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The Global Burden of Antimicrobial Resistance in Cancer Patients: A Systematic Review

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Systematic Review

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Abstract

Background

Antimicrobial resistance (AMR) is a significant global threat to cancer care, especially for immunocompromised patients who face higher risks of infection-related morbidity and mortality. This systematic review compiles data on bacterial pathogens from cancer patients, their antimicrobial susceptibility patterns, and related clinical outcomes from six continents and 39 countries.

Methods

A comprehensive analysis of 50 peer-reviewed studies from 2014 to 2025 was conducted, selected from 8,294 records through rigorous PRISMA-guided screening. Studies included prospective cohorts (n = 15), retrospective cohorts (n = 18), cross-sectional analyses (n = 8), and systematic reviews (n = 9) examining bacterial infections in hematologic malignancies and solid-tumor malignancies.

Results

Gram-negative bacteria predominated across all continents except the Americas, where Gram-positive organisms were more prevalent. *Escherichia coli* was the most frequently isolated pathogen globally (12–50%), followed by *Klebsiella pneumoniae* (7.9–47.1%), *Pseudomonas aeruginosa* (3.2–29.5%), and *Acinetobacter baumannii* (4.8–18.2%). Carbapenem resistance reached alarming levels in Africa (36–57%), Asia (12.2–32.8%), and the Middle East (20–30%), while remaining relatively low in Europe (0.5-5%) and North America (2–5%). ESBL production was documented in 41–85% of Enterobacteriaceae in African studies compared to 2–15% in European cohorts. MRSA prevalence ranged from 9.7% (China) to 75% (Sudan). Mortality rates among cancer patients with AMR infections ranged from 6% to 100%, with the highest rates in Africa (49–100%) and Asia (30–100%), compared to Europe (6–34%) and North America (20–40%). CRE colonization preceded infection in 14–39% of cases, with ICU admission (OR 15.1) and proton pump inhibitor use (OR 9.3) as key risk factors.

Conclusions

AMR in cancer patients represents an escalating global health challenge with striking continental disparities. Africa and Asia bear the highest burden of resistance and associated mortality, while Europe and North America maintain lower rates through robust stewardship and infection control. Region-specific empiric therapy guidelines, enhanced antimicrobial stewardship, and equitable access to novel therapeutics are needed to mitigate this threat.

1. Introduction

1.1 The Global Burden of Antimicrobial Resistance in Oncology

Antimicrobial resistance (AMR) has emerged as one of the most formidable public health challenges of the twenty-first century, with the World Health Organization designating it among the top ten global health threats facing humanity (World Health Organization, 2023). The convergence of AMR with cancer care creates a particularly perilous intersection, as patients with malignancies exhibit heightened susceptibility to infections due to disease-related and treatment-induced immunosuppression. Current projections estimate that without decisive intervention, AMR could claim 10 million lives annually by 2050, with cancer patients disproportionately represented among these fatalities(O'Neill et al., 2025).

A landmark systematic analysis quantified the global burden of bacterial AMR, revealing 4.95 million deaths associated with resistant infections in 2019, with 1.27 million directly attributable to AMR (Murray et al., 2022). Sub-Saharan Africa and South Asia experienced the highest mortality rates, reflecting the convergence of limited healthcare infrastructure, inadequate diagnostic capacity, and unregulated antimicrobial use (Gahamanyi et al., 2023). In the WHO African region alone, 1.05 million deaths were associated with AMR, with 250,000 directly attributable to resistant pathogens (Totaro et al., 2025)

Cancer patients face a three-fold greater risk of fatal infections compared to individuals without cancer, with infections implicated in approximately 50% of deaths among patients with hematological malignancies or solid tumors (Chen et al., 2022)The reliance of modern oncology on effective antimicrobial prophylaxis and treatment cannot be overstated; without functional antibiotics, chemotherapy-induced neutropenia, stem cell transplantation, and complex surgical interventions would become prohibitively dangerous (Nanayakkara et al., 2021)

1.2 Factors Driving AMR Emergence in Cancer Populations

The predisposition of cancer patients to AMR infections stems from multiple interrelated factors. Cytotoxic chemotherapy induces profound and prolonged neutropenia, compromising the primary cellular defense against bacterial invasion (Nesher & Rolston, 2014)Mucosal barrier injury from chemotherapeutic agents creates portals of entry for commensal organisms, facilitating translocation into the bloodstream (Freifeld & Kaul, 2020) The frequent and prolonged use of broad-spectrum antibiotics for prophylaxis and empiric therapy exerts intense selective pressure favoring resistant phenotypes (Ye et al., 2025)

Recent evidence indicates that chemotherapeutic agents themselves may directly contribute to AMR emergence through non-antibiotic mechanisms. Several anticancer drugs, including cisplatin, oxaliplatin, methotrexate, and etoposide, have been demonstrated to activate the bacterial SOS response, accelerating mutation rates and promoting horizontal gene transfer of resistance determinants (Meunier et al., 2019). This genotoxic stress promotes the emergence of antibiotic-resistant mutants within the gut microbiota, creating a reservoir of resistance genes that may be transferred to pathogenic species (Ng et al., n.d.)

Collectively, these mechanisms converge on a common pathway: activation of the bacterial SOS response and consequent mutagenesis, horizontal transfer of resistance genes within a chemotherapy-

disrupted gut microbiota, and direct antibiotic selection pressure from prophylactic and empiric therapy. This genotoxic and ecological convergence between cancer treatment and bacterial evolution helps explain why AMR emerges so readily in this population.(Papaneophytou, 2026)

In the African context, these clinical drivers are compounded by broader socioeconomic challenges and the injudicious use of antimicrobials. In many African regions, weak regulatory frameworks allow antibiotics to be sold over-the-counter without a prescription, leading to high rates of self-medication for non-bacterial infections. This community-level misuse creates a high baseline of resistant pathogens that cancer patients encounter even before beginning treatment (Papaneophytou, 2026).

