White Paper

Safeguarding Progress in Hematology-Oncology: Addressing The Growing Threat of Antimicrobial Resistance

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Foreword by the Union for International Cancer Control

Remarkable advances in hematology-oncology have transformed the outlook for many people living with blood cancers. Novel immunotherapies, targeted treatments, stem-cell transplantation, and increasingly personalized approaches have extended survival and created new opportunities for patients around the world. Yet these therapeutic gains depend on something that is often taken for granted: the ability to prevent, diagnose, and effectively treat infections.

Antimicrobial resistance (AMR) is increasingly challenging this foundation of modern cancer care. People living with hematological malignancies are particularly vulnerable to infections due to both disease-related and treatment-related immune suppression. As resistant pathogens become more common, infections can result in treatment delays, interruptions, prolonged hospital stays, increased healthcare costs, and poorer outcomes. Evidence suggests that AMR is already having a substantial impact on this patient population, with resistant infections associated with higher mortality and increased healthcare utilization.

This white paper comes at an important moment. As innovation continues to expand treatment possibilities in hematology-oncology, there is growing recognition that infection prevention, antimicrobial stewardship, diagnostics, and surveillance are integral components of successful cancer care. The challenge is not simply one of infectious disease management. It is also about protecting the effectiveness, accessibility, and sustainability of cancer treatment in an increasingly complex global health landscape.

The findings presented here draw on published literature, clinical trial analysis, and broader insights from real-world practice. Together, they highlight the central message that infections remain among the most significant complications of hematological cancer care, and that AMR is amplifying this burden. The white paper shows that infection risk is closely linked to treatment exposure, that resistant infections are associated with worse outcomes, and that important gaps remain in our understanding of how AMR affects patients across different geographies and healthcare settings. At the same time, it identifies opportunities to generate better evidence, strengthen surveillance, and better integrate infection-related considerations into clinical development, healthcare delivery, and policy planning.

These observations are reinforced by emerging evidence from the broader literature. A recent global scoping review commissioned by the Union for International Cancer Control Task Force on Antimicrobial Resistance and Cancer Care found that the pooled prevalence of AMR bacterial infections in patients with hematological malignancies was 35%, with resistant bloodstream infections representing a particularly important concern. The review also found that nearly two-thirds of studies reporting mortality demonstrated higher mortality among patients with AMR infections and highlighted major gaps in surveillance and evidence generation, particularly in low- and middle-income countries (LMICs).

Importantly, this white paper should not be viewed as a critique of any individual stakeholder. Rather, it highlights an opportunity for collaboration. Pharmaceutical companies, researchers, regulators, healthcare professionals, patient organizations, and global health partners all have important roles to play in ensuring that advances in cancer treatment continue to translate into meaningful improvements in patient outcomes. Investments in better infection surveillance, microbiology capacity, diagnostics, antimicrobial stewardship, infection prevention and control, real-world evidence generation, and supportive care can strengthen both patient safety and healthcare system resilience. These efforts can also help ensure that cancer therapies developed today remain effective and deliver value across diverse patient populations and healthcare settings.

The white paper also reminds us that geography matters. Significant evidence gaps remain in regions facing both a growing cancer burden and

a high prevalence of resistant infections. Better representation of these settings in research, surveillance, and clinical development will be essential to understanding the full impact of AMR on cancer care and to designing solutions that are relevant, equitable, and effective across different contexts. As the published literature has shown, the current evidence base remains heavily concentrated in high-income settings, leaving important questions unanswered for many parts of the world.

Ultimately, the goal is to ensure that people living with hematological malignancies can continue to benefit from advances in cancer treatment without having those gains undermined by preventable or difficult-to-treat infections. Achieving this goal will require stronger evidence, greater collaboration across disciplines, and a commitment to viewing infection prevention, management, and AMR mitigation as integral components of quality cancer care.

This white paper is an important contribution to that effort. By bringing together perspectives from oncology, infectious diseases, public health, policy, and real-world evidence, it helps highlight an area that has received relatively limited attention despite its growing significance. Most importantly, it provides a foundation for action. Through continued collaboration and investment in data, surveillance, innovation, and implementation, we can build more resilient cancer care systems and improve outcomes for patients.

Introduction

Historically, hematological cancers have served as proving ground for many of oncology's most innovative therapies, with several treatment modalities first demonstrating clinical success in blood cancers before expanding into solid tumors. Advances in immuno-oncology, targeted small molecules, and other novel biologics have transformed survival prospects for many patients.[1] However, these therapeutic gains depend heavily on the ability to safely deliver treatments that often induce profound immunosuppression.

Infections are among the most common and serious complications in this setting. They can worsen patient outcomes, delay or interrupt cancer treatment, and place additional strain on healthcare systems. Infections may also affect clinical research and the development of new therapies, with implications for the timely generation of evidence and patient access to innovation. The challenge is compounded by the accelerating global rise in AMR, particularly antibacterial resistance, which threatens the effectiveness of the antibiotics relied upon to prevent and treat these infections.

This paper explores how rising bacterial resistance could constrain the delivery of immuno-oncology therapies and affect treatment outcomes, especially in emerging markets where the prevalence of resistant pathogens is highest.[2] It examines whether AMR is receiving sufficient attention as a strategic risk in the development of oncology therapies and care delivery, and considers the implications for patients, healthcare systems, regulators, and industry.

The findings presented in this paper are informed by three complementary sources of evidence: a structured review of the literature on infection burden and AMR in hematological cancers; an analysis of 27 completed late-phase hematology-oncology clinical trials; and illustrative insights from clinicians and people living with hematological cancers. Combined, these sources provide insight into the epidemiology and clinical drivers of infection risk, the reporting of infections and their relationship with trial outcomes, and the lived experience of patients and clinicians navigating infection-related disruption in hematological cancer care.



Section I. Setting the context

Hematological cancer care in an era of rising antimicrobial resistance

Hematological cancers remain among the most prevalent cancer types globally, accounting for 6.6% of all cancer diagnoses and 7.2% of cancer-related mortality.[3,4] In the United States alone, someone is diagnosed with a hematological cancer every three minutes, and a related death occurs every nine minutes.[5] This heterogeneous group of diseases encompasses multiple malignancies with distinct biological features and treatment paradigms, and most of them are managed with intensive, and often immunosuppressive, therapeutic regimens.

Over the past three decades, advances in diagnostics, supportive care, and innovative therapies have significantly improved outcomes for many patients with hematological cancers.[6] While mortality has declined in many high-income countries, largely due to earlier diagnosis and the introduction of targeted therapies and immunotherapies such as chimeric antigen receptor T-cell (CAR-T) agents, these gains have not been experienced equally across all settings.[7] In many LMICs, limited access to diagnostics and advanced cancer care continues to contribute to poorer outcomes. Across all settings, however, the safe delivery of effective hematology-oncology care depends on the ability to prevent and manage infectious complications throughout the treatment pathway.

Despite therapeutic progress, infections remain among the most common and serious complications in hematological cancer care. The disease itself, together with treatments such as chemotherapy, stem cell transplantation, and cellular therapies, can leave patients profoundly immunocompromised and highly susceptible to infection. Bloodstream infections, pneumonia, and sepsis remain important causes of morbidity and mortality, with Gram-negative pathogens posing a particular concern because of their association with severe disease and limited treatment options when resistance emerges.[8,9]



Consequently, AMR is one of the most salient threats in public health, directly responsible for taking the lives of approximately 1.27 million people in 2019 and contributing to an estimated 4.95 million deaths globally.[10] Driven by the misuse and overuse of anti-infectives, AMR disproportionately affects LMICs while threatening many of the gains of modern medicine. For these and other reasons, this phenomenon has the potential to undermine therapeutic progress across multiple disease areas, including cancer.

