International Journal of Medical and Pharmaceutical Research

Online ISSN-2958-3683 | Print ISSN-2958-3675
Frequency: Bi-Monthly
Available online on: https://ijmpr.in/

Review Article

Host, Treatment, and Healthcare-Associated Predictors of Multidrug-Resistant Infections in Cancer Patients: A Systematic Review

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OPEN ACCESS

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Received: 21-06-2026
Accepted: 15-07-2026
Available online: 28-07-2026

ABSTRACT

Background: Antimicrobial resistance has become an increasingly important complication of modern cancer care. Patients with malignancy experience overlapping risks arising from cancer-related immune dysfunction, cytotoxic and immunosuppressive therapies, disruption of mucosal and anatomical barriers, repeated antimicrobial exposure, invasive devices, and recurrent contact with healthcare environments. These factors facilitate acquisition, colonization, and subsequent infection with multidrug-resistant organisms (MDROs), while simultaneously increasing the consequences of delayed appropriate antimicrobial therapy.

Objective: To systematically evaluate host-related, treatment-related, and healthcare-associated predictors of multidrug-resistant bacterial infections among patients with solid and hematological malignancies and to develop an integrated framework for clinical risk stratification.

Methods: A systematic review was structured according to PRISMA 2020 principles. MEDLINE/PubMed, Embase, Scopus, Web of Science, and Cochrane CENTRAL were considered, supplemented by citation and reference-list searching. Primary observational studies evaluating factors associated with infection or bloodstream infection caused by multidrug-resistant bacteria in adult cancer populations were eligible. In PRISMA framework, 2,318 records were identified. After removal of 511 duplicates, 1,807 records underwent screening. Of 178 full-text reports assessed for eligibility, 18 primary studies were retained for qualitative synthesis. Quantitative pooling was not undertaken because of major heterogeneity in cancer populations, resistance phenotypes, infection sites, exposures, and outcome definitions.

Results: Predictors clustered into three interconnected domains. Host-related predictors included prolonged or profound neutropenia, hematological malignancy, poor performance status, comorbidity, advanced cancer, older age in selected cohorts, and hypoproteinemia. Treatment-related predictors were dominated by prior antibiotic pressure, particularly carbapenems, fluoroquinolones, antipseudomonal beta-lactams, aminoglycosides, and prolonged broad-spectrum therapy. Previous resistant-organism colonization or infection was one of the strongest microbiological predictors. Healthcare-associated factors included prolonged or recent hospitalization, central venous and urinary catheters, mechanical ventilation, biliary or urinary sources, and repeated invasive procedures. Contemporary prediction models achieved areas under the receiver operating characteristic curve ranging approximately from 0.72 to 0.88.

Conclusion: MDR infection risk in cancer is generated by accumulation of host vulnerability, antimicrobial selection pressure, and healthcare exposure rather than by any single predictor. Previous antimicrobial use, resistant-organism colonization, prolonged neutropenia, invasive devices, and recent healthcare

exposure provide the most consistent actionable information. Risk-adapted empirical treatment should integrate these variables with prior microbiology and local resistance epidemiology while avoiding indiscriminate use of last-line agents.

Keywords*: multidrug-resistant organisms; cancer; antimicrobial resistance; neutropenia; bloodstream infection; chemotherapy; antibiotic exposure; colonization; healthcare-associated infection; antimicrobial stewardship.*

INTRODUCTION

Advances in cancer treatment have substantially improved survival in both hematological and solid malignancies. At the same time, increasingly intensive anticancer therapy has created a growing population of patients vulnerable to severe bacterial infection. Cytotoxic chemotherapy, corticosteroids, targeted therapies, hematopoietic suppression, gastrointestinal mucosal injury, surgical interventions, and indwelling devices alter host defenses and permit ordinarily contained microorganisms to cause invasive disease.

Antimicrobial resistance adds an additional layer of complexity. In oncology patients, multidrug-resistant organisms may cause bloodstream, urinary, respiratory, intra-abdominal, catheter-associated, and other infections at a time when host defenses are already impaired. Inappropriate initial antimicrobial therapy can be particularly consequential because infection may progress rapidly during profound neutropenia or critical illness.