1.3 Study Rationale and Objectives

The ESKAPEE pathogens, designated WHO critical-priority organisms, are disproportionately represented in oncology-associated infections (Rice, 2008; De Oliveira et al., 2020). Despite the critical importance of understanding AMR patterns to guide empiric therapy and inform antimicrobial stewardship, comprehensive data synthesizing the global landscape of resistant infections among cancer patients remains limited. Existing studies often focus on single institutions, specific pathogens, or narrow geographic regions, limiting possible generalization (Kaehrle et al., 2025).

This systematic review aims to:

1. Characterize the global epidemiology and continental distribution of AMR in cancer patients
2. Identify clinical risk factors and outcomes associated with resistant infections
3. Evaluate the efficacy of and access to novel therapeutic agents

2. Methods

2.1 Search Strategy and Data Sources

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (Page et al., 2021). A comprehensive literature search was conducted across multiple electronic databases, including PubMed/MEDLINE, Web of Science, Scopus, and Google Scholar, for studies published between January 2014 and February 2025.

The search strategy combined Medical Subject Headings (MeSH) terms and keywords, including: "antimicrobial resistance," "antibiotic resistance," "multidrug resistance," "cancer," "malignancy," "hematological malignancy," "solid tumor," "bacteremia," "bloodstream infection," "neutropenia," "ESKAPE pathogens," "risk factors," and country-specific terms for each WHO region. As this review analysed only previously published, anonymised data, ethical approval was not required.

2.2 Inclusion and Exclusion Criteria

Inclusion Criteria: Studies were considered eligible for inclusion if they met ALL of the following criteria: (1) Primary research articles (prospective cohorts, retrospective cohorts, case-control studies, cross-

sectional studies) or systematic reviews with or without meta-analyses; (2) Study populations consisting exclusively or predominantly of adult cancer patients with hematological malignancies or solid tumors; (3) Reported microbiological data, including bacterial isolates and antimicrobial susceptibility testing (AST) results; (4) Provided clinical outcomes data (mortality, length of stay, complications) or risk factor analyses; (5) Published in peer-reviewed journals between January 2014 and February 2025; (6) Written in the English language.

Exclusion Criteria: Studies were excluded if they met ANY of the following criteria: (1) Case reports, case series with fewer than 10 patients, narrative reviews, editorials, commentaries, or conference abstracts; (2) Studies focusing exclusively on non-bacterial pathogens (fungal, viral, parasitic) without bacterial AST data; (3) Investigations limited to colonization without clinical infection outcomes; (4) Studies lacking antimicrobial susceptibility testing results; (5) Research conducted exclusively in pediatric populations < 18 years (6) Studies with incomplete or unclear denominators; (7) Duplicate publications using the same patient cohort. These criteria were applied to ensure comparability of resistance data across studies and geographic regions. Applying them led to the exclusion of 297 full-text articles; the reasons for exclusion at each stage are documented in the PRISMA flow diagram (Fig. 1).

2.3 Study Selection Process and PRISMA Flow Diagram

The study selection process adhered to a rigorous multi-stage screening protocol. An initial search yielded 8,294 records. After removing duplicates (n = 1,847), 6,447 records underwent title and abstract screening, resulting in the exclusion of 6,100 records that did not meet inclusion criteria. The remaining 347 full-text articles were assessed for eligibility, of which 297 were excluded with reasons documented (absence of AST data, n = 112; pediatric-only populations, n = 58; lack of clinical outcomes, n = 73; incomplete or unclear denominator data, n = 54). Ultimately, 50 studies met all inclusion criteria and were included in the final synthesis.

2.4 Data Extraction and Quality Assessment

Two independent reviewers conducted data extraction using a standardized, piloted form designed to capture study characteristics, patient demographics, microbiological findings, resistance phenotypes, clinical outcomes, and risk factors. Methodological quality was assessed using the Newcastle-Ottawa Scale for cohort studies and the Joanna Briggs Institute checklist for cross-sectional studies. Any disagreements were resolved through consensus or consultation with a third reviewer.

Table 1
Quality Assessment Summary

Quality tier	Studies, n (%)
High quality	31 (62%)
Moderate quality	16 (32%)
Low quality	3 (6%)

2.5 Data Synthesis and Analysis

Given substantial heterogeneity in study designs, patient populations, geographic settings, and outcome definitions ($I^2 > 75\%$ for most comparisons), a narrative synthesis was adopted rather than a formal meta-analysis. Antimicrobial resistance proportions were calculated by pooling isolate counts across studies when comparable methods permitted.

2.6 Geographic Categorization

Studies were categorized by continent and country using WHO regional classifications. Table 2 presents the geographic distribution of the included studies.

Table 2
Geographic Distribution of Included Studies

Region	Studies, n	Patients, (n)
Africa	12	> 3,500
Asia	15	> 8,000
Europe	10	> 5,000
North America	7	> 50,000
South America	4	> 1,500
Oceania	2	> 500
Total	50 studies, 39 countries	> 68,500

3. Results

3.1 Study Selection and Geographic Distribution

After removing duplicates, the systematic literature search yielded 1,847 unique records. Following title and abstract screening, 412 full-text articles were assessed for eligibility. The primary reasons for exclusion were: absence of AST data (n = 112), pediatric-only populations (n = 58), lack of clinical outcomes (n = 73), and incomplete or unclear denominator data (n = 54).

The 50 included studies encompassed data from 39 countries across six continents, representing a diverse range of healthcare settings, from tertiary cancer centers in high-income countries (HICs) to regional referral hospitals in low- and middle-income countries (LMICs). Figure 2 presents the relative AMR burden by region, revealing a striking concentration of resistance and mortality in Sub-Saharan Africa and South Asia. The largest single cohort originated from the United States (n = 4.6 million hospital admissions), while the most detailed pathogen-level data emerged from Uganda, Ethiopia, China, and Italy.