As shown in table 1, the global burden of AMR is projected to rise substantially over the coming decades, with modelling suggesting millions of additional deaths by 2050. The burden is expected to fall disproportionately on older adults and on regions such as South Asia, Latin America and the Caribbean, and sub-Saharan Africa, where 70% of cancer deaths are already taking place.[11] These same regions are expected to register some of the fastest growth in demand for hematology-oncology services, creating a geographic overlap between increasing cancer burden and growing infection-related risk.

Table 1. The global toll of AMR and projections through 2050

METRIC	PROJECTION THROUGH 2050
Annual attributable deaths	Approximately 1.91 million (from 1.27 million in 2019)[12]
Cumulative direct AMR deaths (2025-2050)	Approximately 39 million[13]
Annual associated deaths (some role of AMR)	Approximately 8.22 million[14]
Regional hotspots	South Asia, Latin America and the Caribbean, and sub-Saharan Africa[15]
Age distribution	Roughly 66% of attributable deaths in ≥70-year-olds[16]
Economic burden	US$1 trillion/year in direct health costs and gross domestic product losses up to 3 to 3.8% annually by 2030-2050[17]

Current surveillance data also reveals substantial geographic variation in resistance among key Gram-negative pathogens, a group of bacteria frequently associated with severe bloodstream and other life-threatening infections in immunocompromised patients. As shown in table 2, for *Escherichia coli*, resistance to third-generation cephalosporins remains relatively low in high-income countries such as Australia, the United Kingdom, and the United States, but is considerably higher in several emerging markets such as Thailand, Saudi Arabia, Tanzania, Indonesia, Kenya, and India. Similarly, marked regional differences are observed for *Klebsiella pneumoniae* resistance to carbapenems. Resistance remains uncommon in Australia, the United Kingdom, and the United States, but reaches substantially higher levels in Saudi Arabia, Argentina, Brazil, India, and Türkiye.

Table 2. Resistance of *Escherichia coli* to third-generation cephalosporins and of *Klebsiella pneumoniae* to carbapenems

COUNTRY (YEAR OF DATA SOURCE)	*E. COLI* RESISTANCE TO THIRD-GENERATION CEPHALOSPORINS (%)	*K. PNEUMONIAE* RESISTANCE TO CARBAPENEMS (%)
Argentina (2023)	9	31
Australia (2023)	8	1
Brazil (2023)	20	40
India (2023)	67	50
Indonesia (2023)	56	22
Kenya (2023)	58	20
Pakistan (2023)	72	25
Saudi Arabia (2023)	38	23
Tanzania (2023)	52	8
Thailand (2023)	32	23
Türkiye (2023)	55	56
United Kingdom (2023)	9	1
United States (2016)	15	3

Sources: Global Antimicrobial Resistance Surveillance System (GLASS),[18] Surveillance Network,[19] and Central Asian and European Surveillance of Antimicrobial Resistance Network (CAESAR)[20]

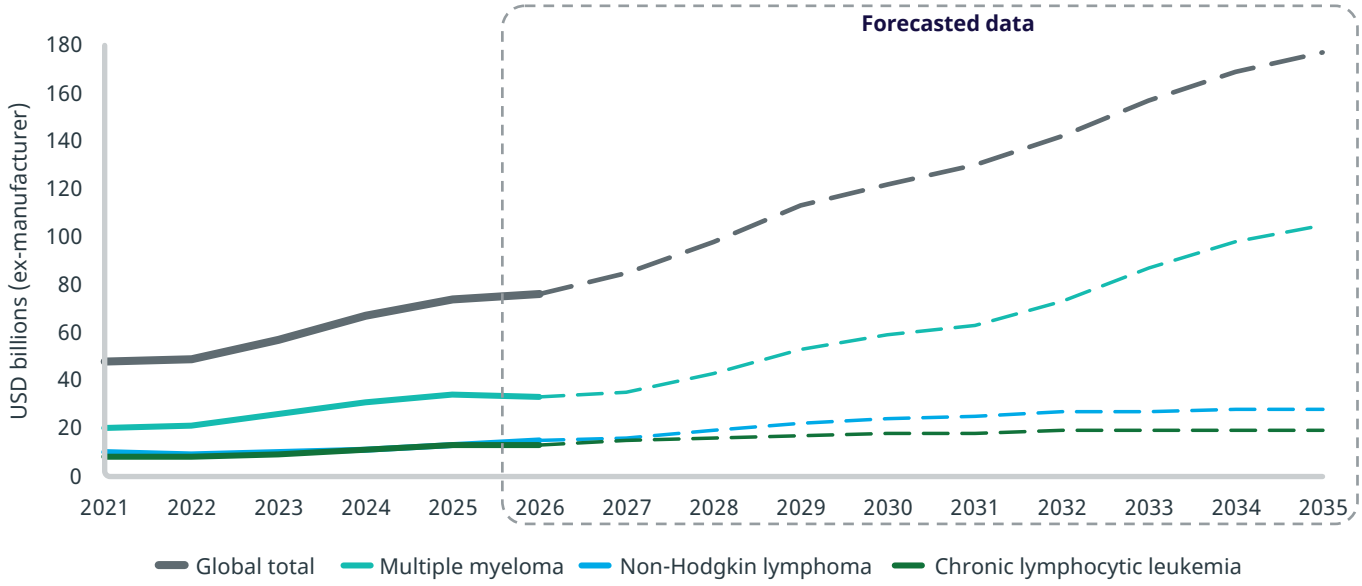
These findings are consistent with the literature reviewed for this paper, which identified multidrug-resistant Gram-negative organisms as an increasing threat in patients with hematological cancers, particularly in LMICs, where bloodstream infections are common and access to detailed resistance surveillance may be limited. As access to advanced cancer therapies expands globally, resistance patterns may increasingly constrain the ability to prevent and manage infectious complications, potentially affecting both treatment delivery and patient outcomes.

Market expansion and increasing global access for hematological cancer therapies

Understanding the scale of this challenge requires consideration of the broader evolution of the hematology-oncology therapeutic landscape. Although significant disparities in access to novel agents persist between and within countries, advances in treatment are gradually reaching a broader range of healthcare settings. This expanding therapeutic footprint is increasing the global importance of hematological cancer care, even more so in regions where cancer burden is rising rapidly and healthcare systems are simultaneously confronting high AMR rates. In such geographies, the ability to prevent and manage infections may become an increasingly important determinant of whether patients can fully benefit from therapeutic innovation.[21]

As figure 1 shows, the market for hematological cancer therapies is entering a period of sustained expansion, driven by continued innovation in targeted treatments, immuno-oncology agents, bispecific antibodies, and cellular therapies. IQVIA data reveals that the global market across major hematological cancers is projected to grow from approximately US$74.1 billion in 2025 to US$176.6 billion by 2035. Multiple myeloma represents the largest segment, accounting for an estimated US$33.8 billion in 2025, followed by non-Hodgkin lymphoma (US$12.8 billion) and chronic lymphoid leukemia (US$12.5 billion). This growth reflects both the increasing prevalence of hematological cancers and the rapid adoption of novel therapies that are delivering meaningful improvements in patient outcomes across multiple disease areas.

