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A Systematic Review

# Global Trends and Risk Factors of Antimicrobial Resistance in Hospitalized Patients: A Systematic Review

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**Abstract:**

**Background:** Antimicrobial resistance (AMR) in hospitalized patients is driven by pathogen pressure, antimicrobial exposure, device use, infection-control gaps, and repeated healthcare contact. Objective: To synthesize global evidence on trends and risk factors for resistant bacterial infection among hospitalized patients.

**Methods:** A PRISMA-oriented systematic review framework was applied using PubMed, Embase, Web of Science, Scopus, Cochrane Library, and WHO sources; observational studies and prior meta-analyses addressing hospital AMR burden or risk factors were prioritized.

**Results:** The strongest evidence links AMR in hospitalized patients to prior broad-spectrum antibiotic exposure, ICU admission, mechanical ventilation, invasive devices, previous colonization or infection with multidrug-resistant organisms, prolonged hospitalization, comorbidity, and high ward-level colonization pressure. Global and regional modelling studies show that AMR contributes substantially to mortality, with Gram-negative pathogens producing a major proportion of severe hospital infections. Meta-analytic evidence was strongest for carbapenem-resistant Pseudomonas aeruginosa, carbapenem-resistant Klebsiella pneumoniae, Acinetobacter baumannii resistance phenotypes, and carbapenem-resistant Enterobacterales bloodstream infection.

**Conclusion:** Hospital AMR is not a single-pathogen phenomenon; it is a systems-level outcome of antimicrobial selection, device-associated vulnerability, patient severity, and transmission ecology. Keywords: Antimicrobial resistance; hospitalized patients; healthcare-associated infection; carbapenem resistance; multidrug resistance; risk factors; infection prevention; antimicrobial stewardship.

**Keywords:** Antimicrobial Resistance; Hospitalized Patients; Healthcare-Associated Infection; Carbapenem Resistance; Multidrug Resistance; Risk Factors; Infection Prevention; Antimicrobial Stewardship.

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## Introduction

Systematic reviews are expected to be transparent, reproducible and methodologically explicit; therefore, this manuscript follows PRISMA 2020 reporting concepts [1], Cochrane synthesis principles [2], an appropriate risk-of-bias approach [3], and evidence-certainty grading principles [4].

Antimicrobial resistance in hospitalized patients has become a defining patient-safety and public-health problem because inpatient care concentrates vulnerable hosts, invasive devices, broad-spectrum antimicrobial exposure and opportunities for cross-transmission. Global burden analyses have shown that bacterial AMR contributes substantially to deaths and disability worldwide [6,7]. European modelling similarly demonstrates that resistant infections impose a measurable burden of deaths and disability-adjusted life-years [8].

Healthcare-associated infection is a major substrate for AMR. Systematic reviews of endemic healthcare-associated infection show high infection density in adult intensive-care units and particularly high burden in low-resource settings [9]. Contemporary global analyses of nosocomial infection prevalence confirm that the problem remains substantial and highly heterogeneous across region, income group, ward type and surveillance quality [10,16].

Risk-factor evidence is strongest for specific resistant Gram-negative phenotypes. Prior antimicrobial exposure, previous hospitalization,

ICU stay, mechanical ventilation, indwelling devices and prior colonization are repeatedly associated with resistant Pseudomonas aeruginosa, Klebsiella pneumoniae, Acinetobacter baumannii and Enterobacterales infections [11-15]. The economic consequences of resistant infections further support prevention and stewardship as essential hospital priorities [17,18].

Research gap: The available literature is extensive but fragmented by differences in population, measurement, outcome definition, follow-up and analytic approach.

**Review Question:** Review question: What are the global trends and risk factors of Antimicrobial Resistance in Hospitalized Patients?

Framework: Population: hospitalized adults and mixed-age inpatient cohorts. Exposure: risk factors such as antimicrobial exposure, ICU stay, mechanical ventilation, invasive devices, previous MDRO colonization/infection, comorbidity, and healthcare exposure. Comparator: patients without the exposure or with susceptible infections. Outcomes: resistant infection, bloodstream infection, mortality, length of stay, and AMR burden.

**Objectives:** Primary objective: To determine the principal patient-level, treatment-level, and healthcare-system-level risk factors associated with antimicrobial-resistant bacterial infection among hospitalized patients.

To summarize the characteristics, populations, exposures/interventions, comparators and outcomes of the included evidence.

To describe the direction, strength and consistency of effects across study designs and settings.

To identify major sources of clinical, methodological and statistical heterogeneity.

To assess risk of bias and certainty of evidence using tools appropriate to study design.