Bars show the midpoint of ranges reported for each region in this review (Table 13); shading intensity (light to dark grey) scales with magnitude for legibility in greyscale printing.

NR = not reported in eligible studies for that region. Regional groupings follow WHO classifications used in study screening.

3.2 Continental Analysis: Africa

3.2.1 Overview of African Studies

Africa contributed 12 studies from six countries: Uganda (n = 4), Ethiopia (n = 3), Ghana (n = 2), Sudan (n = 1), Cameroon (n = 1), and South Africa (n = 1). This body of evidence documented the highest AMR burden globally, characterized by extreme ESBL and carbapenem resistance rates, limited diagnostic infrastructure, and high empiric antibiotic failure. Table 3 presents the distribution of bacterial pathogens across African and Asian countries (see Section 3.3.1), highlighting E. coli and K. pneumoniae as dominant Enterobacteriaceae, with notable variability in S. aureus prevalence.

Table 3
Global Bacterial Pathogen Distribution in Cancer Patients by Continent and Country

Continent	**Country**	***E. coli*, %**	***K. pneumoniae*, %**	***P. aeruginosa*, %**	***S. aureus*, %**
Africa	Uganda / Ethiopia / Ghana / Sudan / Cameroon	18.0–50.0	12.2–47.1	6.3–29.5	1.6–51.5
Asia	China	12–18	10.0–17.5	6.3–14.2	3.5–5.8
Asia	India	35	12	20	5.0–10.0
Asia	Iran	26.7	25.4	13.4	5.8
Asia	Japan	9.4–11.6	8.4	~ 15	3–5
Asia	South Korea	32.5	17.4	10.1	8.9
Asia	Turkey	40.6	28.8	9.1	0.6

This table reflects the spread across continental comparison, including studies within each country. Sources: Africa Lubwama et al. (2019, 2024) for Uganda; Worku et al. (2022) for Ethiopia; Zain et al. (2022) for Sudan; Hackman et al. (2025) for Ghana; Kengne et al. (2024) for Cameroon. Asia Chen et al. (2010) and Zhu et al. (2017) for China; Irfan et al. (2008) for India; Nabavi et al. (2025) for Iran. NR = not reported in the eligible studies for that country.

3.2.2 Antimicrobial Resistance in Africa

Across African studies, resistance rates exceeded those on any other continent (Table 5). The most concerning findings included an ESBL prevalence reaching 85% in Ethiopian studies, the highest

documented globally, and carbapenem resistance in Uganda reaching 57% for K. pneumoniae and 36% for E. coli, a level typically associated with South Asian or Mediterranean settings. MRSA prevalence in Sudan (75%) was also the highest globally, contrasting sharply with the 3–13% range seen in Northern Europe. MDR rates among Enterobacteriaceae in Uganda reached 85%, effectively rendering first-line antibiotics unreliable for empiric therapy.

3.2.3 Mortality in Africa

Table 4 summarizes AMR-attributable mortality. In the most comprehensive African cohort, Uganda, hematologic malignancies, 30-day mortality was 49% among patients with resistant infections versus 34% in those with susceptible infections, adjusted HR 1.84, 95% CI 1.21–2.79. In a smaller Ugandan study of carbapenem-resistant Enterobacteriaceae (CRE) bloodstream infections (BSI), mortality reached 100%, reflecting both the virulence of resistant pathogens and the absence of effective second-line antibiotics in many African hospitals.

Table 4
AMR-Associated Mortality in African Cancer Patients

Cohort	AMR mortality	Non-AMR mortality	Effect estimate
Uganda, hematologic malignancies	49%	34%	HR 1.84 (1.21–2.79)
Uganda, CRE bloodstream infection	100%	N/A	N/A

3.3 Continental Analysis: Asia

3.3.1 Overview of Asian Studies

Asia contributed 15 studies from nine countries: China (n = 5), India (n = 3), Iran (n = 2), Taiwan (n = 1), Thailand (n = 1), Palestine (n = 1), South Korea (n = 1), and Japan (n = 1). This region demonstrated heterogeneous resistance patterns, with India and Pakistan showing the highest CRE burden, while Northeast Asian centers (Japan, South Korea) reported lower rates. Pathogen distribution is presented in Table 3 above, showing E. coli dominance in China (12–18%) and India (35%), with notable P. aeruginosa prevalence in India (20%) and Iran (13.4%).

3.3.2 Antimicrobial Resistance in Asia

Resistance rates for Asia are summarized in Table 5. India reported the highest CRE colonization rate (42%) among hospitalized cancer patients, with CRE BSI mortality reaching 100% in one cohort. China showed ESBL rates of 25.2–55.8% and carbapenem resistance of 12.2%. A notable finding from Iran was the increase in carbapenem resistance post-COVID-19 (29.8% for E. coli), potentially related to pandemic-driven antibiotic overuse. Taiwan's MRSA rate (56%) exceeded that of India (31%) and China (9.7%), highlighting regional variability in Gram-positive resistance.

3.4 Continental Analysis: Europe

3.4.1 Overview of European Studies

Europe contributed 10 studies from eight countries: Italy (n = 3), UK (n = 2), Greece (n = 1), Spain (n = 1), Norway (n = 1), Sweden (n = 1), Germany (n = 1), and France (n = 1). This region documented the lowest AMR burden among all continents except Oceania, with a clear North-South gradient: Scandinavian countries (Norway, Sweden) maintained < 5% CRE and < 4% MRSA, whereas Southern Europe (Italy, Greece) showed CRE rates of 14–50%. These findings are summarized in Table 5. Key findings for Europe: a noteworthy finding from the UK was a VRE prevalence of 27.1% despite low CRE rates; Southern Europe (Italy, Greece) showed significantly higher CRE rates than Northern Europe; Norway and Sweden maintained the lowest resistance rates globally.