Figure 1. Global hematological cancer therapeutics market (2021-2035)



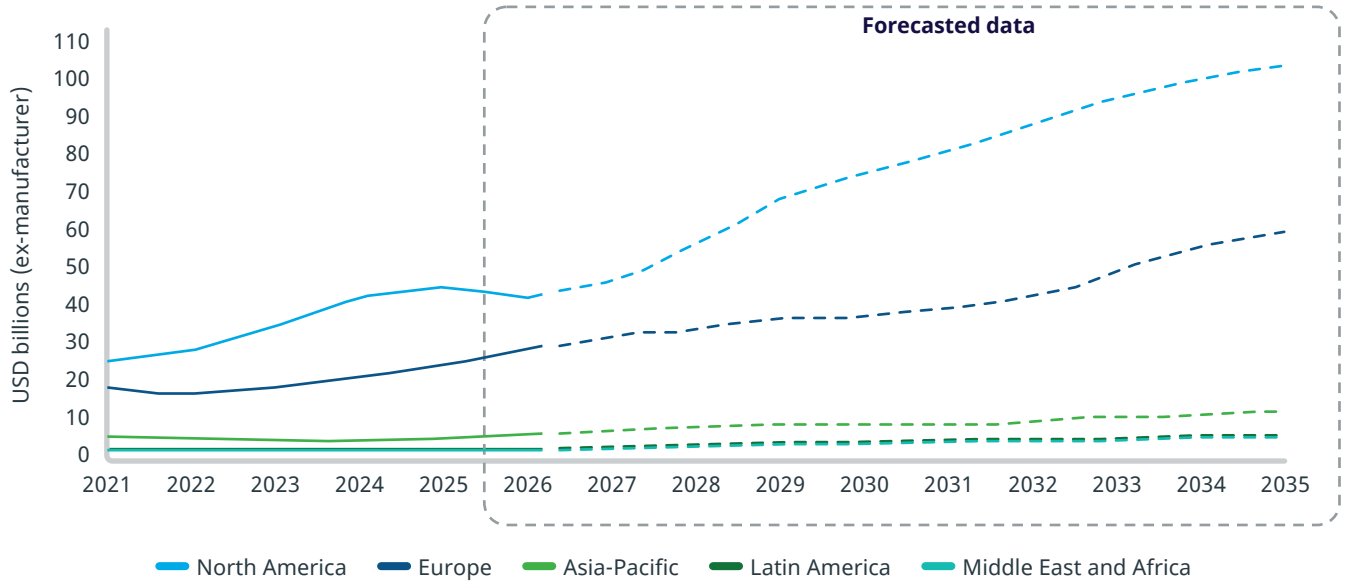
Source: IQVIA Forecast Link

Notes: Historical data is shown for 2021-2025. Values from 2026 onward are projected using IQVIA Forecast Link estimates. Amounts in USD billions (ex-manufacturer) across nine disease categories.

Beyond established markets, emerging economies are expected to contribute an increasing share of future growth. Rising healthcare expenditure, expanding diagnostic capabilities, broader insurance coverage, and improving access to innovative therapies are projected to drive an increase in treatment uptake between 2025 and 2035 across Asia-Pacific (+17.2%), Latin America (+7.7%), and the Middle East and Africa (+24.0%). Although the latter show the highest forecast compound annual growth rate, this is occurring from a relatively small market base. From an absolute value perspective, Asia-Pacific contributes substantially more incremental market growth over the forecasted period.

As healthcare systems invest more heavily in cancer care infrastructure and reimbursement pathways evolve, patients in these regions are gaining access to therapies that were previously limited to higher-income markets. The growing availability of biosimilars is also helping to expand access while creating headroom for investment in newer treatment modalities. Figure 2 summarizes trends in emerging markets.

Figure 2. Hematological cancer market by region (2021-2035)



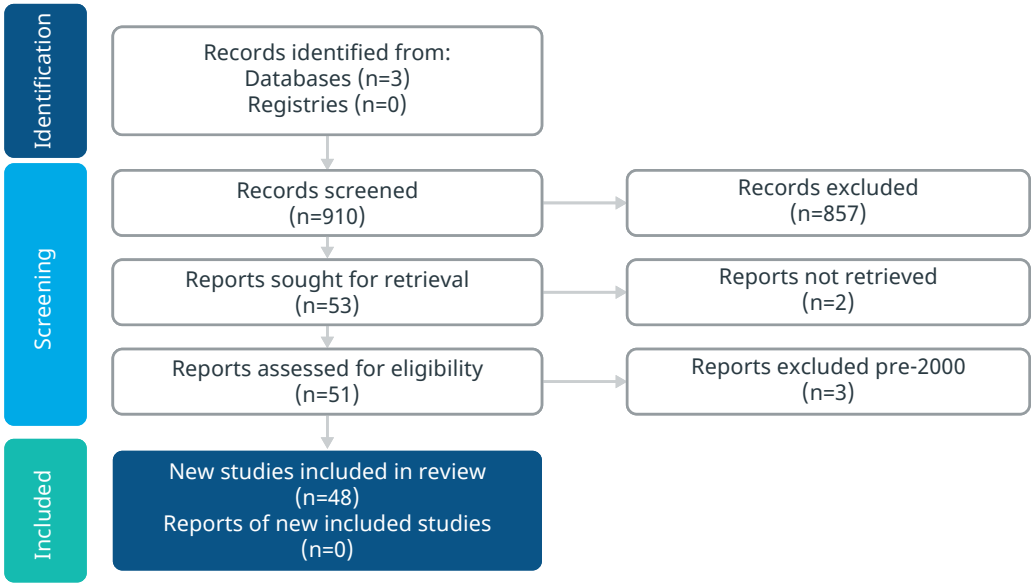
Source: IQVIA Forecast Link
Notes: Historical data is shown for 2021-2025. Values from 2026 onward are projected using IQVIA Forecast Link estimates. Amounts in USD billions (ex-manufacturer) across nine disease categories.

At the same time, the full value of these therapeutic advances will depend on the ability of healthcare systems to manage the infectious complications that frequently accompany the treatment of hematological cancers. As the market continues to shift toward highly effective but often profoundly immunosuppressive therapies, the burden of infection and AMR could play a more prominent role in shaping both clinical outcomes and healthcare resource utilization. In this context, investments in infection prevention, antimicrobial stewardship, diagnostics, and surveillance should be viewed not only as public health priorities but also as critical enablers of sustainable growth and value realization within the global hematology-oncology market.

The threat of infections in the treatment of hematological cancers: What the literature suggests

This literature review covered 48 studies across several geographies, including Europe, North America, Latin America, East Asia, South Asia, the Middle East, and Oceania. It revealed that people living with hematological cancers are particularly vulnerable to severe infections, the epidemiology of which has shifted markedly over the past two decades. Bloodstream infections, occurring when bacteria enter the blood, are now more commonly caused by Gram-negative bacteria and are a major cause of infection-related death in this patient group. *E. coli* and *K. pneumoniae*, as indicated earlier, have emerged as leading causes of sepsis in patients receiving intensive cancer therapy, especially those with neutropenia, a condition marked by very low levels of infection-fighting white blood cells.[22,23]

Figure 3. Identification of new studies through databases and registers



Notes: PRISMA screening flow: 910 records screened and 48 studies included in the review. The literature encompassed high AMR burden settings, including Argentina, China, India, Pakistan, and Türkiye.

High infection risks are closely linked to underlying immune dysfunction. Hematological cancers often impair the immune system even before treatment begins. Many patients have reduced antibody production, as seen in chronic lymphocytic leukemia and multiple myeloma, or weakened T-cell function, which increases susceptibility to viral, fungal, and certain bacterial infections.[24] Some patients also have functional or anatomical loss of the spleen, making them more vulnerable to specific bacterial pathogens.[25] Additional disease-related factors, such as bone marrow involvement, disruption of protective barriers like the gut lining, and poor nutritional status, further reduce the body's ability to prevent and effectively respond to infection.