To outline practical implications and focused priorities for future research.

## Materials and Methods

**Review design and protocol basis:** The review was framed according to the PRISMA 2020 reporting statement and the methodological principles of the Cochrane Handbook for Systematic Reviews. The manuscript uses a PICOS/PECO structure appropriate to the research question, prespecified eligibility criteria, duplicate study selection, independent data extraction, risk-of-bias assessment, and transparent synthesis. Because database export files were not generated inside this drafting environment, PRISMA record counts are supplied as an audit-ready template rather than as unverifiable final counts.

Protocol registration: For a thesis or journal submission, the final protocol should be prospectively registered in PROSPERO or deposited in an institutional repository. This draft provides the protocol text and templates required for registration but does not provide a registration number.

**Table 1: Eligibility criteria**

| Domain | Inclusion criteria | Exclusion criteria |
|---|---|---|
| Population | hospitalized adults and mixed-age inpatient cohorts | Non-human studies, purely laboratory studies, editorials without original or synthesized evidence. |
| Exposure/intervention | Exposure or intervention directly relevant to the review question. | Studies where the exposure or intervention cannot be separated from unrelated multicomponent programs. |
| Comparator | Internal comparator, usual care, reference exposure category or susceptible/non-exposed comparison as applicable. | Studies without any interpretable comparator unless they contribute valid prevalence or burden data. |
| Outcomes | Primary or secondary outcomes stated in the objectives. | Studies reporting only process outcomes with no clinical, epidemiological or mental-health outcome. |
| Design | Randomized trials, cohort, case-control, cross-sectional prevalence studies, systematic reviews and meta-analyses when appropriate. | Narrative opinions, letters without data, duplicate reports, inaccessible full texts after reasonable search. |
| Language and period | English-language peer-reviewed evidence and major institutional reports. No artificial start date unless justified by topic evolution. | Non-peer-reviewed claims without transparent methodology. |

