses that have historically limited mortality. Its greatest danger lies not simply in the emergence of resistant organisms, but in the progressive loss of reliable treatment for infections that remain widespread, transmissible, and potentially life-threatening.

WHY TUBERCULOSIS MAY BE THE GREATEST PRESENT BACTERIAL THREAT

When transmissibility, mortality, global prevalence, antimicrobial resistance, and persistence are considered collectively, Mycobacterium tuberculosis emerges as arguably the greatest established bacterial threat to global health. Unlike pathogens whose impact depends primarily on explosive outbreaks or healthcare-associated transmission, tuberculosis combines airborne dissemination, prolonged infectiousness, an extensive reservoir of latent infection, incomplete vaccine protection, and persistent socioeconomic barriers to prevention, diagnosis, and treatment.[4,9]

The magnitude of this threat is substantial. In 2024, an estimated 10.7 million people developed tuberculosis worldwide and 1.23 million died, while approximately 390,000 developed multidrug-resistant or rifampicin-resistant tuberculosis (MDR/RR-TB).[4] The capacity of resistant strains to spread directly between individuals further compounds the challenge, allowing antimicrobial resistance to propagate independently of prior treatment exposure.[10]

Tuberculosis is particularly difficult to eliminate because its epidemiological persistence extends beyond clinically apparent disease. Latent infection creates a large reservoir of individuals at risk of future progression, while delayed diagnosis, prolonged treatment requirements, inadequate healthcare access, and social vulnerability sustain transmission and preventable mortality.[4,9] Tuberculosis therefore represents more than a pathogen with theoretical pandemic potential: it is an enduring global epidemic of pandemic

proportions. Its exceptional significance lies in the convergence of sustained airborne transmission, substantial mortality, persistent infection reservoirs, and transmissible antimicrobial resistance, making it a particularly formidable contemporary bacterial threat.