Figure 4. Risk factors for infection in people living with hematological cancers

Disease-related factors	Treatment-related factors	Iatrogenic factors	Additional factors
Reduced antibody production (e.g., CLL, myeloma)	Chemotherapy and radiotherapy: neutropenia and mucosal injury	Repeated or prolonged antibiotic courses	Older age
Impaired T-cell function	Corticosteroids and TNF-α inhibitors	Frequent and prolonged hospitalization	Co-morbidities and frailty
Functional or anatomical asplenia	Anti-CD20 antibodies, proteasome and JAK inhibitors	Recurrent outpatient clinic visits	Regional resistance patterns
Bone marrow infiltration	Reactivation risk: hepatitis B, tuberculosis, and herpesviruses	Indwelling lines and catheters	Socio-economic barriers to care
Disruption of mucosal barriers	Stem cell transplant: GvHD and slow immune reconstitution	Invasive diagnostic procedures	Limited access to diagnostics and antimicrobials
Nutritional deficiencies	CAR-T and bispecific antibodies: prolonged cytopenia, B-cell aplasia	Colonization with multidrug-resistant organisms	Prior colonization or infection history
	Checkpoint inhibitors: immune dysregulation		Limited microbiology and surveillance capacity

Abbreviations: CAR-T = Chimeric antigen receptor T-cell (therapy), CD20 = Cluster of differentiation 20 (B-cell surface antigen targeted by anti-CD20 antibodies), CLL = Chronic lymphocytic leukemia, GvHD = Graft-versus-host disease, JAK = Janus kinase, and TNF-α = Tumor necrosis factor alpha.

Many modern therapies, corticosteroids, anti-CD20 antibodies, proteasome inhibitors, tumor necrosis factor α inhibitors, and Janus kinase inhibitors, suppress specific immune pathways and are associated with well-recognized infection risks such as hepatitis B, tuberculosis reactivation, and herpesvirus infections.[26-29] Stem cell transplantation further extends the period of immune vulnerability, as immune recovery may take several months.

Newer immunotherapies have added additional layers of complexity. Treatments such as CAR-T therapy and bispecific antibodies often lead to prolonged low blood counts, loss of normal B cells, and reduced antibody levels, leaving patients vulnerable to infection long after treatment initiation.[30-32] Immune checkpoint inhibitors, while not traditionally immunosuppressive, can disrupt normal immune balance and have been linked to unusual or opportunistic infections, although the underlying mechanisms are still being clarified. In conjunction, these factors create a clinical environment in which infections are frequent, difficult to manage, and linked to significant clinical and health system impact.

People living with hematological cancers are also notably exposed to resistant bacteria due to the nature of their care. Many receive repeated or prolonged courses of antibiotics, experience long hospital admissions, and have frequent contact with healthcare environments.[33,34] These factors amplify both the likelihood of acquiring resistant organisms and the risk that colonization, such as bacteria carried in the gut, will later lead to invasive infection. Despite this, detailed and consistent epidemiological data in this population remains limited, and relatively few studies have clearly shown how colonization translates into subsequent bloodstream infection.[35,36]



These overlapping risk factors create a clinical environment in which infections are both more frequent and more difficult to manage effectively. The growing prevalence of resistant Gram-negative pathogens, combined with profound and prolonged immune suppression, places considerable pressure on existing treatment paradigms. For clinicians, this translates into narrowing therapeutic options and greater reliance on timely, targeted intervention. For healthcare systems and industry stakeholders, it highlights an area of persistent unmet need, where improved diagnostics, preventive strategies, and novel anti-infective approaches could substantially improve outcomes for a highly vulnerable patient population.

Figure 5. Summary of findings of the literature review

Burden and pathogens	Resistance and risks	Global picture and response
1 Infections remain a major cause of morbidity and mortality in patients with hematological malignancies	4 Multidrug-resistant (MDR) organisms are becoming more prevalent, challenging effective treatment	7 Low- and middle-income countries report higher burdens of MDR infections than high-income countries
2 Bloodstream and respiratory infections were the most frequently reported infectious complications	5 Intensive chemotherapy, stem cell transplantation and CAR-T therapy carry the highest infection risk	8 Geographic variation in resistance patterns demands locally tailored empirical antibiotic strategies
3 Gram-negative pathogens, particularly *E. coli* and *K. pneumoniae*, are increasingly dominant causes	6 Prolonged, severe neutropenia is consistently the most important risk factor for serious infection	9 Prevention, surveillance and antimicrobial stewardship are critical to improving outcomes

The human impact of infections in hematological cancers

To illustrate the lived experience of people living with hematological cancers, in-depth interviews were conducted with three individuals in high-income and middle-income settings. Additionally, two hematology clinicians from the United Kingdom were also consulted. Across these perspectives, infections emerged as central to care, shaping treatment experiences, influencing quality of life, disrupting care pathways, and creating emotional, financial and clinical burdens, alongside mounting concerns about AMR and the increasing complexity of infection management. Clinical trials and real-world data studies document infection occurrence, but patient experience reveals the downstream impact on treatment continuity, support needs, and the implicit costs of intensified care, underscoring the need for people-centered outcome measures and more nuanced reporting.

Patients often describe infections not as discrete clinical events, but as experiences marked by profound uncertainty. Kirstin Molven, treated in Norway during the COVID-19 pandemic, developed neutropenic sepsis caused by her own bacteria. "I could never have gone through this type of treatment without effective antibiotics, as the risk would have been too high. Access made it safer to receive induction treatment as I was continuously on prophylactic treatment to avoid pneumocystis pneumonia. And when I got sepsis, access to several lines of antibiotics made it possible for my treatment team to effectively change when first-line treatment did not work. I do not think it is always easy to know exactly when to change drugs, but I know that in my case it needed to be done quickly, so that I could continue treatment as scheduled." Although she knew sepsis was a possibility, she did not appreciate how quickly she could deteriorate, and later found dose reduction for her cancer treatment concerning despite reassurance that it followed protocol. Her infection episode, period of isolation, and recovery also imposed anxiety, fear of hospitalization, and ongoing vigilance with hand hygiene, mask use and limiting visitors, mirroring the lived experience of many hematology-oncology patients. Her story underlines how modern cancer care depends on prophylaxis, rapid diagnosis, and multiple antimicrobial options integrated into comprehensive psychosocial support, and highlights the importance of continuous patient education to manage infection risk.

Magalí Yáñez, treated for stage IIIB Hodgkin lymphoma in Argentina, experienced fungal pneumonia, recurrent urinary tract infections, and shingles after bone marrow transplantation. Her pneumonia delayed chemotherapy by two weeks: "That was the day they told my mother I could die." She endured monthly urinary tract infections for almost two years, repeated antibiotic courses, prolonged hospitalizations and emotional distress, yet tolerated chemotherapy. Infections added substantial financial strain when her family sold property and rented a place near Buenos Aires to facilitate access to care. Her case highlights regional disparities where travel, accommodation, and out-of-pocket expenses amplify infection burdens, especially in middle-income countries where social safety nets are thin. Compared with high-income settings, follow-up care and rehabilitation support are less readily available, exacerbating long-term vulnerability.

Maximiliano Morales, a physician with nine years of treatment for Hodgkin lymphoma, reflected on his own experience with prolonged neutropenia, transplantation, and severe infection. "The worst thing about having a white cell count of zero is that you feel nothing. You can think everything is fine while internally it is not." He experienced a catheter-associated infection treated with vancomycin and noted how infections disrupted work, family life, and mental wellbeing. His dual perspective as patient and clinician also shaped his outlook on the need for shared decision-making and clear communication when adjusting treatment in the face of infection, advocating for anticipatory guidance and peer support networks.

These patient experiences mirror clinician observations. Dr. Katrina Ferrell, consultant hematologist in Scotland, noted that "infections can impair our delivery of potentially curative treatment to people with potentially curable cancers. It is not necessarily the blood cancer that patients struggle with most. Sometimes it is infections themselves."



Recurrent respiratory infections, prolonged antibiotics, persistent symptoms, and repeat hospital visits frequently overshadow the malignancy itself. These effects extend beyond clinical metrics to cognitive burden, fatigue, and reduced social participation, dimensions that are rarely captured in standard adverse event reporting. Ferrell advocates for integrating quality of life measures that capture infection burden into trial endpoints and routine care.

"It is not necessarily the blood cancer that patients struggle with most. Sometimes it is infections themselves."