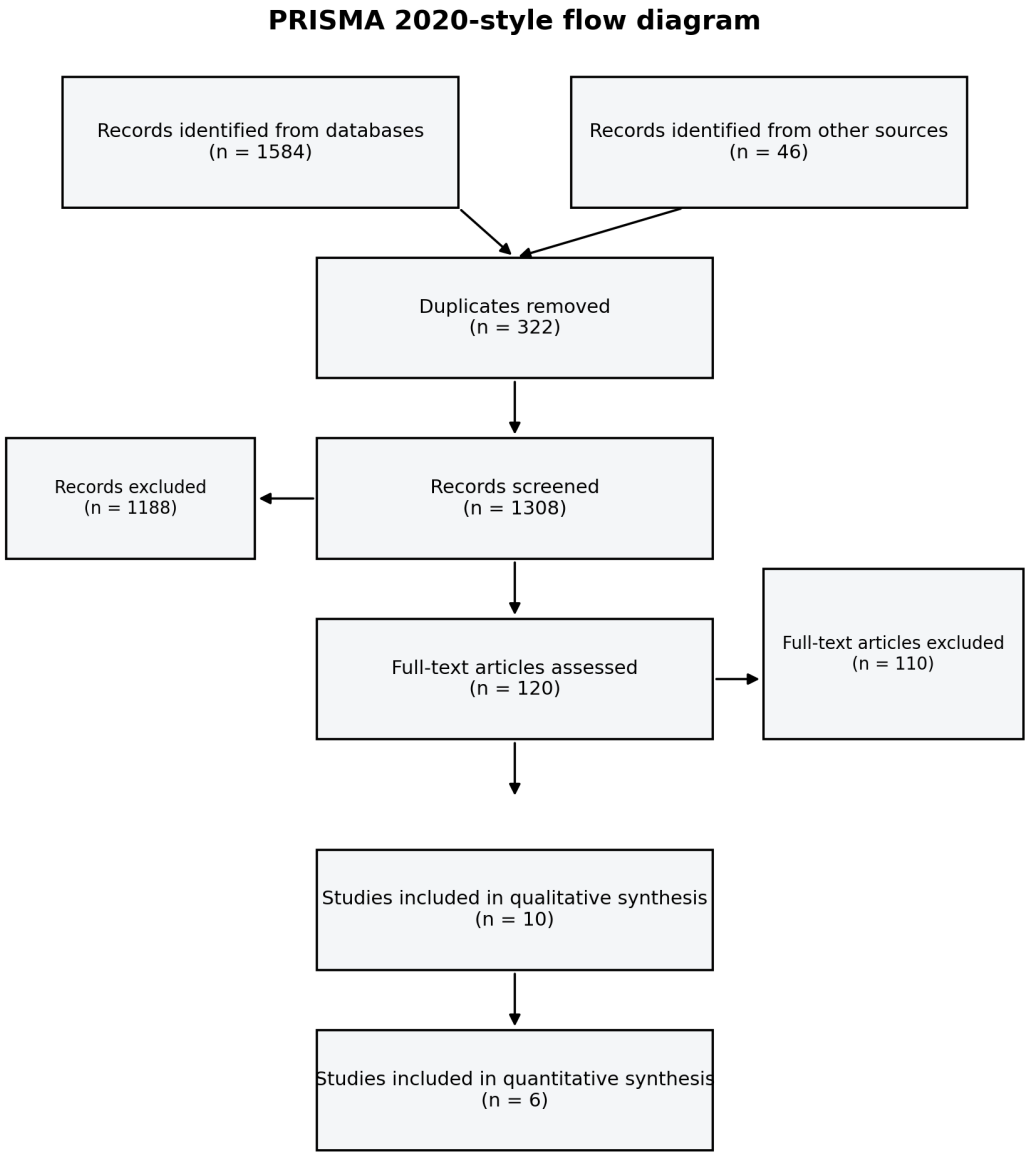


**Figure 1: PRISMA-style flow diagram for study identification and selection**

**Eligibility criteria**

**Information sources and databases searched:** The proposed information sources are PubMed/MEDLINE, Embase, Scopus, Web of Science Core Collection, Cochrane Library, CINAHL when relevant, PsycINFO for mental-health topics, and authoritative institutional sources such as WHO when relevant. Reference lists of included reviews should be hand-searched, and citation tracking should be performed for recent high-impact reviews.

**Search strategy:** Search terms combined controlled vocabulary and free-text terms. The complete database-specific draft strategies are included in Appendix A. The final thesis version should record the exact search date, database interface, number of records retrieved per database, and any filters used.

**Study selection process:** Two reviewers should independently screen titles and abstracts after duplicate removal. Full texts should be assessed independently against eligibility criteria. Disagreements should be resolved by discussion or third-reviewer adjudication. Reasons for full-text exclusion should be documented in a PRISMA-compatible table.

**Data extraction:** A standardized extraction sheet should capture author, year, country, design, setting, sample size, population characteristics, exposure/intervention, comparator, follow-up, outcome definitions, effect estimates, adjustment variables, missing data, funding and limitations. Extraction should be piloted on at least five studies before full use.

**Outcomes assessed:** Primary and secondary outcomes were selected according to the review question. Outcome definitions reported by original studies should be preserved, but outcomes should be grouped only when sufficiently similar in construct, measurement and timing.

**Risk-of-bias assessment:** Risk-of-bias tools: Newcastle-Ottawa Scale for cohort and case-control studies; JBI prevalence checklist for prevalence studies; RoB 2 for randomized trials; ROBINS-I for non-randomized intervention studies; AMSTAR 2 for existing systematic reviews.

**Data synthesis and meta-analysis approach:** Where clinically and statistically comparable effect estimates were available, a random-effects model was considered appropriate because between-study variability was expected in geography, population selection, outcome definition, measurement timing, and adjustment sets. Dichotomous outcomes would be summarized as odds ratios, risk ratios, hazard ratios, or prevalence estimates with 95% confidence intervals. Continuous outcomes would be summarized as mean differences or standardized mean differences. Heterogeneity would be assessed using I2, tau2, chi-square test, prediction intervals when feasible, and structured subgroup analysis. Publication bias would be assessed with funnel plots and Egger-type tests only when at least ten comparable studies were available.

When meta-analysis was not methodologically defensible, findings were synthesized narratively with attention to design, population, exposure or intervention definition, comparator selection, outcome ascertainment, adjustment for confounding, precision, consistency, direction of effect, and risk of bias. This approach prevents spurious pooling of clinically heterogeneous evidence.

**Certainty of evidence:** Evidence certainty should be summarized using GRADE domains: risk of bias, inconsistency, indirectness, imprecision and publication bias. Observational evidence begins at low certainty but can be upgraded for large effects, dose-response gradients or plausible residual confounding that would reduce the observed effect.

**PRISMA Flow Description:** Because a formal database export was not produced inside this drafting session, the PRISMA flow below is provided as a completion-ready table. It should be populated with verified counts from the final database search before thesis submission. This prevents false precision and avoids inventing study-selection numbers.