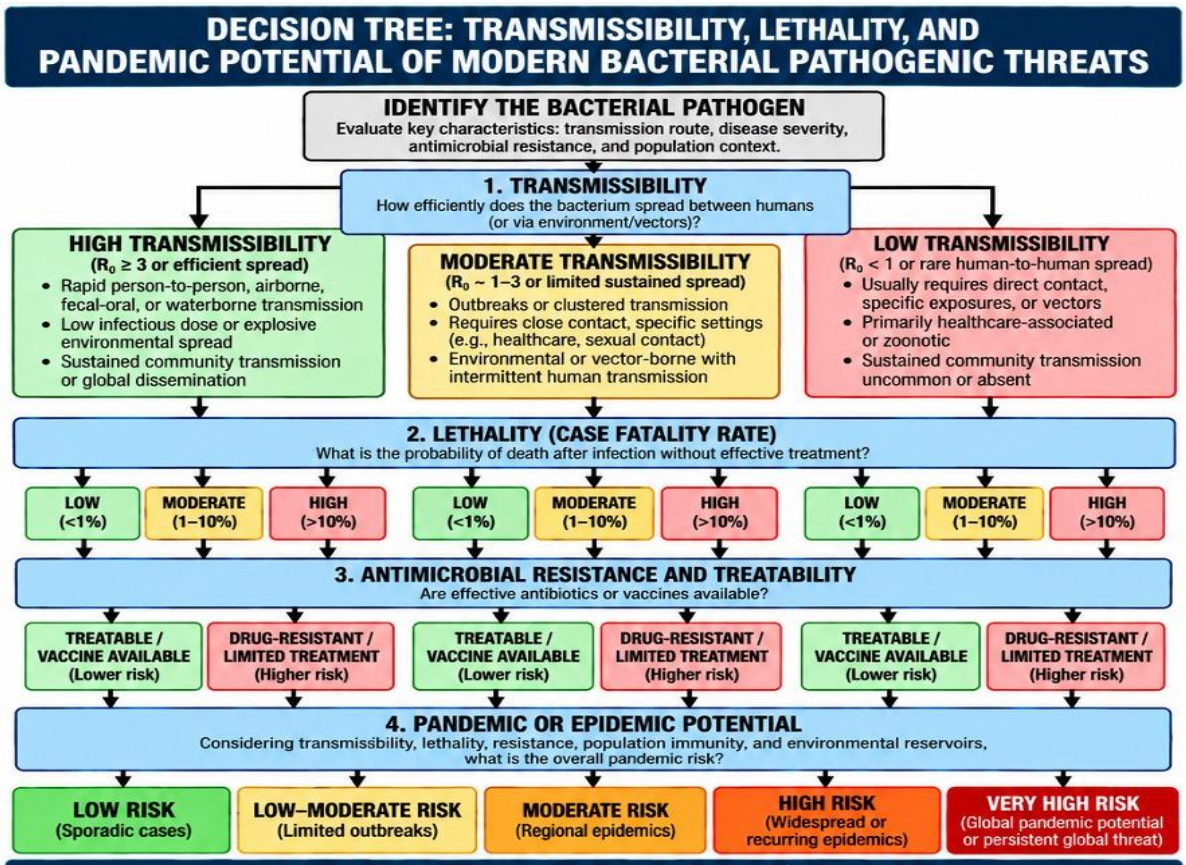
THE GREATEST FUTURE BACTERIAL THREAT MAY BE EVOLUTIONARY RATHER THAN NOVEL

Although pandemic preparedness frequently emphasizes the emergence of previously unknown pathogens, future bacterial threats may arise from the evolution of established organisms rather than the introduction of novel species. Of particular concern is the convergence of efficient transmission, multidrug resistance, invasive pathogenicity, and environmental persistence, which could substantially increase the clinical and epidemiological impact of an already widespread bacterium.[2,6]

Bacterial evolution is especially consequential because antimicrobial resistance can disseminate through horizontal gene transfer, including plasmids, transposons, and other mobile genetic elements. These mechanisms enable resistance determinants to spread across bacterial strains and, in some circumstances, species, allowing resistance emerging in one ecological reservoir to become established in clinically important pathogens elsewhere.[6,23] Antimicrobial selection pressure, international travel, healthcare-associated transmission, and interconnected human, animal, and environmental reservoirs further facilitate this process. The pandemic potential of modern bacterial pathogenic threats is shown in Figure 1 below.

The World Health Organization's 2024 Bacterial Priority Pathogens List reflects these concerns, identifying 24 antibiotic-resistant pathogens across 15 bacterial families. Critical priorities include carbapenem-resistant *A. baumannii*, resistant Enterobacterales, and rifampicin-resistant *M. tuberculosis*, while other priority categories encompass resistant *Salmonella, Shigella, Staphylococcus aureus, Pseudomonas aeruginosa*, and *N. gonorrhoeae*.[3]

The greatest future bacterial threat may therefore emerge not through the appearance of an unfamiliar pathogen, but through the evolutionary transformation of a common organism into one that is increasingly transmissible, invasive, persistent, and difficult to treat. This possibility underscores the importance of integrating antimicrobial stewardship, genomic surveillance, infection prevention, vaccine development, and coordinated human, animal, and environmental health strategies into global pandemic preparedness.



EXAMPLES OF MODERN BACTERIAL PATHOGENIC THREATS

(Approximate values; vary by strain, region, and healthcare context)

Bacterial Pathogen (Examples)	Typical Transmission	Relative Transmissibility	Typical Case Fatality Rate (Without Treatment)	Antimicrobial Resistance Concern	Current Pandemic/ Epidemic Potential	Overall Risk Category
Mycobacterium tuberculosis (TB, MDR-TB)	Airborne	High	~15% (untreated) (~1–5% treated)	High (MDR/XDR)	Very high (global)	VERY HIGH
Vibrio cholerae (Cholera)	Water/food (fecal-oral)	High	1–5% (can be >50% if untreated)	Moderate (increasing)	High (ongoing 7th pandemic)	HIGH
Yersinia pestis (Plague)	Flea vector; respiratory (pneumonic)	Moderate	High (30–100% untreated)	Low–moderate	Low–moderate (historical potential)	MODERATE
Neisseria meningitidis (Meningococcal disease)	Respiratory secretions (close contact)	Moderate	10–15% (despite treatment)	Moderate	Moderate (outbreak potential)	HIGH
Staphylococcus aureus (MRSA)	Contact (skin, fomites, healthcare)	Moderate	Variable (higher in invasive disease)	High (MRSA)	Moderate (healthcare/community)	HIGH
Enterobacterales (CRE: Klebsiella, E. coli)	Contact, food, healthcare, endogenous flora	Moderate	High (invasive infection)	Very high (carbapenem resistance)	Moderate (global dissemination)	HIGH
Acinetobacter baumannii (CRAB)	Healthcare environment (contact)	Low–moderate	High (in critically ill)	Very high	Moderate (hospital outbreaks)	HIGH
Pseudomonas aeruginosa	Healthcare environment, water, devices	Low–moderate	High (in vulnerable patients)	High	Moderate	MODERATE–HIGH
Salmonella Typhi (Typhoid fever)	Fecal-oral (contaminated food/water)	Moderate	10–20% (untreated)	High (drug-resistant strains)	Moderate (regional outbreaks)	HIGH
Shigella spp.	Fecal-oral (very low infectious dose)	High	<1% (usually low)	High (increasing)	Moderate–high (outbreak potential)	HIGH
Neisseria gonorrhoeae (Gonorrhea)	Sexual contact	Moderate	Rarely fatal	High (extensive resistance)	High (global endemic)	MODERATE
Streptococcus pneumoniae (Pneumococcus)	Respiratory secretions	Moderate	Variable (higher in invasive disease)	Moderate (increasing)	Moderate (global disease burden)	MODERATE