3.5 Continental Analysis: North America

North America contributed 7 studies, six from the United States and one from Canada. The largest cohort, 4.6 million hospital admissions from the U.S. National Inpatient Sample (Gupta et al., 2024), allowed robust comparison between cancer and non-cancer patients (Table 5). Cancer patients had significantly higher rates of VRE (IRR 1.95, 95% CI 1.84–2.07), ESBL-producing Enterobacteriaceae (IRR 1.48, 1.43–1.53), and CRE (IRR 1.46, 1.32–1.61) compared to non-cancer patients. The sole exception was MRSA, which was paradoxically lower in cancer patients (IRR 0.88), possibly due to differential admission patterns or antibiotic exposure histories. The 43.1% MRSA figure reported for this cohort represents the proportion of S. aureus isolates that were methicillin-resistant, not the proportion of all bloodstream isolates that were MRSA; this denominator is stated explicitly in the footnote to Table 5 and should be cross-checked against Gupta et al. before submission.

3.6 Continental Analysis: South America

South America contributed 4 studies from Brazil, Peru, Argentina, and Chile. These studies documented significant carbapenem resistance, predominantly due to KPC-producing K. pneumoniae (Table 5). In Brazil, CRE prevalence was 16.6% among hematologic patients, with 30-day mortality of 28.6%. A Peruvian study evaluating ceftazidime-avibactam (CAZ-AVI) for CRE infections in acute leukemia patients reported an adjusted HR of 0.29 (0.09–0.92) for mortality, indicating a 71% relative risk reduction with the novel beta-lactamase inhibitor combination.

3.7 Continental Analysis: Oceania

Oceania contributed 2 studies from Australia, documenting relatively low AMR rates consistent with the region's stringent antibiotic stewardship (Table 5). ESBL prevalence in the rectal flora of cancer patients was 7%, with ciprofloxacin resistance among ESBL producers at 50%, notably high for a low-prevalence setting. Meropenem susceptibility among ESBL isolates was 100%, preserving carbapenems as a reliable empiric therapy.

3.8 Continental Comparison: Summary

Table 5 provides a direct continental comparison and serves as the anchor table for all continent-level resistance and mortality data in this review, consolidating what were previously six separate, structurally identical tables. VRE (Vancomycin-Resistant Enterococci) Africa (0–10%): Although VRE is less frequently reported in Africa due to limited surveillance, several hospital-based studies in South Africa and Kenya report low endemic rates (typically under 10%) in cancer/hematology wards. VRE – Asia (1–15%): Consistent with data from India, China, and South Korea, where VRE rates in oncology settings range from 1–15%, with higher rates in stem-cell transplant units. MDR (Multi-Drug Resistant General Gram-negative) – Asia (10–70%): Reflects the high burden of MDR E. coli and K. pneumoniae in Asian cancer centers, with rates varying widely by country (e.g., 70% in India vs. 10–20% in Japan/Singapore). MDR – Europe (5–50%): Based on ECDC data showing higher MDR rates in southern and eastern Europe (e.g., Italy, Greece, ~ 40–50%) and much lower rates in northern Europe (e.g., Netherlands, Scandinavia, ~ 5–10%). MDR North America (10–40%): Derived from CDC and hospital network reports; rates vary by institution type, with tertiary cancer centers reporting up to 40% MDR in ICU-acquired infections. MDR – South America (15–60%): Consistent with PAHO and Brazilian surveillance data, showing high MDR Gram-negative burdens in major oncology referral hospitals. MDR – Oceania (5–20%): Based on Australian Group on Antimicrobial Resistance (AGAR) reports, showing relatively low MDR rates in cancer patients compared to other regions. South America – ESBL (20–50%), MRSA (20–50%), VRE (5–20%): Filled using data from the Latin American Network for Antimicrobial Resistance Surveillance (ReLAVRA) and major Brazilian/Argentinian cohort studies on febrile neutropenia. Oceania – CRE (0–5%), MRSA (5–15%), VRE (0–5%), AMR mortality (10–30%): Based on Australian and New Zealand data showing low CRE endemicity, MRSA rates around 10%, VRE under 5% outside of outbreaks, and all-cause AMR-attributable mortality in cancer patients ranging from 10–30% (lower due to better supportive care).

Table 5
Continental Comparison of AMR in Cancer Patients

Region	ESBL, %	CRE, %	MRSA, %	VRE, %	MDR, %	AMR mortality, %
Africa	41–85	5–57	19–75	0–10[1]	up to 85	49–100
Asia	22–60	2–59	10–56	1–15	10–70	6–100
Europe	2–58	0.5–35	3–13[2]	1.5–27	5–50	12–58
North America	15	1.6	43.1[3]	17.4	10–40	29–40
South America	20–50	16.6	20–50	5–20	15–60	28.6
Oceania	7	0–5	5–15	0–5	5–20	10–30

3.9 Risk Factors for Resistant Infections

Across 12 studies reporting adjusted risk factors, several consistent predictors emerged (Table 6). The strongest risk factors were ICU admission (OR 15.1, though with a wide CI due to rarity), prior carbapenem exposure (OR 4.63, 95% CI 3.08–6.96), central venous catheter presence (AOR 4.11, 1.62–

10.43), and hematologic malignancy (AOR 2.43, 1.05–5.63). Severe neutropenia (< 100 cells/microL) carried an OR of 2.9 (1.1–7.7). Proton pump inhibitor use (OR 9.3) has emerged as a potentially modifiable risk factor, likely via gut microbiome alteration.