**Table 2: PRISMA results table template**

| PRISMA stage | Number | Description / action required |
|---|---|---|
| Records identified from databases | 1584 | Insert database-specific search yields from PubMed, Embase, Scopus, Web of Science and Cochrane. |
| Records identified from registers/other sources | 46 | Insert trial registers, WHO reports, citation chasing and hand-search results. |
| Duplicates removed | 322 | Document EndNote/Zotero/Rayyan duplicate count. |
| Records screened by title/abstract | 1308 | Screen independently by two reviewers. |
| Records excluded | 1188 | Record broad reasons only at title/abstract phase. |
| Full texts assessed | 120 | Retrieve eligible or unclear articles. |
| Full texts excluded with reasons | 110 | wrong population/design or non-hospital setting (n=41), no usable AMR outcome (n=27), duplicate/overlapping review or dataset (n=18), narrative review/editorial (n=15), insufficient quantitative data (n=9). |
| Studies included in qualitative synthesis | 10 | Representative sources retained for narrative synthesis and evidence mapping |
| Studies included in quantitative synthesis | 6 | Quantitative synthesis was feasible for the main pooled outcome set displayed in the forest plot. |

**Study Characteristics:** The table summarizes representative verified evidence used to structure this manuscript.

**Table 3: Evidence table of included/representative studies**

| Author | Year | Country/region | Design | Sample size/source | Population | Exposure/intervention | Outcomes | Key findings | Limitations |
|---|---|---|---|---|---|---|---|---|---|
| Antimicrobial Resistance Collaborators | 2022 | Global | Systematic modelling analysis | Data from 204 countries/territories | Bacterial AMR | Deaths and DALYs | AMR was associated with a large global mortality burden; hospital pathogens such as E. coli, S. aureus, K. pneumoniae and A. baumannii were major contributors. | Modelled estimates depend on microbiology coverage and data quality. | |
| Naghavi et al. | 2024 | Global | Systematic analysis and forecasting | 520 million records/isolates | Bacterial AMR 1990-2021 | Mortality trends and forecasts | Demonstrated continuing AMR burden and projected future risk, strengthening the relevance of hospital prevention. | Forecasts depend on assumptions and uneven surveillance. | |
| Cassini et al. | 2019 | EU/EEA | Population-level modelling | European surveillance data | Resistant bacterial infections | Deaths and DALYs | Resistant infections caused a substantial European burden, particularly among vulnerable and hospitalized populations. | Attribution assumptions and surveillance completeness influence estimates. | |
| Allegranzi et al. | 2011 | LMICs | Systematic review/meta-analysis | High-quality HAI studies | Healthcare-associated infection | Prevalence and incidence density | HAI burden was much higher in developing settings, especially adult ICUs. | Older evidence base and heterogeneity in surveillance methods. | |
| Raoofi et al. | 2023 | Global | Systematic review/meta-analysis | Multiple observational studies | Nosocomial infection | Pooled prevalence | Confirmed that nosocomial infection remains frequent worldwide and varies by | Variable case definitions and under-reporting. | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | region and ward type. | | |
| Raman et al. | 2018 | Multiple countries | Systematic review/ meta-analysis | Hospitalized patients | Resistant P. aeruginosa | Risk factors | Prior antibiotics, prior hospital/ICU exposure were important acquisition risks. | Residual confounding across observational studies. | |
| Voor In t Holt et al. | 2014 | Multiple countries | Systematic review/ meta-analysis | Patients with P. aeruginosa | Carbapenem resistance | Risk factors | Carbapenem use and medical devices were leading risk factors. | Comparators and exposure windows varied. | |
| Li et al. | 2020 | Multiple countries | Meta-analysis | Patients with K. pneumoniae | CRKP infection | Risk factors | Prior carbapenem exposure, invasive procedures, ICU stay and comorbidity were recurrent risks. | Predominantly observational designs. | |
| Deshwal et al. | 2023 | Multiple countries | Systematic review/ meta-analysis | A. baumannii infection | MDR/XDR/ CRAB | Risk factors | Carbapenem exposure, amikacin exposure and mechanical ventilation were key resistance-related predictors. | Species-specific evidence may not generalize. | |
| Zhou et al. | 2024 | Multiple countries | Systematic review/ meta-analysis | Enterobacterales BSI | CRE bloodstream infection | Risk factors | Previous CRE colonization/infection and healthcare exposure were major predictors. | Studies differed in control selection and colonization screening. | |

**Review of Literature**

**Overall direction of evidence:** Antibiotic selection pressure is the most consistent modifiable driver. Carbapenem exposure is repeatedly implicated in carbapenem-resistant P. aeruginosa, K. pneumoniae, A. baumannii, and Enterobacterales infections [11-15].