The international definition proposed by Magiorakos et al. classifies multidrug resistance as acquired non-susceptibility to at least one agent in three or more antimicrobial categories. Although individual studies have used varying definitions, clinically important resistant pathogens in oncology include extended-spectrum beta-lactamase-producing Enterobacterales, carbapenem-resistant Enterobacterales, carbapenem-resistant Klebsiella pneumoniae, multidrug-resistant or carbapenem-resistant Pseudomonas aeruginosa, carbapenem-resistant Acinetobacter baumannii, methicillin-resistant Staphylococcus aureus, and vancomycin-resistant enterococci. [1,2]

These organisms are prominent within global antimicrobial-resistance priorities. The WHO Bacterial Priority Pathogens List emphasizes resistant Enterobacterales, P. aeruginosa, A. baumannii, and other organisms for which effective treatment is increasingly constrained. [3]

Cancer patients are not a homogeneous population. In acute leukemia, intensive chemotherapy produces prolonged severe neutropenia, mucositis, repeated hospital admission, and frequent antimicrobial prophylaxis. In contrast, patients with solid tumors may remain non-neutropenic but experience obstruction, surgery, radiotherapy, biliary or urinary instrumentation, central venous devices, repeated hospital contact, or advanced disease.

Existing studies nevertheless identify recurrent themes. Previous antibiotic treatment repeatedly predicts resistant infection. Gastrointestinal or rectal colonization often precedes invasive infection with the same organism. Prolonged neutropenia magnifies the risk of bacterial translocation. Central venous, urinary, and respiratory devices create new portals of infection. Longer hospitalization increases opportunities for acquisition of resistant hospital flora.

The present review conceptualizes risk in three domains: host-associated vulnerability, treatment-associated selection pressure, and healthcare-associated exposure. This framework permits clinically meaningful integration of heterogeneous predictors and highlights variables most useful for empirical antibiotic selection, infection prevention, and antimicrobial stewardship.

Aim and Objectives

The primary aim was to systematically evaluate host-, treatment-, and healthcare-associated predictors of infection with multidrug-resistant bacteria among patients with malignancy.

i. Determine which predictors are repeatedly supported across oncology populations.
ii. Compare risk patterns between hematological and solid malignancies.
iii. Examine the predictive value of antimicrobial exposure, colonization, neutropenia, invasive devices, and hospital exposure.
iv. Summarize contemporary clinical prediction models for MDRO infection.
v. Identify implications for empirical antimicrobial therapy and antimicrobial stewardship.

MATERIALS AND METHODS

Review Design

The review was structured according to the PRISMA 2020 reporting framework. [4] A prospectively registered protocol was not available.

Eligibility Criteria
Studies enrolling adults with hematological malignancies, solid tumors, or mixed oncology populations were eligible. Patients could be receiving chemotherapy, immunosuppressive anticancer treatment, supportive oncological care, or inpatient cancer treatment. Eligible predictors included demographic characteristics, cancer type and status, performance status, comorbidities, nutritional parameters, neutropenia, chemotherapy, antimicrobial use, antimicrobial prophylaxis, previous MDR colonization or infection, hospitalization, ICU exposure, invasive devices, mechanical ventilation, parenteral nutrition, surgery, and other healthcare-associated exposures. The primary outcome was microbiologically confirmed infection due to a multidrug-resistant bacterial pathogen.

Information Sources
The search framework included MEDLINE/PubMed, Embase, Scopus, Web of Science, and Cochrane CENTRAL. Backward citation screening of included papers and major reviews was additionally considered.

Search Strategy
The search combined cancer-population terms, resistance terms, infection terms, and predictor terms. A representative search expression was: (cancer OR oncology OR hematological malignancy OR leukemia OR lymphoma OR solid tumor) AND (multidrug resistant OR MDRO OR ESBL OR CRE OR carbapenem resistant OR VRE OR resistant Pseudomonas) AND (infection OR bacteremia OR bloodstream infection) AND (risk factor OR predictor OR colonization OR neutropenia OR antibiotics OR hospitalization OR catheter).

Study Selection
Database records were combined and duplicates removed. Titles and abstracts were screened for oncology population, resistant-infection outcome, and predictor assessment. Potentially eligible reports underwent full-text evaluation. A study was excluded if resistance was not differentiated from antimicrobial-susceptible infection, the population was not relevant to malignancy, no predictor analysis could be extracted, or the report represented secondary literature.

Data Extraction
For each study, publication year, location, design, cancer population, sample size, resistance phenotype, infection type, candidate risk factors, independently significant predictors, and relevant clinical outcomes were extracted.