Another clinician, whose name is not disclosed, confirmed a growing burden: "We are definitely seeing more infections. We are giving more treatment to more patients and many more older patients, and we are using more antibiotics than ever because we are employing multiple lines of treatment." Patients now survive longer, receive more therapies, and benefit from novel agents, but these gains create larger populations of heavily pre-treated, immunocompromised individuals vulnerable to infection for extended periods. CAR-T and bispecific therapies, for example, lead to later infections outside predictable chemotherapy-induced neutropenia periods, requiring vigilance months after initial treatment. The clinician emphasized the need for extended follow-up protocols and multidisciplinary infection management clinics.

Antibiotic use has increased accordingly. Clinicians treat febrile episodes, manage recurrent infections, and sometimes have to use antibiotics for prophylaxis. One of the clinicians reported her institution deliberately decided against routine antibacterial prophylaxis during neutropenia because of concerns about resistance, *Clostridioides difficile* and methicillin-resistant *Staphylococcus aureus*, although she noted that the calculus may differ in settings with higher baseline infection rates. Meanwhile, Yáñez described self-medication with ciprofloxacin for recurrent urinary tract infections until advised otherwise, suspecting reduced effectiveness later. Both examples highlight tensions between immediate patient need and long-term stewardship objectives that require nuanced guidelines and patient education. There is a clear demand for local antibiograms and stewardship teams embedded in oncology centers to inform practice in real time.

AMR is increasingly visible to clinicians, though not yet a primary determinant of treatment choice in most high-income settings. One of the clinicians could not recall a patient being denied curative treatment solely due to resistant infection but acknowledged the situation may change: "At the moment, antimicrobial resistance is not affecting our choice of therapy, but it might in the future." Ferrell described losing effective antibiotics as terrifying: "Our ability to treat blood cancers is entirely dependent on having antibiotics that work." Growing local resistance patterns, especially to Gram-negative organisms, are already complicating empiric choices, reinforcing the need for rapid diagnostics and access to newer agents. Clinicians support investment in new antibiotic development and regulatory pathways that recognize hematology-oncology as a high-priority field.

"Our ability to treat blood cancers is entirely dependent on having antibiotics that work."

Patients and clinicians aligned on recommendations. Patients underscored the importance of trust, transparency, clear guidance on infection risks, and psychosocial support, including counselling for anxiety and navigating infection-induced treatment changes. Clinicians advocated stronger microbiology services, better surveillance, improved diagnostics to distinguish bacterial from viral and fungal infections, and more detailed infection reporting in clinical trials, including management approaches and prophylaxis effectiveness. They also called for investment in infection prevention infrastructure such as clean rooms, HEPA filtration, and telemedicine support to reduce unnecessary hospital visits. Additionally, interviewees indicated that governments and life sciences should support global stewardship initiatives, tailor guidelines to immunosuppressed populations, and fund research into vaccines and prophylactic strategies specific to hematology-oncology.

These perspectives lay bare a fact often obscured in clinical trial reports. Infections influence treatment delivery, quality of life, healthcare utilization, emotional wellbeing, and survival. They also impose additional cost and capacity burdens on health systems. As hematology-oncology evolves towards more complex, immunosuppressive therapies, understanding and mitigating infection risk will be essential for protecting patients and preserving antimicrobial effectiveness. Future research should prioritize lived experience metrics, integrate infection reporting with patient-reported outcomes, and support global stewardship initiatives that recognize the unique needs of this population. Robust policy frameworks are also needed to ensure equitable access to infection prevention and treatment across regions.

Section II. What do clinical trials reveal about infections in hematological cancers?

To understand how infections are captured in late-stage evidence for hematological cancers, this paper examined 27 multinational and multisite phase III interventional clinical trials, reflecting the global nature of contemporary hematology research. These studies enrolled 11,969 participants, providing a substantial evidence base for assessing how frequently infectious complications occur, how they are reported, and how they relate to treatment intensity and trial outcomes.

Trials were identified from the IQVIA clinical trials database, obtained through an internal information request covering all oncology portfolio trials from 2010 onwards. This provided an extensive dataset of studies, which was then screened and narrowed to hematology-oncology trials completed by December 2023 with published results. Geographically, the trial dataset was dominated by Europe, North America, and East Asia (Republic of Korea, Japan, and Taiwan), signaling a focus on high-income settings.

The analysis looked for recurring patterns across multiple clinical trials to determine what factors best explained differences in infection rates. By comparing treatment groups, cancer types, and study populations, it assessed whether infections were more strongly influenced by the treatment patients received or by underlying disease characteristics. Statistical analyses were used to distinguish meaningful associations from random variation and identify the factors most closely linked to infection risk.

Figure 6. Hematological cancers in scope (not an exhaustive list)

Leukemias	Lymphomas	Plasma cell and myeloid neoplasms
Acute lymphocytic leukemia	Diffuse large B-cell lymphoma	Multiple myeloma
Acute myeloid leukemia	Hodgkin lymphoma	Myelodysplastic syndrome
Chronic lymphocytic leukemia	Non-Hodgkin lymphoma	Myelofibrosis
Chronic myeloid leukemia	Mantle cell lymphoma	Waldenström macroglobulinemia
	Peripheral T-cell lymphoma	

The purpose of this review was not to compare the efficacy of individual drugs but to identify patterns in infection burden, reporting practices, and downstream trial consequences such as treatment discontinuation and mortality. In doing so, the analysis highlights both what publicly available trial evidence reveals and what remains insufficiently captured or described about infection risk in hematological cancer care.

The review of these trials resulted in the following observations:

Infections are reported unevenly across trials

One of the key findings from this analysis is the extreme variation in reported infection burden across phase III trials. When infection events were standardized as events per 100 participants to allow comparison between studies of different sizes, rates varied by more than 300-fold. Some trials reported very few infections, while others reported infection rates that exceeded one event per participant over the course of follow-up.

While infection events, including microbiology and AMR data, are captured in many cases, this information may not be made available in granular detail due to current reporting requirements and practices, which usually consolidate data into larger categories for sponsors and regulatory authorities. In some instances, data may not be captured at all. As a result, there can be a marked difference between the data associated with the management of trial participants and the level of data shared as part of a trial's evaluation.

This variation reflects a combination of factors that differ substantially between studies, including the underlying disease population (e.g., newly diagnosed versus relapsed or refractory disease); treatment intensity and duration; degree and type of immune suppression; follow-up length; and how infections are defined and reported in publications or trial registries.

While the trials analyzed met regulatory standards for phase III evidence, the infection signal they exposed was far from uniform or predictable. This has implications for how confidently infection risk can be inferred from headline trial outcomes alone.

High rates of treatment non-completion are the norm, not the exception

Alongside infection burden, the analysis examined treatment non-completion, defined as patients who did not finish the assigned regimen for any given reason. In this instance, as occurred with infection

reporting, the range was wide. In phase III oncology trials, non-completion matters because it affects the dose and duration of therapy delivered; the interpretation of efficacy endpoints; patient safety; and the extent to which results can be translated into routine clinical practice.

While non-completion can result from many factors, including disease progression, patient choice or non-infectious toxicity, infections are a plausible and important contributor. The key point is that attrition is common and substantial in many hematological-oncology trials, and infection risk needs to be understood as part of this broader operational reality rather than as a marginal adverse event.

A consistent clinical pattern is evident despite significant heterogeneity

Although infection rates varied widely, the types of infections reported were remarkably consistent across studies. When events were grouped into broad clinical categories, several clear patterns emerged.

Across the full analysis:

- Respiratory infections dominated, accounting for roughly half of all recorded events. Pneumonia and lower respiratory tract infections were especially prominent.
- Sepsis and sepsis-related syndromes formed the second largest category and appeared repeatedly across different regimens.
- Other infection types, including urinary tract, skin and soft tissue, gastrointestinal, and non-specific infections, accounted for a smaller yet still meaningful share of reported events.
- Viral and fungal pathogens also featured across the dataset, contributing a smaller but notable proportion of cases.