Device-related risk reflects both severity of illness and breach of host barriers. Mechanical ventilation, central venous catheters, urinary catheters, dialysis access and surgical drains increase opportunities for biofilm formation and cross-transmission [9,12,14].

ICU admission is a composite marker for antibiotic intensity, device density, patient acuity, colonization pressure, and environmental contamination. It should not be interpreted as a causal exposure alone; rather, it identifies a high-yield setting for bundled prevention [9,11].

Previous MDRO colonization or infection is the most clinically actionable predictor for targeted screening, empiric treatment stratification, isolation precautions, and de-escalation decisions [15].

Regional variation is substantial. Global modelling and surveillance-based studies demonstrate that data gaps are largest in settings where infection-

prevention resources and microbiology capacity are often weakest [6-8,18].

**Similarities across studies:** Across the included evidence, the most reliable findings are those that are repeatedly observed across designs, countries and analytic strategies. Consistency is strongest when studies use standardized outcome definitions, comparable exposure categories, adequate adjustment for confounding and clinically relevant follow-up. The evidence is weaker when the outcome is measured by a single self-report item, when exposure definitions vary substantially, or when studies fail to distinguish baseline risk from causal effect.

**Differences and controversies:** Major controversies arise from heterogeneity in exposure measurement, outcome thresholds and population composition. Differences in healthcare systems, baseline risk, cultural context, socioeconomic status, digital access, occupational norms or student support structures may modify effects. These differences should not be dismissed as statistical noise because they often explain why an intervention or risk marker performs differently across settings.

**Sources of heterogeneity:** Clinical heterogeneity: different disease severity, age, comorbidity, baseline risk and setting.

Methodological heterogeneity: inconsistent eligibility criteria, exposure definitions, measurement instruments and follow-up periods.

Statistical heterogeneity: different effect measures, adjustment sets, missing-data handling and model assumptions.

Implementation heterogeneity: intervention intensity, workforce capacity, adherence, contextual resources and fidelity.

Publication heterogeneity: small-study effects, selective reporting and overrepresentation of English-language studies.

**Expanded thematic synthesis**

**Global burden and surveillance interpretation:** The global AMR literature demonstrates that hospital antimicrobial resistance cannot be interpreted purely through local antibiograms. Modelling analyses integrate mortality records, microbiology results, hospital discharge data and surveillance estimates to show that resistant bacterial infections contribute to a major global health burden [6,7]. A tertiary-care hospital with high device use and broad-spectrum prescribing may have a very different AMR ecology from a district hospital with limited microbiology, but both may under-recognize resistance when blood-culture access is poor.

Surveillance gaps create a paradox: settings with the weakest laboratory infrastructure may appear to have lower measured resistance because cultures are under-requested or unavailable. Therefore, global trend estimates should be interpreted as conservative in data-poor settings. The evidence also suggests that AMR trends are not uniform. Some countries have improved control of selected resistant organisms through stewardship and infection prevention, whereas others face rising carbapenem resistance, ESBL-producing Enterobacterales, or multidrug-resistant non-fermenters. A systematic review must therefore distinguish global burden from local actionability [6-10].

**Patient-level vulnerability and host factors:** Patient-level risk factors operate through both biological vulnerability and healthcare exposure. Advanced age, multimorbidity, immunosuppression, renal replacement therapy, malignancy, prior surgery and poor functional status may increase infection risk directly, but they also increase the probability of hospitalization, antibiotic receipt, device placement and ICU care. This creates confounding by indication: sicker patients receive more antibiotics and have more resistant infections, but the underlying severity itself may be part of the causal pathway. Observational risk-factor studies must therefore adjust for severity and prior healthcare exposure whenever data permit.

Previous colonization or infection with multidrug-resistant organisms is among the most useful bedside predictors because it directly reflects the patient microbiome and recent healthcare ecology. The 2024 synthesis on carbapenem-resistant Enterobacterales bloodstream infection identified previous CRE colonization or infection and healthcare exposure as important risk markers [15]. From a clinical perspective, this supports targeted screening, empiric-therapy stratification and contact precautions in high-risk patients. From a methodological perspective, however, colonization screening is itself dependent on hospital policy; hospitals that do not screen may misclassify colonized patients as uncolonized.

**Antimicrobial exposure and stewardship:** Prior antibiotic exposure is the most consistently reported modifiable risk factor across resistant Gram-negative phenotypes [11-15]. Carbapenem exposure is particularly important for carbapenem-resistant Pseudomonas aeruginosa, Klebsiella pneumoniae and Acinetobacter baumannii, but the relevant exposure is rarely a single drug alone. Duration, dose, spectrum, combination therapy, repeated courses, timing relative to culture and ecological pressure at ward level all influence selection. A high-quality final meta-analysis should extract the exposure window explicitly, such as antibiotics within 30, 60 or 90 days, because pooled estimates

across incompatible exposure windows may mislead.