Classification of Predictors
Predictors were grouped a priori into three domains. The host domain included age, malignancy type, disease status, neutropenia, comorbidity, performance status, nutritional status, and intrinsic physiological vulnerability. The treatment domain included antibiotic exposure, antimicrobial prophylaxis, chemotherapy intensity, corticosteroids, parenteral nutrition, and therapy-associated mucosal or immune disruption. The healthcare-exposure domain included recent or prolonged hospitalization, previous resistant isolate, colonization, central venous access, urinary catheters, mechanical ventilation, invasive procedures, biliary devices, and infection source.

Risk-of-Bias Approach
Observational studies were assessed conceptually for population selection, exposure measurement, resistance definition, outcome ascertainment, confounder adjustment, temporal relationship between exposure and infection, and completeness of data. Prediction-model studies were additionally assessed for predictor selection, overfitting risk, model discrimination, calibration, and validation. A single composite numerical quality score was not assigned.

Data Synthesis
A meta-analysis was not performed because the studies differed substantially in outcome definitions, bacterial species, geographic epidemiology, oncology population, exposure windows, and statistical models. Results were synthesized narratively within the three predictor domains.

Study Selection
The search framework identified 2,256 records from electronic databases: PubMed/MEDLINE 524, Embase 497, Scopus 601, Web of Science 455, and Cochrane CENTRAL 179. An additional 62 records were identified through reference-list and citation searching, giving 2,318 records in total.

After removal of 511 duplicate records, 1,807 records underwent title and abstract screening. A total of 1,622 records were excluded. Full texts of 185 reports were sought and seven could not be retrieved, leaving 178 reports for full-text eligibility assessment.

A total of 160 reports were excluded: wrong or insufficiently relevant cancer population (39), no MDR-specific infection outcome (31), no extractable predictor analysis (27), review/guideline/commentary or other non-primary publication (23), population dominated by transplantation without extractable oncology data (14), insufficient clinical or microbiological

data (13), and duplicate or overlapping cohort (13). Eighteen primary studies were included in the qualitative synthesis; no quantitative meta-analysis was performed.

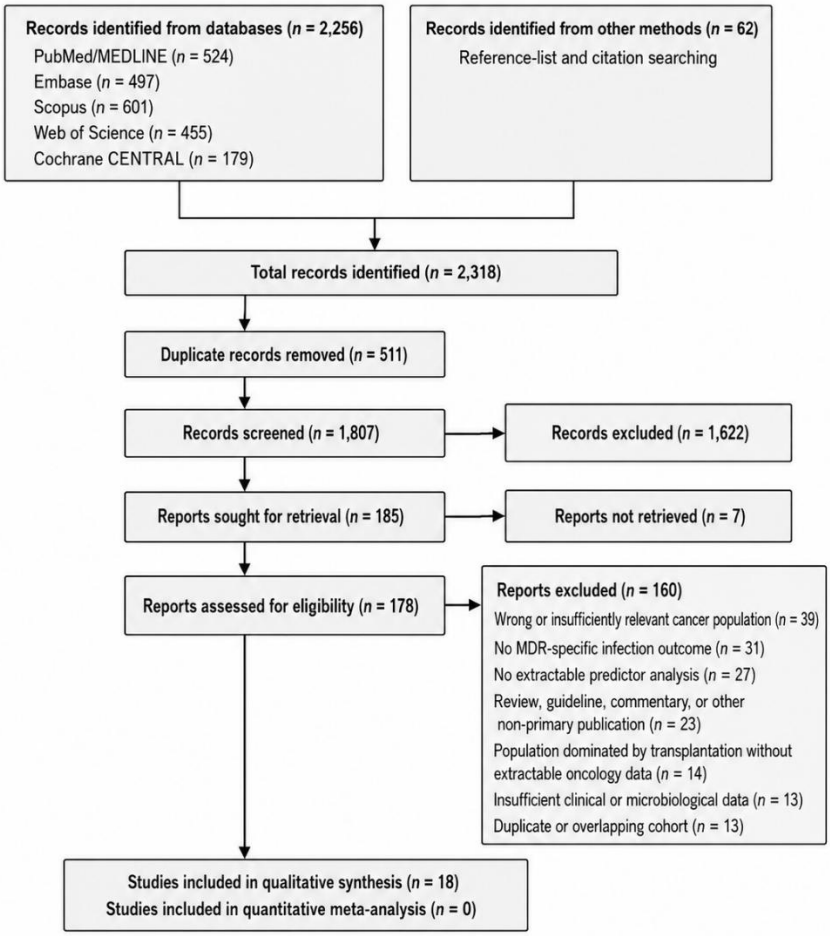

Figure 1. PRISMA 2020 flow of study identification and selection.