This consistency is notable and relevant. It suggests that, despite differences in trial design and reporting detail, the dataset reflects a recognizable and clinically plausible infection landscape for patients with hematological cancers. This helps to conclude that infections are not random or incidental, but follow patterns aligned with known vulnerabilities in immunocompromised populations.[37,38]

Infection patterns differ by treatment type

To explore whether infection burden reflects the nature of therapy, treatments were grouped into four broad categories:

- **Monoclonal antibody monotherapy:** Lowest overall risk

  When used alone, often in maintenance settings, monoclonal antibodies showed the lowest overall infection burden. Infections were predominantly respiratory, while severe bloodstream and sepsis related events were less common. This pattern is consistent with selective impairment of the immune system.

- **Cytotoxic chemotherapy:** Predictable but serious risk

  Cytotoxic chemotherapy arms showed a moderate-to-high infection burden, dominated by respiratory infections and sepsis. These patterns align with well-established effects of chemotherapy, including neutropenia and damage to mucosal barriers, which increase susceptibility to both local and systemic infections.

- **Targeted small-molecule therapies and immunomodulatory agents:** Variable but potentially very high-burden

  These therapies showed the highest pooled infection burden overall, driven in part by specific agents used in high-risk, heavily pre-treated populations. While respiratory and sepsis-related events again dominated, these regimens also showed a broad mix of other infections, including catheter- and device-associated events. This reflects prolonged immune modulation, cumulative exposure, and treatment in patients with advanced disease.



- **Combination regimens:** Additive vulnerability

  Combination regimens produced the broadest and most diverse infection profiles. Respiratory infections remained most common, but sepsis and a wide range of other infections were also frequent. This likely reflects additive or synergistic immune suppression when multiple therapeutic mechanisms are combined, alongside longer treatment courses and more intensive supportive care requirements.

Across all classes, the analysis reinforces the critical point that treatment modality is a major determinant of infection risk in hematological cancer trials.

Infections occur even when neutropenia is rarely reported

Reported neutropenia across most trials, including those involving cytotoxic chemotherapy and combination regimens, was generally low, with higher rates in combination arms. This does not necessarily suggest that neutropenia was genuinely uncommon, and may instead reflect variation in definitions, thresholds, and reporting practices across trials. Given this uncertainty, the low reported rates cannot be used to infer the relative contribution of neutropenic versus non-neutropenic mechanisms to the infections observed.

Independent of this reporting limitation, this pattern aligns with the current clinical understanding that hematological cancers and their treatments impair immune function through multiple, overlapping mechanisms, including B-cell dysfunction, T-cell impairment, innate immune disruption, and cumulative treatment-related immunosuppression. This supports the view that infection risk in these populations is unlikely to be attributable to neutrophil suppression alone, though the extent to which each pathway contributes cannot be determined from the present data.

Section III. Integrated findings from the literature review and trial analysis

This white paper set out to understand how infections shape outcomes in hematological cancers, and whether current clinical trial evidence adequately reflects the risks observed in real-world practice. By integrating a structured literature review with a detailed analysis of 27 phase III hematological cancer trials, several clear and interrelated findings emerge.

At a high level, both evidence streams converge on infections as a frequent, clinically consequential, and treatment-shaped burden in hematological cancer care. Although infections are routinely reported as adverse events in trials, the limited detail provided often constrains the utility of trial-generated infection data, exposing structural limitations in the evidence base that underpins therapeutic development, regulatory decision-making, and market planning.

Main findings

1. **Infections are the baseline and a central clinical burden:**

   Across both the published literature and the phase III trial analysis, infections consistently ranked among the most common adverse events in hematological cancers. While absolute rates varied widely by regimen and population in the trial data, respiratory infections, particularly pneumonia, appeared as the dominant category, accounting for roughly one-third to one-half of all reported events. Sepsis and sepsis-related complications formed the second most prominent category across studies.

   This pattern closely mirrors the literature, which repeatedly identifies pneumonia and bloodstream infections as leading causes of morbidity and mortality in hematological cancer populations. Therefore, the two evidence streams confirm that infections are not peripheral complications but core determinants of patient safety, treatment continuity, and outcomes, with their impact strongly shaped by therapeutic exposure.

2. **Treatment exposure, not diagnosis, is the primary driver of risk:**

   Both the literature and the trial analysis demonstrate that infection risk is far more closely linked to treatment modality than to cancer type.

   The strongest and most statistically robust association observed in the trial dataset was between treatment class and infection risk. More intensive or immunomodulatory regimens were clearly associated with higher infection rates, confirming that treatment selection plays a central role in shaping susceptibility. The following evidence was captured as part of the analysis:

   - **Chemotherapy and combination regimens** were consistently associated with neutropenic sepsis and bacterial pneumonia across both sources, reflecting prolonged myelosuppression and mucosal barrier injury.
   - **Monoclonal antibody monotherapy**, particularly in maintenance settings, showed a lower overall infection burden, dominated by respiratory infections and occasional skin or soft tissue events.
   - **Targeted small-molecule therapies and immunomodulatory agents** produced the most complex signal. In the trial dataset, they showed the highest pooled infection rate, affecting roughly 40% or more of participants and translating to a high number of infection events per 100 patients.

   By contrast, no meaningful association was observed between infection risk and cancer type, underscoring that diagnosis alone is a poor predictor of infectious burden once treatment exposure and patient context are factored in. This finding aligns with clinical experience and supports a shift away from diagnosis-centric models of infection risk toward treatment and exposure-based frameworks.

3. **Treatment class matters, but context and population matter just as much:**

   While infection risk varies by treatment class in both sources of evidence, the magnitude and interpretation of that risk depend strongly on patient selection and trial design.

   The phase III trial analysis showed that infection rates were often highest in studies involving relapsed or refractory disease, heavily pre-treated patients, or populations with greater cumulative immune compromise. In these settings, the burden of infection frequently exceeded what would be expected from the treatment mechanism alone.

   Differences in follow-up duration, adverse event reporting, and eligibility criteria also contributed to substantial variation across trials, even within the same therapeutic class. In contrast, the literature generally reports more moderate infection risks, mainly in less heavily pre-treated populations. This divergence highlights the importance of disease stage, prior therapy, and trial inclusion criteria, and cautions against attributing infection risk solely to drug mechanism in isolation.

4. **Infection burden is linked to trial outcomes, but it is incompletely reported:**

   Beyond frequency, the analysis explored how infections relate to broader trial outcomes. A moderate positive association between infection burden and mortality was observed: trial arms with higher infection rates tended to report higher death rates. While this relationship does not establish causality, it is consistent with the clinical reality that serious infections both contribute to, and signal, poorer outcomes in immunocompromised populations.

   The relationship between infections and treatment discontinuation was weaker overall and not statistically significant. However, important nuances came to the fore. In monoclonal antibody arms, where baseline toxicity is low, even small increases in infection burden appeared to exert a disproportionate effect on treatment discontinuation. In combination regimens, by contrast, high infection rates were observed irrespective of completion status, suggesting that other drivers such as cumulative toxicity or disease progression also shaped attrition.

   Concurrently, these findings seem to suggest that infections may influence mortality and treatment continuity, but current trial reporting does not consistently link infections to downstream outcomes, limiting interpretability. This limitation is highly relevant given growing evidence that infections drive substantial morbidity and mortality in patients with hematological cancers, underscoring the need for more systematic reporting of infection-related outcomes.[39]

5. **There is a critical divergence between what trials report versus what clinicians observe:**

   Despite broad agreement on the importance of infections, the two evidence bases diverge sharply in the level of detail reported.

   The literature places strong emphasis on bloodstream infections and multidrug-resistant Gram-negative bacteria, particularly third-generation cephalosporin- and carbapenem-resistant Enterobacterales and vancomycin-resistant Enterococci. These pathogens are repeatedly contributing to treatment failure, prolonged hospitalization, and excess mortality in real-world cohorts.