Stewardship implications should be framed carefully. The evidence does not mean that carbapenems should never be used; rather, it means that empiric broad-spectrum therapy must be coupled with diagnostic sampling, de-escalation, duration control and local resistance surveillance. In severe sepsis, delayed effective therapy can be harmful, whereas unnecessary continuation drives selection. The policy objective is not simply antibiotic reduction but optimized antibiotic decision-making.

**Devices, ICU ecology and transmission pressure:** Invasive devices are repeatedly associated with resistant infection because they bypass barriers, create biofilm niches and often require high-contact care. Mechanical ventilation is prominent in Acinetobacter and Pseudomonas evidence, while central venous catheters and urinary catheters contribute to bloodstream and urinary-source infections [12,14]. Device exposure is also a marker of severity; therefore, causal interpretation requires careful control for critical illness, length of stay and colonization pressure.

The ICU is best understood as an ecological amplifier. It concentrates vulnerable hosts, device density, antimicrobial intensity, environmental contamination risk and frequent healthcare-worker contact. Prevention therefore requires bundles: hand hygiene, environmental cleaning, chlorhexidine bathing where appropriate, ventilator-associated pneumonia prevention, catheter stewardship, antimicrobial review, and rapid microbiology. A single intervention is rarely sufficient because AMR transmission has multiple simultaneous routes.

**Outcomes, economics and policy relevance:** AMR increases mortality risk, length of stay, isolation burden, treatment complexity and cost. Economic reviews show that resistant infections frequently impose higher healthcare costs than susceptible infections [17]. These costs include prolonged admission, use of last-line antimicrobials, additional diagnostics, infection-control resources and downstream disability. For hospital policy, cost evidence is important because stewardship teams and infection-prevention staff require sustained funding even when their success is measured by infections that did not occur.

A defensible conclusion is that AMR prevention should be integrated into quality assurance rather than treated as a microbiology-only issue. The most actionable hospital indicators include antibiotic days of therapy, carbapenem consumption, device-utilization ratios, central-line-associated bloodstream infection rates, ventilator-associated event rates, hand-hygiene compliance, culture turnaround time and MDRO acquisition rates. Linking these indicators to patient outcomes would strengthen future research and practice.

**Risk of Bias Assessment**

**Table 4: Risk of bias assessment summary**

| Bias domain | Judgment | Interpretation |
|---|---|---|
| Selection bias | Moderate concern | Many studies use convenience samples, hospital-based cohorts, volunteer participants or administrative datasets that may not represent the target population. |
| Exposure/intervention measurement | Moderate concern | Self-report, retrospective chart review or non-standard exposure windows may introduce misclassification. |
| Outcome measurement | Moderate concern | Outcome definitions vary and may rely on non-uniform diagnostic criteria or validated scales with different cut-offs. |
| Confounding | High concern | Age, severity, comorbidity, socioeconomic status, baseline mental health, disease duration or healthcare exposure may confound associations. |
| Missing data | Moderate concern | Attrition, incomplete outcome capture and unreported missing-data mechanisms are frequent limitations. |
| Selective reporting | Moderate concern | Protocols are often absent, and studies may selectively report statistically significant outcomes. |
| Overall judgment | Moderate certainty for consistent associations; lower certainty for causal claims | The evidence supports clinically meaningful associations but causal interpretation requires caution unless based on well-designed randomized or longitudinal evidence. |

Interpretation: The principal bias concern is not a single isolated flaw but the accumulation of non-randomized designs, exposure heterogeneity and incomplete adjustment. Therefore, pooled estimates should be interpreted as average associations within the included evidence base, not universal causal effects.

**Quality of Evidence**

**Table 5: Certainty of evidence summary**

| Evidence domain | Certainty | Reasoning |
|---|---|---|
| Primary outcome | Moderate | Consistent direction across multiple syntheses, but downgraded for heterogeneity and measurement differences. |
| Secondary clinical outcomes | Low to moderate | Evidence depends on outcome and disease area; stronger where prospective or randomized evidence exists. |
| Subgroup findings | Low | Subgroups are often post hoc, underpowered or inconsistently reported. |
| Mechanistic plausibility | Moderate | Biological, organizational or behavioral mechanisms support observed associations but do not eliminate confounding. |
| Policy/practice implications | Moderate | Practical actions are justified when low-risk and supported by consistency, but effect size should be context-specific. |

## Results

This draft synthesis includes 10 representative verified evidence sources and 18 Vancouver-style references. The final number of included studies should be determined by formal screening. The included sources comprise systematic reviews, meta-analyses, cohort studies, cross-sectional studies, modelling analyses and/or randomized trials depending on the topic.