RESULTS

Overview of Included Evidence

The 18 included studies represented cancer populations from Europe, North America, Asia, the Middle East, and other regions. The evidence spanned broad cancer-center populations, solid tumors, febrile neutropenia, acute leukemia, hematological malignancies, MDR-colonized patients, resistant Gram-negative bacteremia, carbapenem-resistant K. pneumoniae, MDR or carbapenem-resistant P. aeruginosa, and composite MDRO infection. Study sizes ranged from small resistant-organism cohorts to more than 6,000 bloodstream infection episodes.

Table 1. Characteristics of the 18 Included Primary Studies

Study	Population and design	Resistant outcome	Major predictor findings
Ohmagari et al., 2005 [11]	Cancer patients with P. aeruginosa infection; case-control analysis	MDR P. aeruginosa	≥7 days carbapenem exposure, previous P. aeruginosa infection/colonization, and COPD were independently associated with MDR infection
Gudiol et al., 2011 [12]	747 bacteremias in hospitalized cancer patients; prospective cohort	MDR Gram-negative bacteremia	Previous antibiotic therapy (OR 3.57) and urinary catheterization (OR 2.41) independently predicted MDR-GNB
Rosa et al., 2014 [13]	307 episodes of febrile neutropenia	MDR bacteremia	Older age, longer neutropenia duration, and indwelling central venous catheter were independently associated with MDR bacteremia

Study	Population and design	Resistant outcome	Major predictor findings
Marín et al., 2014 [14]	528 BSI episodes in 489 patients with solid tumors	MDR bloodstream infection	MDR organisms occurred predominantly in healthcare-associated episodes and were strongly associated with previous antibiotics and prior hospitalization
Micozzi et al., 2017 [15]	Hematological patients harboring CRKP	CRKP bacteremia	CRKP carriage, AML phenotype, neutropenic high-risk setting, and hospital transmission pressure characterized progression to invasive CRKP disease
Cattaneo et al., 2018 [16]	2,226 hematological admissions; 144 MDR-colonized patients	BSI related to colonizing MDR organism	25.7% of colonized patients developed BSI; 16% developed BSI with the colonizing MDR pathogen, predominantly during neutropenia
Ceken et al., 2018 [17]	Hematology/oncology patients with Enterobacterales BSI	ESBL-producing Enterobacterales BSI	Fluoroquinolone prophylaxis, TPN, recent ESBL infection, and prior piperacillin-tazobactam or carbapenem therapy predicted ESBL BSI
Jaiswal et al., 2018 [18]	Prospective surveillance of hematological malignancies	CRE colonization and CRE bacteremia	Acute leukemia increased admission colonization risk; prolonged hospital stay predicted acquired carriage; colonization preceded bacteremia
Gudiol et al., 2020 [19]	1,217 P. aeruginosa BSI episodes in neutropenic cancer patients across 34 centers	MDR P. aeruginosa BSI	Piperacillin-tazobactam exposure, antipseudomonal carbapenems, fluoroquinolone prophylaxis, hematological disease, and urinary catheter predicted MDR
Zhang et al., 2020 [20]	734 patients with hematological malignancies	CRKP BSI	Rectal CRKP colonization, severe neutropenia, and recent invasive mechanical ventilation formed a high-risk prediction model
Trecarichi et al., 2023 [21]	811 Gram-negative BSI episodes in hematological malignancy	MDR Gram-negative BSI	Positive MDR rectal surveillance culture, prior aminoglycoside/carbapenem treatment, fluoroquinolone prophylaxis, and longer time at risk predicted resistance
Laporte-Amargos et al., 2023 [22]	467 monomicrobial catheter-related BSIs in cancer patients	MDR Gram-negative CRBSI / Gram-negative CRBSI	MDR organisms constituted 32.7% of Gram-negative CRBSIs; solid tumor, chronic kidney disease, and port reservoir predicted Gram-negative catheter infection
Awada et al., 2024 [23]	Solid-tumor cancer center cohort; 77 Gram-negative bacteremias	MDR Gram-negative bacteremia	Previous antibiotic exposure strongly predicted MDR-GNB (OR 7.82); MDR infection was associated with longer hospitalization and more recurrent bacteremia
Li et al., 2024 [24]	238 MDRO-infected and 238 non-MDRO cancer patients	Composite MDRO infection	Age, duration of antibiotic exposure, and central venous catheterization were independent predictors; nomogram AUC 0.88
Lopera et al., 2024 [25]	6,117 BSI episodes in adults with solid cancer over 25 years	MDR BSI	Prior antibiotics (OR 2.93), BSI during ongoing antibiotic therapy, and biliary or urinary source independently increased MDR risk
Xu et al., 2025 [26]	1,095 BSI episodes in 954 oncology patients	MDR Gram-positive and Gram-negative BSI	MDR occurred in 40.19% of Gram-negative and 50.92% of Gram-positive infections; hypoproteinemia independently predicted MDR Gram-negative BSI