   By contrast, the phase III trial dataset rarely reports microbiologically defined bloodstream infections. Instead, serious infections are largely aggregated under broad clinical labels such as “sepsis” or “infection,” with no information on causative organisms, resistance patterns, or colonization status. This systematic difference reflects a structural coding and reporting gap between controlled regulatory trials and observational or real-world studies.

As a result, current phase III trials capture the presence of infections, but not their drivers. This is a limitation that becomes increasingly consequential in an era of rising AMR.

6. **Neutropenia explains part of the risk but not all of it:**

   The role of neutropenia further illustrates the gap between trial reporting and clinical experience. The literature strongly links prolonged neutropenia, most commonly following intensive chemotherapy, stem cell transplantation, or CAR-T therapy, with invasive bacterial and fungal infections. In contrast, the phase III trial dataset reported very low rates of treatment-emergent neutropenia, generally below 10% across drug classes.

   This discrepancy may be explained by selective adverse-event grading and trial composition, particularly the absence of stem cell transplantation and CAR-T therapies from the dataset. Other mechanisms such as lymphocyte dysfunction, impaired humoral immunity, mucosal damage, and disease-related immune compromise clearly play a substantial role, while remaining insufficiently captured by standard trial adverse-event reporting frameworks.

7. **Geography matters and trials miss the highest risk settings:**

   Geographic coverage represents one of the most consequential structural differences between the two evidence streams. As indicated earlier, the phase III trials analyzed were concentrated in Europe, North America, and parts of East Asia, notably Japan, South Korea, and Taiwan. By contrast, the literature draws on data from high-burden and rapidly growing regions, including Latin America, South Asia, the Middle East, and China, settings that continue to exhibit the highest prevalence of multidrug-resistant infections.

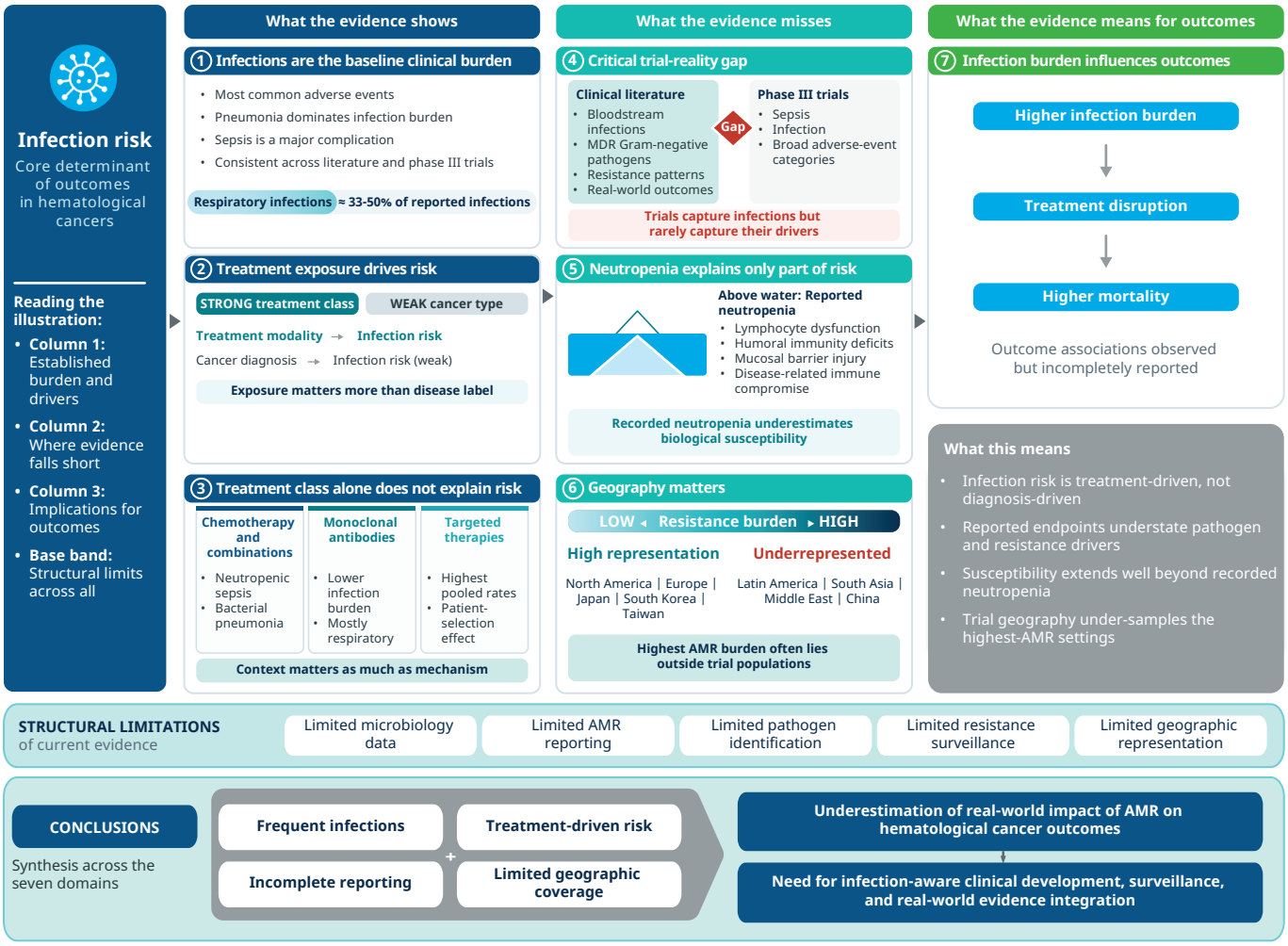
   The failure of trial datasets to report an AMR signal is likely driven primarily by the lack of sufficiently granular data, as the information required to demonstrate the impact of AMR is not routinely collected for regulatory purposes. The mismatch between trial locations and future growth markets further compounds this limitation and means that current trial reports may underestimate the clinical and operational challenges that will emerge as hematology-oncology therapies expand into regions with the highest resistance burden.

Overall, these findings show that infections are frequent, outcome-shaping, and highly dependent on treatment exposure, yet remain systematically underreported in late-stage clinical trials. The absence of microbiological and AMR data, combined with limited geographic representation, creates a gap between controlled trial conditions and real-world clinical practice.

As hematology-oncology innovation increasingly relies on complex, long-term, and globally deployed therapies, accurate measurement and interpretation of infection risk is critical. This task should then become a prerequisite for ensuring that therapeutic gains observed in trials translate into durable, equitable benefits for patients, and into sustainable value for health systems and payers.



Figure 7. Summary of findings



Recommendations

AMR is no longer only a clinical risk but represents a system level challenge that cuts across innovation, regulation, access, and market sustainability in the hematology-oncology space. Safeguarding future progress will require coordinated action by industry, national authorities, and civil society.

While AMR underpins many of these challenges, the most immediate and tangible risk for patients and providers is infection itself, particularly when it disrupts or prevents treatment delivery. Framing the issue through infection risk and management helps anchor these recommendations in real-world clinical decision-making, while maintaining focus on AMR as the underlying systemic threat.