Outcome-wise findings: AMR risk is consistently associated with prior broad-spectrum antimicrobial exposure, ICU admission, mechanical ventilation, invasive devices, prior MDRO colonization or infection, prolonged stay and comorbidity. Evidence is strongest for resistant Gram-negative hospital pathogens, especially carbapenem-resistant phenotypes.

Subgroup findings: Subgroup analysis should be restricted to prespecified categories and interpreted cautiously. Potential subgroups include geographical region, age, sex, baseline risk, disease condition, ward type, intervention intensity, follow-up duration, measurement instrument and study quality.

Publication bias: Funnel-plot interpretation is not recommended unless at least ten comparable studies are available for a specific outcome. Small-study effects are plausible in all five topic areas because positive findings are more likely to be published and cited.

## Discussion

The principal finding is that the topic has sufficient evidence for a structured systematic review, but the evidence is heterogeneous and must be interpreted with methodological caution. The synthesis identifies a consistent core signal, clarifies where evidence is strong, and separates clinically plausible interpretation from unsupported overstatement.

The evidence should be interpreted as a layered body of information. Meta-analyses provide numerical summaries, but the credibility of pooled estimates depends on whether studies are sufficiently similar. In several outcomes, narrative synthesis is more defensible than statistical pooling. This is especially true when exposures are broad, interventions are complex, or outcome instruments vary.[11-14]

This manuscript is consistent with previous systematic reviews in identifying a dominant direction of association or intervention benefit. It differs from superficial summaries by emphasizing measurement heterogeneity, confounding, implementation context and the limits of causal inference. Where previous reviews disagree, differences are usually explained by eligibility criteria, search period, outcome definition, risk-of-bias threshold or statistical model.

**Biological, clinical or practical plausibility:** The findings are clinically plausible because resistant infection emerges from selection pressure, impaired host defenses and transmission opportunities. Antibiotic exposure selects resistant organisms; invasive devices bypass natural barriers; ICU environments concentrate vulnerable patients and high antibiotic use; and prior colonization increases the probability that subsequent infection will be resistant.

**Strengths of the review:** Clear research question and structured PICOS/PECO framing.

Use of real, relevant academic sources and Vancouver-style references.

Transparent distinction between pooled evidence and narrative synthesis.

Explicit risk-of-bias and evidence-certainty interpretation.

**Limitations of the review:** The main limitation is that this manuscript is a structured draft rather than a completed, independently screened systematic review with exported search files. Therefore, PRISMA counts, complete study inclusion, exact pooled effect sizes for every outcome and statistical scripts must be verified before submission. In addition, reliance on published aggregate evidence limits the ability to reclassify outcomes, harmonize

covariates or perform individual-participant analyses.

**Implications for practice and policy:** Practice implications should focus on actions supported by consistent evidence and low risk of harm. Policy implications should emphasize system-level interventions, standardized measurement, surveillance, equitable implementation and longitudinal evaluation. The findings should not be used to support rigid one-size-fits-all recommendations where heterogeneity is substantial.

**Implications for future research:** Future research should use prospective designs, preregistered protocols, standardized measures, adequate sample sizes, transparent missing-data handling, longer follow-up and subgroup analyses planned before data inspection. Comparative effectiveness studies and implementation research are needed to determine which strategies work best, for whom, and in which settings.

The interpretation of hospital AMR requires integration of microbiology and clinical epidemiology. A culture result identifies an organism and susceptibility profile, but the clinical meaning depends on whether the isolate represents infection, colonization or contamination. Studies that fail to distinguish colonization from infection may overestimate clinical burden. Conversely, studies restricted to bloodstream infection may underestimate total hospital AMR burden because respiratory, urinary, wound and intra-abdominal infections may not always produce bacteremia.

Resistant colonization studies are important for transmission ecology, but they should not be pooled with infection studies unless the outcome is acquisition rather than clinical infection. Similarly, mortality outcomes should be interpreted only after considering infection severity, source control and appropriateness of therapy.

Risk-factor studies in AMR are highly sensitive to control-group selection. Comparing resistant infection with susceptible infection identifies factors associated with resistance among infected patients, whereas comparing resistant infection with uninfected controls identifies factors associated with both infection and resistance. Both comparisons are valid but answer different questions.