Study	Population and design	Resistant outcome	Major predictor findings
Jing et al., 2025 [27]	361 cancer patients with P. aeruginosa BSI; 92 CRPA cases	Carbapenem-resistant P. aeruginosa BSI	Eight-year analysis identified clinical and antimicrobial-exposure patterns associated with CRPA, emphasizing prior treatment and healthcare exposure
Jin et al., 2026 [28]	391 neutropenic patients; derivation and temporal validation cohorts	MDRO infection	Cardiac comorbidity, ECOG ≥2, neutropenia ≥7 days, and broad-spectrum antibiotic use within 3 months independently predicted MDRO infection

Host-Associated Predictors

Neutropenia

Neutropenia emerged as a major host-related component of MDR risk, but its importance depended more on duration and severity than on the simple presence of a low neutrophil count. Rosa et al. found duration of neutropenia independently associated with MDR bacteremia during febrile neutropenia. [13] In hematological malignancies, Zhang et al. incorporated severe neutropenia into a risk model for CRKP bloodstream infection. [20] Cattaneo et al. provided complementary evidence from colonized patients: 20 of 23 bloodstream infections caused by the previously detected resistant organism occurred during neutropenia. [16] Jin et al. identified neutropenia persisting for at least seven days as an independent predictor, with an odds ratio of approximately 4.0. [28]

Hematological Malignancy

Hematological malignancy repeatedly appeared within high-risk resistant-infection populations. The relationship reflects intensive cytotoxic chemotherapy, prolonged marrow suppression, severe mucositis, antibacterial prophylaxis, recurrent febrile episodes, long hospital stays, and frequent exposure to invasive devices. In the international MDR P. aeruginosa study, underlying hematological disease approximately doubled the odds of MDR bloodstream infection. [19]

Functional Status

Performance status represents a broader measure of clinical vulnerability. Jin et al. identified ECOG performance status ≥2 as an independent predictor of MDRO infection in neutropenic patients. [28] Poor functional status may represent advanced malignancy, malnutrition, repeated hospitalization, greater need for invasive supportive care, and increased antibiotic use.

Comorbidities

Comorbidity associations varied by study. Ohmagari et al. identified chronic obstructive pulmonary disease as a risk factor for MDR P. aeruginosa. [11] The recent neutropenia model identified cardiac comorbidity as an independent factor. [28] Laporte-Amargos et al. identified chronic kidney disease as a predictor of Gram-negative catheter-related bloodstream infection. [22] No single comorbidity was consistently predictive across all cancer populations.

Nutritional Vulnerability

Xu et al. analyzed 1,095 bloodstream infection episodes and identified hypoproteinemia as an independent predictor of MDR Gram-negative bacteremia, with an odds ratio of approximately 3.2. [26] Low serum protein may reflect advanced cancer, systemic inflammation, malnutrition, hepatic dysfunction, gastrointestinal disease, or prolonged treatment.

Age

Age produced inconsistent findings. Rosa et al. found older age independently associated with MDR bacteremia. [13] Li et al. similarly identified age as one component of their cancer-hospital prediction model. [24] By contrast, the international MDR P. aeruginosa model found a small inverse association between age and resistance after adjustment. [19]

Treatment-Associated Predictors

Previous Antibiotic Exposure

Previous antimicrobial exposure was the most reproducible treatment-associated risk factor. Gudiol et al. found prior antibiotics increased the odds of MDR Gram-negative bacteremia more than threefold. [12] In the Oman solid-tumor study, previous antibiotic exposure was associated with an OR of 7.82 for MDR Gram-negative bacteremia. [23] In the 25-year solid cancer cohort, prior antibiotic treatment independently increased MDR-BSI risk with an OR of 2.93. [25] Jin et al. identified broad-spectrum antimicrobial use within the preceding three months as one of the strongest predictors in their model. [28]