Figure 1

THE MOST DANGEROUS COMBINATION

Assessing bacterial pandemic potential requires extending the conventional transmissibility-lethality framework to incorporate antimicrobial resistance, population susceptibility, and ecological persistence. A particularly consequential threat would emerge from the convergence of efficient human-to-human transmission, high invasive-disease lethality, extensive antimicrobial resistance, limited vaccine protection, prolonged asymptomatic or presymptomatic carriage, persistent environmental or animal reservoirs, and capacity for international dissemination.[2,6]

No major contemporary bacterial pathogen fully combines these characteristics. Instead, existing organisms exhibit distinct combinations of epidemiological and clinical risk factors. *M. tuberculosis* integrates sustained airborne transmission, a vast reservoir of latent infection, substantial mortality, and transmissible drug resistance.[4] *V. cholerae* demonstrates explosive epidemic potential through contaminated water, whereas *N. meningitidis* combines respiratory transmission with rapidly progressive, potentially fatal invasive disease.[7,16] *Y. pestis* retains exceptional untreated lethality, zoonotic reservoirs, and the capacity for respiratory transmission in pneumonic plague.[14]

Among antimicrobial-resistant opportunistic pathogens, carbapenem-resistant *Enterobacterales* combine invasive disease with mobile resistance determinants capable of dissemination across bacterial populations.[21,23] Carbapenem-resistant *A. baumannii* exhibits extensive resistance and environmental persistence within healthcare settings, while methicillin-resistant *S. aureus* combines widespread colonization, community and healthcare transmission, and potentially severe invasive infection.[19,24]

The greatest prospective bacterial threat would arise from the convergence of these characteristics in a pathogen capable of sustained transmission despite effective public health interventions and progressively diminishing therapeutic options. Although such convergence remains hypothetical, the continued evolution and dissemination of antimicrobial resistance demonstrate why bacterial pandemic preparedness must anticipate changes in established pathogens rather than focus exclusively on novel organisms.

VIRAL VERSUS BACTERIAL PANDEMIC THREAT

Viral and bacterial pandemic threats share fundamental determinants, including transmissibility, virulence, population susceptibility, and ecological opportunity, but differ in important mechanisms of emergence, persistence, and therapeutic resistance. For emerging viral pathogens, a central concern is the acquisition or optimization of efficient human-to-human transmission in susceptible populations. For established bacterial pathogens, an increasingly consequential threat is the progressive loss of effective antimicrobial treatment in organisms already capable of sustained transmission.[2,6]

SARS-CoV-2 demonstrated the capacity of a novel respiratory virus to disseminate rapidly through an immunologically susceptible global population, whereas Mycobacterium tuberculosis illustrates how an airborne bacterial pathogen can sustain widespread transmission and substantial mortality over centuries.[4,40] These contrasting patterns underscore the distinction between rapid pandemic emergence and persistent global endemicity.

Antimicrobial resistance introduces an additional evolutionary challenge. Although viruses also develop resistance to antiviral therapies, bacteria can disseminate resistance determinants through horizontal gene transfer, enabling adaptive traits to spread across genetically distinct populations and, in some circumstances, species.[6] Moreover, antimicrobial selection pressure can favor resistant bacterial strains without requiring increased intrinsic virulence or transmissibility, allowing previously treatable infections to become progressively more difficult to manage.[2,6]

Thus, while a major emerging viral pandemic may depend on a pathogen acquiring efficient human transmission, a future bacterial crisis could arise from an already

widespread organism progressively losing susceptibility to effective treatment. This distinction highlights the complementary importance of surveillance for emerging pathogens and sustained efforts to prevent antimicrobial resistance in established bacterial populations.

A PRACTICAL RANKING OF MODERN BACTERIAL THREATS

When transmissibility, mortality, global disease burden, antimicrobial resistance, epidemic potential, and healthcare vulnerability are considered collectively, the following qualitative ranking provides a practical assessment of major contemporary bacterial threats. Although inherently context-dependent, this framework distinguishes pathogens responsible for sustained global transmission from those posing exceptional risks through explosive epidemics or antimicrobial resistance.[3,4]