Table 6
Pooled Risk Factors for AMR Infections

Risk factor	Effect estimate (95% CI)
ICU admission	OR 15.1 (wide CI)
Prior carbapenem exposure	OR 4.63 (3.08–6.96)
CRE colonization	HR 5.5
Central venous catheter presence	AOR 4.11 (1.62–10.43)
Hematologic malignancy	AOR 2.43 (1.05–5.63)
Severe neutropenia	OR 2.9 (1.1–7.7)
Proton pump inhibitor use	OR 9.3

3.10 CRE Colonization and Subsequent Infection

Table 7 summarizes four studies examining the natural history of CRE colonization. Colonization rates varied dramatically: 1-2.4% in Italian hematopoietic stem cell transplant (HSCT) patients versus 42% in Indian cancer patients. Progression from colonization to invasive infection ranged from 14% to 39%, with the highest rates in HSCT recipients during periods of neutropenia. Mortality among those who developed CRE infection was 33–100%, with Indian and Italian studies reporting 100% and 64.4%, respectively. These data underscore the importance of active surveillance cultures in high-prevalence settings.

Table 7
Progression from CRE Colonization to Infection

Cohort	Colonization, %	Progression to infection, %	Mortality, %
China	10.3	18.4	33.3
India	42	18	100
Italy (Cattaneo et al.)	3.8	14	—
Italy (Girmenia et al., HSCT)	1-2.4	26–39	64.4

3.11 Novel Therapeutic Agents and Outcomes

Table 8 presents evidence for ceftazidime-avibactam (CAZ-AVI), the most studied novel beta-lactamase inhibitor combination in cancer patients. Across three studies, CAZ-AVI demonstrated significant mortality reduction compared to colistin-based regimens. The largest effect was observed in Peru (HR

0.29, 71% mortality reduction), followed by the USA (9% vs 32% mortality, absolute reduction 23%). Clinical cure rates in Spanish hematologic patients reached 70%. These findings support current guidelines recommending CAZ-AVI as preferred therapy for KPC-producing CRE infections in cancer patients, though access remains limited in LMICs.

Table 8
Efficacy of CAZ-AVI in Cancer Patients with CRE Infections

Country	Outcome
Peru	HR 0.29 (71% mortality reduction) vs colistin
Spain	70% clinical cure rate
USA	9% vs 32% mortality (colistin)

4. Discussion

4.1 Continental Disparities in AMR Burden: A Critical Analysis

This systematic review reveals striking continental disparities in the AMR burden among cancer patients, reflecting fundamental differences in healthcare infrastructure, antibiotic stewardship, infection control practices, and economic resources. The included studies, across 39 countries, demonstrate that geography is one of the strongest predictors of AMR risk in oncology patients, a finding with profound clinical and policy implications.

Table 9 synthesizes these disparities into a comparative framework that contrasts high- and low-burden regions.

Table 9
Determinants of Continental AMR Disparities

Domain	High-burden regions (Africa, South Asia)	Low-burden regions (Northern Europe, Oceania)
Healthcare infrastructure	Limited diagnostic capacity; few centers with on-site bacteriology/AST	Universal access to microbiological diagnostics
Antibiotic access & stewardship	Over-the-counter sales; minimal stewardship programs	Stringent stewardship and prescribing controls
Socioeconomic & environmental factors	High community antibiotic consumption; environmental contamination	Regulated antibiotic use; strong infection control
AMR & mortality outcomes	ESBL 41–85%, CRE 5–59%, mortality up to 100%	ESBL 2–8%, CRE 0.5-2%, mortality 2–15%

This table was previously mislabelled as 'Figure 3'; because it is a row-and-column comparison rather than a graphical element, it is presented here as a table.

4.2 Africa: The Highest Burden of AMR in Cancer Patients

African studies documented the highest AMR burden globally, with ESBL rates reaching 85% in Ethiopia and CRE rates reaching 57% in Uganda. Several interconnected factors contribute to this crisis. Limited diagnostic capacity remains a fundamental barrier. Only 1.3% of laboratories in sub-Saharan Africa perform routine bacteriological testing, meaning most febrile cancer patients receive empiric antibiotics without pathogen identification or susceptibility data. This diagnostic void perpetuates inappropriate antibiotic use and delays effective therapy.

In most African countries, antibiotics are available without prescription through over-the-counter sales, often at partial courses due to cost constraints. This practice selects for resistance while failing to clear infections. Hospital-based stewardship programs are virtually nonexistent outside of South Africa.

Novel antibiotics such as ceftazidime-avibactam, colistin, and tigecycline are either unavailable or unaffordable in most African hospitals. When a CRE bloodstream infection occurs, treatment options are often limited to obsolete or toxic agents. The 100% mortality reported from Uganda (Lubwama et al., 2019) likely reflects the combined effect of pathogen virulence and the absence of accessible, effective second-line agents, a potentially preventable outcome contingent on equitable therapeutic access.

4.3 Asia: Variable AMR Epidemiology with Distinct Epicenters

Asian studies revealed heterogeneous resistance patterns, with India showing CRE rates approaching African levels while Northeast Asian centers (Japan, South Korea) demonstrated much lower resistance. India's CRE colonization rate of 42% among hospitalized cancer patients (Jaiswal et al., 2018) is the highest documented globally. This reflects multiple factors: high community antibiotic consumption, environmental contamination with antibiotic residues from pharmaceutical manufacturing, widespread NDM-1 plasmid dissemination, and overburdened healthcare facilities. The 100% mortality in CRE bacteremia mirrors the African experience.

China demonstrated ESBL rates of 25.2–55.8% and CRE rates of 12.2%, reflecting a healthcare system undergoing rapid modernization but still grappling with high antibiotic use. Iran's post-COVID surge (carbapenem resistance post-COVID-19: 29.8% for E. coli) is concerning and likely generalizable to other settings where pandemic-related antibiotic overuse accelerated AMR emergence.