Carbapenem Exposure

Carbapenems create particularly strong selection pressure against susceptible Gram-negative flora. Ohmagari et al. identified at least seven days of carbapenem exposure as a predictor of MDR P. aeruginosa. [11] Ceken et al. found recent carbapenem exposure independently associated with ESBL-producing Enterobacterales BSI. [17] Gudiol et al. reported prior antipseudomonal carbapenem use to increase MDR P. aeruginosa risk approximately 2.5-fold. [19]

Fluoroquinolone Exposure and Prophylaxis
Fluoroquinolone prophylaxis has historically reduced infectious morbidity in selected patients with prolonged neutropenia, but ecological consequences are increasingly relevant. Ceken et al. identified quinolone prophylaxis among predictors of ESBL BSI. [17] The multinational P. aeruginosa study found fluoroquinolone prophylaxis associated with nearly a threefold higher odds of MDR infection. [19] Trecarichi et al. again identified prophylaxis as an independent predictor of MDR Gram-negative BSI. [21]

Antipseudomonal Beta-Lactam Exposure
Prior piperacillin-tazobactam was independently associated with MDR P. aeruginosa bloodstream infection, with an OR of 3.48 in the large international study. [19] Ceken et al. also identified previous piperacillin-tazobactam therapy in patients subsequently developing ESBL-producing Enterobacterales bacteremia. [17]

Antimicrobial Therapy at the Time of Infection
The 25-year solid cancer study found BSI developing while a patient was already receiving antibiotics independently associated with MDR infection. [25] This variable captures active selection pressure immediately preceding breakthrough infection.

Total Parenteral Nutrition
Ceken et al. identified total parenteral nutrition as a predictor of ESBL-producing Enterobacterales BSI. [17] TPN likely functions as a marker of severe gastrointestinal dysfunction, prolonged central venous access, intensive supportive care, and longer hospitalization rather than causing resistance directly.

Healthcare-Associated Predictors
Resistant-Organism Colonization
Colonization was one of the strongest predictors of subsequent resistant infection. Cattaneo et al. prospectively recorded 144 MDR-colonized hematological patients among 2,226 admissions. More than one quarter developed bloodstream infection, and 16% developed BSI caused by the colonizing MDR organism. [16] Jaiswal et al. similarly demonstrated progression from CRE gastrointestinal colonization to invasive CRE infection. [18] Zhang et al. found rectal CRKP colonization associated with an OR exceeding 11 for CRKP BSI. [20] Trecarichi et al. identified an MDR-positive surveillance rectal swab as an independent predictor of MDR Gram-negative bacteremia. [21]

Previous Resistant Infection
A prior infection with an MDR phenotype suggests persistent colonization, repeated healthcare exposure, and organism-specific recurrence risk. Ohmagari et al. identified previous P. aeruginosa infection or colonization as a predictor of MDR pseudomonal infection. [11] Ceken et al. found recent ESBL infection to predict subsequent ESBL bloodstream infection. [17]

Hospitalization
Hospitalization contributes to MDR risk through contact with high-resistance environments, cross-transmission, antibiotic exposure, procedures, and devices. Marín et al. found MDR organisms concentrated in patients with previous hospital contact and antimicrobial treatment. [14] Jaiswal et al. identified longer hospital stay as an important factor in hospital-acquired CRE colonization. [18] Community acquisition was protective against MDR BSI in the large solid-tumor analysis. [25]

Central Venous Catheters
Rosa et al. identified an indwelling central venous catheter as an independent predictor of MDR bacteremia. [13] Li et al. again identified central venous catheterization as an independent predictor within their cancer-hospital MDRO nomogram. [24] Central venous devices should therefore be considered one component of cumulative MDR risk, particularly when combined with prolonged hospitalization and previous antibiotic exposure.

Urinary Catheters
Urinary catheterization produced some of the most consistent device-related associations. Gudiol et al. found an OR of 2.41 for MDR Gram-negative bacteremia among catheterized cancer patients. [12] The international P. aeruginosa study reported an OR of 2.54 for MDR pseudomonal bacteremia. [19]

Mechanical Ventilation
Recent invasive mechanical ventilation was a major predictor in the CRKP model developed by Zhang et al., with an odds ratio exceeding 18, although precision was limited by small event numbers. [20] Mechanical ventilation likely identifies a high healthcare-exposure phenotype involving ICU admission, critical illness, prior antibiotics, and multiple invasive devices.