1. ***M. tuberculosis***, particularly MDR/RR-TB. Represents the most consequential overall threat through sustained airborne transmission, extensive latent infection reservoirs, substantial global mortality, and transmissible antimicrobial resistance.[4]
2. **Carbapenem-resistant *Enterobacterales***. Constitute a critical global AMR threat because common pathogens, particularly *K. pneumoniae* and *E. coli*, cause severe invasive infections while transferable resistance determinants facilitate international dissemination.[21,23]
3. ***V. cholerae***. Exhibits exceptional epidemic potential through contaminated water and sanitation failures, with the continuing seventh pandemic demonstrating its capacity for widespread outbreaks and substantial preventable mortality.[7,12]
4. **Carbapenem-resistant *A. baumannii***. Poses a critical threat to healthcare systems through environmental persistence, extensive antimicrobial resistance, and severe infections among critically ill and mechanically ventilated patients.[24,25]
5. **Methicillin-resistant *S. aureus***. Remains a globally established cause of community-acquired and healthcare-associated infections, combining widespread colonization, persistent transmission, antimicrobial resistance, and potentially fatal invasive disease.[19,20]
6. **N. meningitidis.** Although less capable of sustained global transmission, invasive meningococcal disease can progress within hours and carries substantial mortality despite appropriate antimicrobial treatment.[16]
7. **Drug-resistant *S. Typhi* and *Shigella***. Represent major enteric threats where inadequate sanitation, efficient fecal-oral transmission, and increasing antimicrobial resistance sustain endemic disease and recurrent outbreaks.[28,31]
8. **Drug-resistant *P. aeruginosa*.** Causes difficult-to-treat invasive infections, particularly among critically ill, immunocompromised, and mechanically ventilated patients, with resistance limiting therapeutic options.[26,27]
9. ***Y. pestis***. Retains exceptional untreated lethality and the capacity for respiratory transmission in pneumonic plague, although effective antibiotics, surveillance, and public health interventions substantially constrain contemporary pandemic potential.[14,15]

10. **Drug-resistant *N. gonorrhoeae***. Presents comparatively low mortality but substantial global morbidity, with widespread sexual transmission and evolving resistance threatening the effectiveness of established treatment regimens.[34,35]

This ranking is an interpretive synthesis rather than a validated quantitative hierarchy. Relative threat varies with regional epidemiology, population susceptibility, resistance prevalence, healthcare capacity, and the outcomes being evaluated. Importantly, the World Health Organization's 2024 Bacterial Priority Pathogens List prioritizes antibiotic-resistant organisms according to public health and research considerations rather than providing a universal ranking of overall pandemic risk.[3]

Taken together, these findings identify tuberculosis as the most consequential established bacterial threat when sustained transmission and mortality are considered jointly, while resistant Gram-negative pathogens represent a particularly urgent challenge to the continued effectiveness of modern antimicrobial therapy.

CONCLUSION

The global threat posed by bacterial pathogens cannot be assessed through transmissibility or case fatality alone. Rather, it reflects the convergence of transmission dynamics, clinical severity, population susceptibility, ecological persistence, healthcare capacity, and antimicrobial resistance (AMR). Among these determinants, AMR represents an increasingly consequential threat because it can transform previously treatable infections into life-threatening diseases while undermining essential medical interventions.[2,3]

M. tuberculosis remains arguably the greatest established global bacterial threat, combining sustained airborne transmission, extensive reservoirs of latent infection, substantial mortality, and transmissible drug resistance. In 2024, tuberculosis caused an estimated 10.7 million incident cases and 1.23 million deaths worldwide, making it the leading cause of death from a single infectious agent.[4] Other pathogens exhibit distinct but consequential threat profiles. *V. cholera*e demonstrates exceptional epidemic potential through contaminated water and sanitation failures, while *N. meningitidis* can cause rapidly progressive invasive disease with case fatality rates of 10% to 15% despite appropriate treatment.[7,16]

Beyond these established threats, the progressive dissemination of AMR may represent the most consequential long-term challenge to bacterial disease control. Carbapenem-resistant *Enterobacterales*, *A. baumannii*, and *P. aeruginosa*, together with resistant *M. tuberculosis*, *S. aureus, Salmonella, Shigella*, and *N. gonorrhoeae*, demonstrate how resistance can compromise treatment across diverse bacterial species, clinical syndromes, and transmission environments.[3]

The greatest prospective bacterial threat would arise from the convergence of efficient transmission, substantial invasive-disease lethality, extensive antimicrobial resistance, persistent reservoirs, and limited preventive or therapeutic options. Although no major contemporary pathogen fully exhibits this combination, ongoing bacterial evolution and resistance dissemination underscore the need for integrated genomic surveillance, antimicrobial stewardship, vaccination, infection prevention, sanitation, and sustained antimicrobial development.

Ultimately, the defining danger of future bacterial pandemics may lie not in the emergence of an unfamiliar pathogen, but in the progressive loss of effective treatment against organisms already capable of widespread transmission. Whereas emerging viral pandemics often depend on the acquisition of efficient human-to-human transmission, a major future bacterial crisis may arise when established pathogens become increasingly resistant to the therapies that have historically controlled them.

Disclosure: The authors did not report any disclosures.

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