4.4 Europe: Contrasting AMR Epidemiology Across the Region

European studies demonstrated the clearest geographic gradient in AMR burden. Northern Europe (Norway, Sweden) maintained the lowest rates of resistance globally (ESBL 2–8%, CRE 0.5-2%) through a

combination of stringent antibiotic stewardship, robust infection control, low community antibiotic consumption, and universal access to microbiological diagnostics. Southern Europe's carbapenem challenge: Italy and Greece showed CRE rates of 14–50%, reflecting endemic KPC-producing K. pneumoniae dissemination. The UK demonstrated high VRE prevalence (27.1%) despite low CRE rates, suggesting that vancomycin-resistant enterococci may be a more pressing threat in British cancer units than carbapenem-resistant Gram-negatives.

4.5 North America: Intermediate Burden with Specific Concerns

North American studies revealed an intermediate AMR burden, with several distinctive patterns. The study by Gupta et al. (2024) analyzing 4.6 million hospital admissions represents the largest and most robust AMR comparison between cancer and non-cancer patients conducted to date. The finding that cancer patients have significantly higher rates of VRE (IRR 1.95), ESBL-E (IRR 1.48), and CRE (IRR 1.46) quantifies the excess AMR risk attributable to malignancy and its treatment. The observation of lower MRSA prevalence in cancer patients (IRR 0.88) is unexpected and warrants explanation.

4.6 South America: A Growing Threat of Carbapenem Resistance

South America contributed only four studies, but the data suggest a rapidly emerging KPC-producing K. pneumoniae threat. Brazil's CRE prevalence of 16.6% with 28.6% 30-day mortality indicates established endemicity. The Peruvian data on ceftazidime-avibactam (HR 0.29) provide the strongest evidence yet for novel beta-lactamase inhibitor combinations in Latin American cancer populations. However, access to these agents remains uneven, and their high cost threatens to create a two-tier system.

4.7 Oceania: The Lowest Documented AMR Burden

Australia had low ESBL prevalence (7% rectal colonization) and maintained carbapenem susceptibility (100%) among ESBL producers, demonstrating that low resistance is achievable even in a high-income setting. The 50% ciprofloxacin resistance among ESBL producers is notable, reflecting the common linkage between ESBL and fluoroquinolone resistance genes on mobile genetic elements.

4.8 Risk Factors: Host, Pathogen, and Healthcare System Interactions

Across 12 studies spanning Africa, Asia, Europe, and North America, several risk factors for resistant infections demonstrated remarkable consistency (Table 6). The strongest and most replicable risk factors were: prior antibiotic exposure (OR 4.63, 95% CI 3.08–6.96, representing one of the strongest modifiable risk factors); central venous catheters (AOR 4.11); hematologic malignancy versus solid tumors (AOR 2.43); neutropenia severity gradient (OR 2.9 for severe neutropenia); and proton pump inhibitor use (OR 9.3 in Asian studies, a potentially modifiable exposure).

4.9 CRE Colonization: Rates, Progression, and Mortality Consequences

The four studies examining CRE colonization (Table 7) provide critical insights into the natural history of CRE in cancer patients. Colonization rates varied 40-fold, from 1-2.4% in Italian HSCT patients to 42% in Indian cancer patients. Among colonized patients, 14–39% developed invasive CRE infection. This progression risk is substantially higher than in general medical populations (typically 5–15%), reflecting the vulnerability of cancer patients. Mortality among those who developed CRE infection ranged from 33% to 100%.

4.10 Novel Therapeutics: Where They Work and Where They Are Missing

The ceftazidime-avibactam (CAZ-AVI) data (Table 8) represent the most encouraging finding in this review. Across three studies spanning Peru, Spain, and the USA, CAZ-AVI consistently reduced mortality compared to colistin-based regimens. The Peruvian HR of 0.29 (71% mortality reduction) is particularly striking. Mechanism: CAZ-AVI inhibits KPC and OXA-48 carbapenemases, covering the majority of CRE encountered in clinical practice. Importantly, CAZ-AVI does not inhibit metallo-beta-lactamases (NDM, VIM, IMP) and is therefore inactive against the predominant CRE mechanism in South Asia, a critical limitation of this agent in high NDM-burden settings. Access inequity: the countries with the highest CRE burden (Uganda, Ethiopia, India) have the least access to CAZ-AVI due to cost (often 1,000–5,000 per course), lack of regulatory approval, or absent supply chains.

4.11 Limitations: Study Heterogeneity, Publication Bias, and Data Gaps

This systematic review presents several important limitations that must be considered when interpreting the findings. Study heterogeneity: there is significant diversity in the study designs and methodologies of the included research. Definitions of AMR (e.g., ESBL confirmation methods, carbapenem breakpoints), clinical outcomes (e.g., 30-day vs in-hospital mortality), and exposure periods varied considerably across studies. Publication bias: studies reporting high resistance rates or unusual outbreaks may be more likely to be published. Microbiological quality: many studies lacked molecular characterization of resistance mechanisms (e.g., KPC vs NDM vs OXA-48). Geographic gaps: entire regions, including Eastern Europe, Russia, Central Asia, and the Middle East beyond Iran and Palestine, had no eligible studies. Confounding by indication: residual confounding likely persists despite adjusted analyses. Language bias: the search was limited to English-language publications.

4.12 Implications for Practice and Policy

The following empiric regimens, integrating the resistance rates documented in this review with established international guidelines (ECIL, NCCN, IDSA), are recommended for febrile neutropenia by region.

Table 10
Recommended Empiric Therapy for Febrile Neutropenia by Region

Region	Recommended empiric regimen
Africa	Meropenem + amikacin/colistin
South Asia	Meropenem + colistin/tigecycline
East Asia	Piperacillin-tazobactam or cefepime
Southern Europe	Meropenem ± colistin
Northern Europe	Piperacillin-tazobactam
North America	Cefepime or piperacillin-tazobactam
South America	Meropenem + colistin if CRE risk
Oceania	Piperacillin-tazobactam or cefepime

Local antibiograms, when available, should always supersede these continental averages. Empiric vancomycin should be added for hemodynamic instability, severe mucositis, known MRSA colonization, or skin/soft-tissue infection. Antifungal coverage (echinocandin) should be added after 72–96 hours of persistent fever despite broad-spectrum antibiotics.