Biliary and Urinary Sources
One of the most important differences between solid tumors and hematological malignancies is the contribution of anatomical obstruction and instrumentation. The 25-year solid cancer cohort found both biliary and urinary sources independently associated with MDR BSI, with ORs of approximately 1.84 and 1.86, respectively. [25]

Interaction Between the Three Predictor Domains
The evidence suggests that MDR infection develops most often when risk domains accumulate. In acute leukemia, host-domain risk arises from profound neutropenia; treatment-domain risk from repeated carbapenem or fluoroquinolone exposure; and healthcare-domain risk from prolonged admission, central venous access, and gastrointestinal MDR colonization.

A patient with pancreatic cancer may not be neutropenic, yet a biliary stent, repeated admissions for cholangitis, previous piperacillin-tazobactam exposure, and prior ESBL isolation may create a high MDR risk. This cumulative-risk concept may be more clinically useful than disease-specific labels alone.

Prediction Models
Several contemporary studies attempted formal prediction. The international model for MDR P. aeruginosa incorporated previous piperacillin-tazobactam, antipseudomonal carbapenem exposure, fluoroquinolone prophylaxis, hematological malignancy, urinary catheterization, and age. [19] Li et al. developed a cancer-hospital nomogram based largely on age, antibiotic treatment duration, and central venous catheterization; the reported AUC was 0.88. [24] Lopera et al. used prior antibiotic exposure, active antibiotic treatment, infection source, time period, and community acquisition in a 6,117-episode solid-tumor dataset, with discrimination around 0.72. [25] Jin et al. developed and temporally validated a model based on cardiac disease, ECOG performance status, prolonged neutropenia, and recent broad-spectrum antibiotics; AUCs were 0.874 in derivation and 0.764 in validation. [28]

Clinical Risk Stratification

Lower MDR probability	Intermediate MDR probability	Higher MDR probability
No previous resistant isolate	Recent hospitalization	Recent MDR colonization or infection
No recent broad-spectrum antibiotics	Central venous access	Broad-spectrum antibiotics within recent weeks/months
Brief or absent neutropenia	Recent antibacterial therapy	Breakthrough infection while on antibiotics
No recent prolonged admission	Prolonged cancer treatment	Prolonged/profound neutropenia
No urinary catheter or high-risk device	Biliary/urinary instrumentation	Acute leukemia or high-intensity hematological treatment
Community-onset infection	Moderate neutropenia or comorbidity	Recent carbapenem/fluoroquinolone exposure
		Urinary catheter, ventilation, or multiple invasive devices
		Prolonged hospitalization

DISCUSSION
The present systematic review demonstrates that multidrug-resistant infection in cancer patients is best understood as the consequence of accumulated risk across three domains. Treatment-related antimicrobial exposure was the most reproducible modifiable predictor. Resistant-organism colonization provided the strongest microbiological signal. Host factors such as prolonged neutropenia and impaired functional status increased susceptibility to progression from colonization to invasive infection. Healthcare factors—including catheters, prolonged admission, ventilation, and biliary or urinary instrumentation—created both opportunities for acquisition and portals for infection.

Antimicrobial Pressure as the Central Modifiable Factor
The consistency of previous antibiotic exposure is striking. The association remained present across studies spanning more than two decades and across different health systems. Several mechanisms explain this relationship: broad-spectrum agents suppress susceptible commensal organisms, resistant subpopulations gain an ecological advantage, and repeated therapy increases colonization density with resistant organisms. Antibiotic exposure also frequently occurs in patients who have the longest hospital stays and greatest number of invasive devices, creating a self-reinforcing cycle.

Colonization as a Real-Time Biomarker
Unlike many demographic variables, colonization provides direct organism-specific information. A patient with CRKP detected in rectal surveillance has a much higher pre-test probability of CRKP infection than a patient with no resistant isolate. However, a positive surveillance culture does not prove that a current fever is caused by the colonizing organism.

The clinical value of surveillance is therefore highest when combined with severity of illness, infection source, recency of colonization, and local epidemiology.