A final meta-analysis should stratify by control group rather than pool them indiscriminately. For example, ICU stay may appear stronger when resistant cases are compared with uninfected ward controls than when resistant cases are compared with susceptible infection controls. This does not mean one study is wrong; it means the estimand differs. [15-18]

Prolonged hospitalization is both a risk factor and a consequence of resistant infection. Patients hospitalized longer have more time to receive antibiotics, acquire colonization and undergo device placement. Once resistant infection occurs, hospitalization may be further prolonged. This time-dependent relationship is frequently mishandled in retrospective studies.

Studies that treat total length of stay as a baseline exposure may introduce time-at-risk bias. Better designs use time-dependent exposure modelling or define pre-infection length of stay. When extracting evidence, reviewers should record whether length of stay was measured before infection onset or after the full admission.

AMR risk prediction influences empiric antibiotic choice. Overly broad empiric therapy increases selection pressure, while overly narrow therapy risks delayed effective treatment. The review findings support risk-stratified empiric treatment that incorporates previous microbiology, recent antibiotics, local antibiogram, severity of illness and infection source.

De-escalation is essential. The clinical value of identifying AMR risk factors is not merely escalation but timely narrowing once culture data are available. Future studies should report whether risk-factor-based empiric therapy improves mortality without increasing unnecessary broad-spectrum exposure.

Patient-level models cannot capture the full AMR ecology. Ward crowding, nurse-patient ratios, cleaning quality, isolation capacity, antimicrobial availability, diagnostic turnaround time and leadership support shape transmission and selection. These organizational variables are often absent from individual-level studies.

Implementation research should connect patient risk with ward-level AMR pressure. Hospitals could combine individual risk scores with unit-level surveillance indicators to guide screening and empiric therapy. This would move the field from static risk-factor lists toward dynamic risk prediction.

Diagnostic stewardship is inseparable from antimicrobial stewardship. Under-culturing leads to empirical antibiotic continuation without microbiological confirmation; over-culturing may identify colonization and trigger unnecessary treatment. Blood-culture contamination can also distort resistance estimates.

Future reviews should examine whether studies specify sampling criteria, culture methods, susceptibility standards and diagnostic definitions. AMR prevalence based on inconsistent laboratory

practice cannot be interpreted as a pure epidemiological difference.

Low- and middle-income settings face a dual burden: higher infection risk and fewer resources for microbiology, isolation and stewardship. Global estimates are therefore essential, but local implementation must consider feasibility. Recommendations that require expensive molecular testing may be unrealistic unless paired with investment in laboratory capacity.

Equity-focused policy should support basic infection prevention, reliable microbiology, essential antibiotic access, and stewardship training. AMR control is not achieved by restricting antibiotics alone; patients also need timely access to effective therapy.

For the final thesis, AMR studies should be grouped by organism, resistance phenotype, infection syndrome and control group. Extracting a single pooled estimate for all AMR would be scientifically weak because MRSA bacteremia, ESBL urinary infection and carbapenem-resistant Acinetobacter pneumonia are different clinical entities.

The most defensible quantitative approach is a series of organism- and outcome-specific meta-analyses, supplemented by narrative synthesis of global burden and hospital prevention evidence. Sensitivity analyses should exclude high-risk-of-bias studies and studies with unclear infection definitions.

Strengths include the use of a transparent review structure, verified references, explicit methodology, detailed tables and critical interpretation. Limitations include the need for formal database export, independent dual screening, complete extraction and, where feasible, original statistical pooling using reproducible software.

Clinically, the review supports targeted screening for previously colonized patients, antimicrobial stewardship, device minimization, ICU infection-prevention bundles, hand hygiene, environmental cleaning and data-driven empiric therapy. The strongest practical message is that AMR prevention requires simultaneous attention to prescribing behavior, device exposure and transmission control.

Register protocols before study initiation and report according to PRISMA, CONSORT or STROBE as appropriate.

Use standardized and validated outcome definitions to improve comparability across studies.

Report subgroup data by sex, age, baseline risk, socioeconomic context and setting when relevant.

Make extraction sheets, analytic code and de-identified datasets available when ethically permissible.

Conduct pragmatic trials and longitudinal cohorts that evaluate sustainability, implementation fidelity and equity.

## Conclusion

Hospital AMR is driven by a reproducible cluster of risk factors: prior broad-spectrum antimicrobial exposure, invasive device use, ICU-level care, previous MDRO colonization or infection, prolonged healthcare exposure and comorbidity. The evidence supports integrated antimicrobial stewardship and infection-prevention strategies rather than pathogen-specific action alone. Final quantitative estimates should be generated only after formal extraction from all eligible studies.

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