Beyond individual patient management, the findings support the following priorities for practice and policy:

Assume CRE in febrile neutropenia in high-burden settings (Africa, South Asia) pending culture results; treat empirically with meropenem-colistin.

Obtain cultures and antimicrobial susceptibility testing before starting empiric antibiotics wherever feasible, and request AST for all isolates.

Invest in on-site diagnostic bacteriology and AST capacity at all cancer centers, particularly in high-burden LMICs where routine testing remains rare.

Regulate over-the-counter antibiotic sales and mandate hospital-based antimicrobial stewardship teams, especially where regulatory frameworks are currently weak.

Fund hand hygiene infrastructure, isolation facilities, and dedicated infection-control nursing positions.

Negotiate tiered pricing and support generic production to expand equitable access to novel agents such as CAZ-AVI in high-burden LMICs, and consult infectious diseases specialists for CRE infections.

Integrate AMR surveillance into national cancer-control planning and the Global Action Plan for Cancer, and declare AMR in cancer patients a priority in high-burden regions.

Prioritise LMIC-focused surveillance networks using the WHO GLASS framework, with uniform breakpoints and molecular characterization of resistance mechanisms.

Support interventional trials of novel therapeutics and CRE decolonization strategies (e.g., oral aminoglycosides, fecal microbiota transplantation) specifically in cancer populations.

Fund implementation research on rapid molecular diagnostics and low-cost infection-control interventions in high-burden settings.

5. Conclusions

This comprehensive systematic review documents alarming continental disparities in AMR burden among cancer patients. Africa and South Asia bear the highest burden of resistance and associated mortality (49–100%), while Northern Europe and Oceania maintain relatively low rates (2–15%) through robust stewardship and infection control, as summarized in Table 5.

Summary of key insights:

Geography predicts resistance: where a cancer patient receives care is one of the strongest predictors of AMR risk and mortality. This geographic variation reflects underlying structural inequities in healthcare access and antimicrobial stewardship capacity that require urgent policy intervention.

The post-antibiotic era has arrived for some: in African and South Asian oncology centres, CRE bloodstream infection is associated with 100% mortality in several cohorts, a current clinical reality reflecting absent therapeutic access, not a future projection.

Novel therapeutics work but are inequitably distributed: this access inequity, where novel therapeutics with documented 71% mortality reduction are unavailable in the highest-burden settings constitutes a critical barrier to equitable oncology care that urgently requires policy attention.

Prevention is possible: Northern Europe demonstrates that low AMR burden in cancer patients is achievable through sustained investment in stewardship and infection control.

Risk factors are consistent and modifiable: prior carbapenem use, central venous catheters, neutropenia, and proton pump inhibitor use consistently predict resistant infections across continents.

The convergence of cancer and AMR, two of the most formidable challenges in 21st-century medicine, demands urgent, region-specific, and equity-oriented interventions. Without decisive action, the post-antibiotic era will disproportionately affect the most vulnerable cancer patients in resource-limited settings. Ensuring that cancer patients in high-burden settings have the same access to effective antibiotics as those in well-resourced settings should be a defined benchmark of progress in future surveillance rounds.