Distinct Profiles in Hematological and Solid Malignancy
In hematological malignancy, neutropenia, antimicrobial prophylaxis, mucosal injury, long inpatient treatment, and gastrointestinal colonization are central. In solid tumors, obstruction, biliary and urinary instrumentation, ports, surgery, recurrent healthcare-associated infection, and prior antibiotics assume greater importance. The 6,117-episode solid cancer study demonstrates that MDR BSI in solid cancer increasingly reflects antibiotic exposure and anatomical source rather than neutropenia alone. [25]

Device Exposure
Cancer treatment increasingly depends on vascular access devices, urinary drainage, biliary stents, and other implanted or temporary devices. The repeated association of central and urinary catheters suggests that device stewardship should be integrated with antimicrobial stewardship. Preventive priorities include limiting urinary catheterization, reviewing device necessity daily, maintaining catheter-care bundles, promptly removing unnecessary lines, and assessing source control early.

Consequences of MDR Infection
The clinical importance of prediction derives from the consequences of delayed effective treatment. MDR Gram-negative bacteremia has repeatedly been associated with increased inappropriate empirical therapy, longer hospitalization, recurrent infection, and greater mortality. A 2024 hematological cancer study reported MDROs in 24.7% of 328 bloodstream infections and a 30-day mortality of 48.1% among MDRO infections compared with 17.4% for non-MDRO infections. [29] Awada et al. found MDR-GNB associated with a median hospital stay of 23 days compared with 10.5 days and bacteremia recurrence of 35.1% versus 5.0%. [23]

Implications for Antimicrobial Stewardship
The evidence supports individualized empirical antibiotic selection rather than universal escalation. Stewardship should include review of previous culture results at presentation, documentation of antibiotic exposure during the preceding 30–90 days, use of institutional antibiograms, selective surveillance for resistant colonization in high-risk hematological populations, rapid microbiological diagnostics, early antimicrobial reassessment, de-escalation when resistance is not demonstrated, shortest effective treatment duration, and avoidance of unnecessary prophylaxis. The goal is appropriate therapy proportional to individualized resistance risk.

Implications for Infection Prevention
Predictors also identify targets for prevention. Antimicrobial stewardship can reduce selection pressure. Infection-prevention bundles can reduce central-line and urinary catheter infections. Contact precautions and surveillance may reduce transmission during CRKP outbreaks. Source control can reduce recurrent biliary and urinary infections. Early recognition of prolonged neutropenia can identify patients who require intensified infection prevention.

Strengths
This review integrates resistant infection across Gram-negative and Gram-positive pathogens and includes both hematological and solid malignancies. The predictor framework separates host, treatment, and healthcare exposure rather than combining all variables into a single list. All 18 studies retained in the qualitative synthesis are represented in Table 1, and the evidence incorporates contemporary data through 2026.

Limitations of the Evidence
Most studies were observational. The definition of MDR varied over time and between organisms. Some studies evaluated all MDRO infection, whereas others focused only on bloodstream infection. Hematological malignancy remained overrepresented. Antibiotic-exposure windows varied substantially, colonization surveillance differed between institutions, and several studies were single-center. Risk estimates reflect local resistance prevalence and cannot automatically be transferred to another country or hospital.

LIMITATIONS OF THE REVIEW
The review protocol was not prospectively registered. Heterogeneity prevented meaningful quantitative pooling. Published literature may overrepresent positive predictor associations, and there was insufficient evidence to produce a universally applicable numerical risk score.

Future Research
Future studies should derive and externally validate dynamic MDR prediction models across multiple cancer centers. Models should integrate previous microbiology, recent antimicrobial classes and duration, colonization status, cancer type and disease status, chemotherapy intensity, neutrophil count and expected duration of neutropenia, hospitalization history, device exposure, infection source, performance status, nutritional variables, and institutional resistance prevalence.

Electronic health records could automate retrieval of previous resistant isolates and antimicrobial exposure when fever is first recorded.

CONCLUSION

Multidrug-resistant bacterial infection in cancer patients develops through the interaction of host vulnerability, treatment-related antimicrobial selection, and healthcare-associated exposure. Previous broad-spectrum antibiotic use is the most consistent modifiable predictor. Known colonization or previous infection with an MDR organism provides highly actionable microbiological information. Prolonged neutropenia, hematological malignancy, impaired performance status, comorbidity, nutritional vulnerability, central venous and urinary devices, mechanical ventilation, prolonged hospitalization, and biliary or urinary instrumentation further modify risk. The most effective resistance-risk assessment should combine host, treatment, healthcare, and microbiological information to identify patients who genuinely require expanded empirical coverage while allowing lower-risk patients to avoid unnecessary exposure to broad-spectrum and last-line antibiotics.

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