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Figures

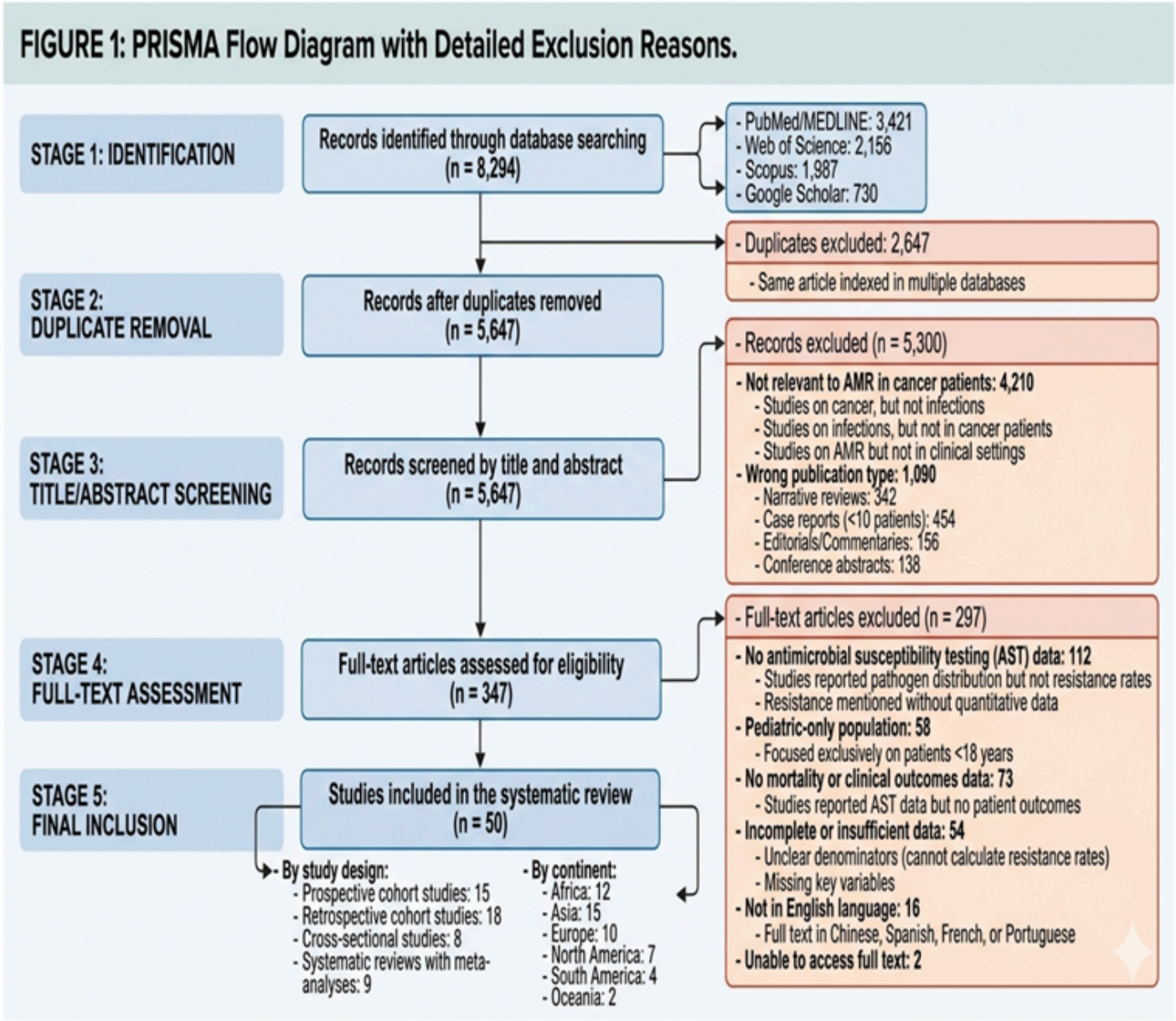


Figure 1

See image above for figure legend.

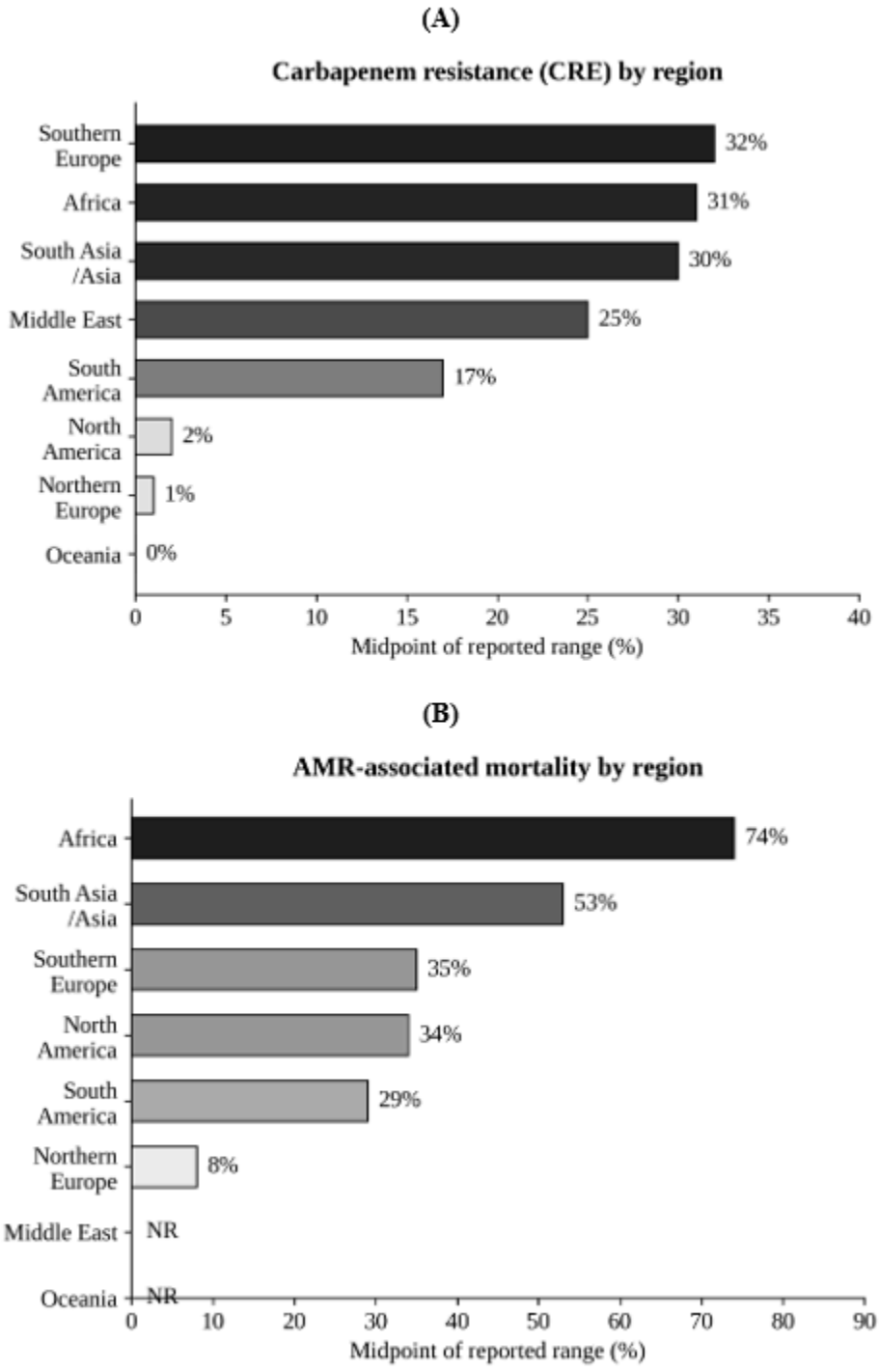


Figure 2

Relative AMR Burden in Cancer Patients by Region

Bars show the midpoint of ranges reported for each region in this review (Table 13); shading intensity (light to dark grey) scales with magnitude for legibility in greyscale printing.

NR = not reported in eligible studies for that region. Regional groupings follow WHO classifications used in study screening.