The recommendations below outline mutually reinforcing actions across these stakeholders:

For industry and clinical developers: Incorporating resilience into innovation and market delivery

- **Embed AMR readiness into clinical development:** Clinical development strategies should explicitly address infection and resistance risk as determinants of trial feasibility and real-world deliverability. This encompasses the integration of relevant considerations into trial design; for example, baseline colonization screening, region-adapted prophylaxis protocols, and structured infection surveillance. These measures strengthen patient safety while generating data that better reflects clinical practice. Complementing this, integrating real-world research alongside clinical development can address key evidence gaps. Linking trial data with clinical datasets, including microbiology, antimicrobial use, hospitalization, and outcomes, provides a more complete picture of infection risk across pathogens, geographies, and treatment exposures. Strategic geographic expansion of trials remains equally important. Ensuring late-stage studies include high-resistance and fast-growing markets improves the relevance of safety and efficacy data, reduces regulatory and payer uncertainty, and helps identify implementation challenges before launch.
- **Integrate point-of-care (POC) diagnostics to enable earlier, targeted intervention:** POC diagnostics can play a critical role in identifying infection risk earlier in the patient pathway, before clinical deterioration leads to treatment discontinuation. Rapid, near-patient testing can support timely and appropriate use of antibiotics, helping clinicians balance the risks of overtreatment, including microbiome disruption and resistance selection, against the need to maintain therapy in immunocompromised patients. Incorporating POC diagnostics into clinical trial protocols and routine care pathways can reduce unnecessary antibiotic exposure, improve patient stability during treatment, and preserve trial continuity. As such, these tools should be considered a complementary investment alongside site-level microbiology, shifting infection management from reactive characterization to proactive prevention.
- **Strengthen microbiology infrastructure, data reporting, and surveillance:** High-quality infection data requires strong diagnostic foundations. Companies are encouraged to invest in site-level microbiology capacity, particularly in high-burden regions, including cultures, rapid antimicrobial susceptibility testing, and resistance gene detection where feasible. Such investments improve trial execution while building longer term health system capability. Linking AMR surveillance directly to adverse event granular reporting allows early identification of geographic- and pathogen-specific risk patterns, enabling proactive mitigation rather than post hoc response. When combined with real-world data linkages, these capabilities can further enhance the granularity and longitudinal understanding of infection and resistance patterns across care settings.
- **Partner on stewardship and prevention:** Infection risk cannot be mitigated through protocol design alone. Embedding antimicrobial stewardship programs within trials can reduce inappropriate antibiotic exposure, limit resistance emergence, and protect patients during prolonged treatment courses. At the same time, codeveloping targeted prevention strategies with infection specialists would safeguard against local and regional resistance patterns. These collaborative prevention strategies would benefit both patient outcomes and study integrity.
- **Broaden the supportive care value proposition:** As infection risk increasingly constrains treatment delivery, supportive care becomes a strategic asset. Companies should explore adjunctive investments or partnerships involving anti-infectives, vaccines, or pathogen-specific monoclonal antibodies relevant to hematology-oncology populations. In high-risk settings, integrated offerings — combining hematology-oncology regimens with infection prevention, treatment, and monitoring solutions — can enhance outcomes, strengthen payer value propositions, and improve adoption in high AMR-burden markets.

For governments and national authorities: Strengthening health system resilience and regulatory readiness

- **Integrate AMR into oncology and cancer control strategies:** National Cancer Control Plans (NCCPs) and oncology guidelines should explicitly recognize AMR as a cross-cutting risk to cancer care, particularly for immunosuppressive therapies. This should encourage the alignment of cancer, infectious disease, and AMR strategies to ensure coherent policy signals, funding priorities, and surveillance frameworks. A recent review conducted by the Union for International Cancer Control (UICC), for instance, found that only two of 98 available NCCPs referenced AMR-related strategies.[40] Therefore, taking action in this regard is essential.
- **Require and enable better infection reporting in trials:** Regulators and ethics committees can play a catalytic role by encouraging or requiring more granular infection reporting in late-stage oncology trials, including microbiological data where feasible. To support this, governments should invest in laboratory infrastructure, workforce training, and digital surveillance systems, most urgently in LMICs where resistance burden is highest.
- **Incentivize trials and innovation in high-burden settings:** Governments and regional authorities should actively incentivize clinical research in high-AMR, high-growth markets, using tools such as fast track review, tax incentives, or public-private partnerships.[41] Such policies help ensure that evidence generation keeps pace with local epidemiological realities and that new therapies are designed with real-world constraints in mind.

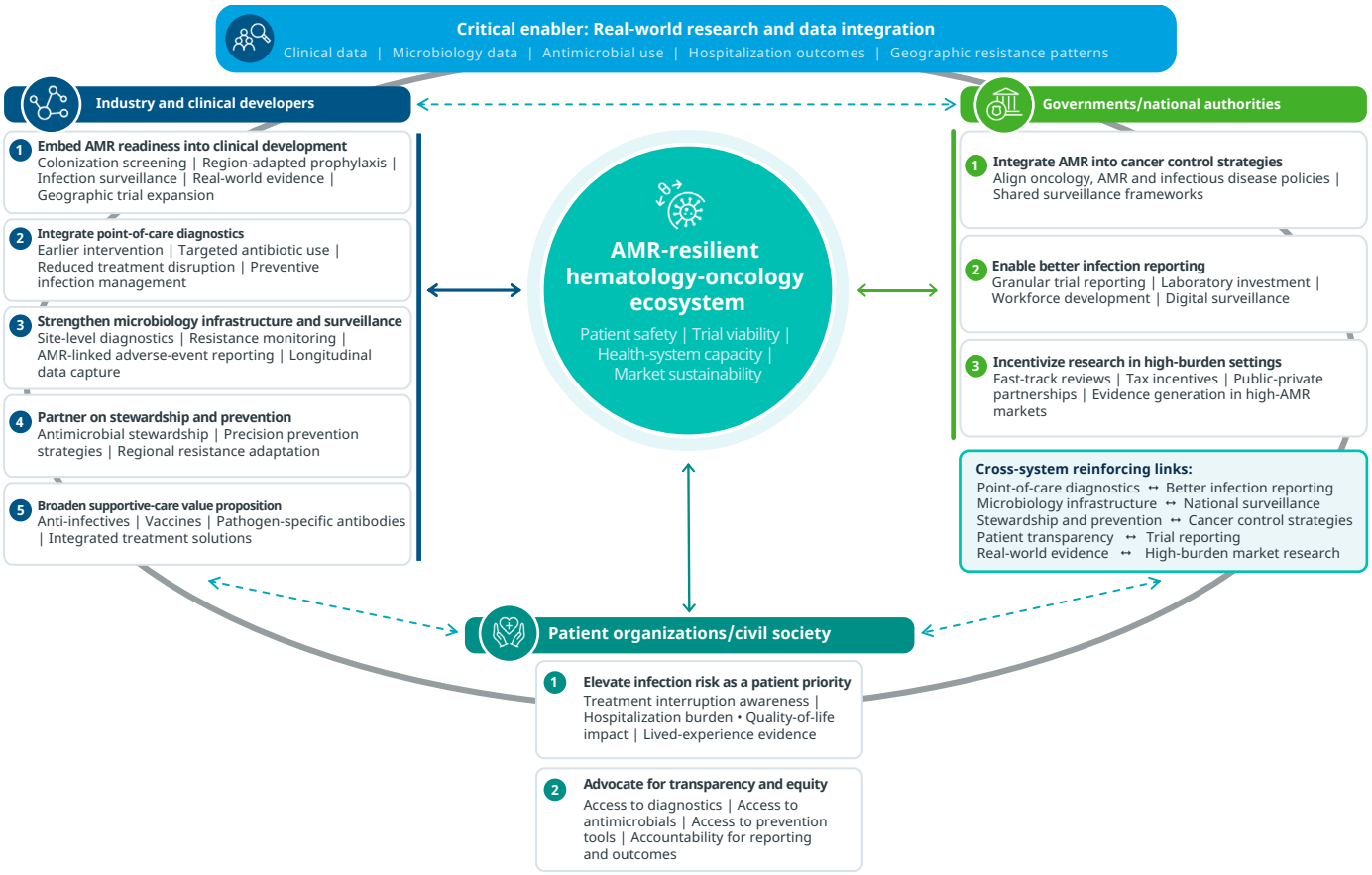
For patient organizations and civil society: Amplifying lived experience and accountability

- **Elevate infection risk as a patient priority issue:** Patient and advocacy organizations have a critical role in framing infection risk and its consequences — not only cancer progression — as major drivers of outcomes, quality of life, and access to care. This includes communicating risks in clear, accessible terms rather than relying solely on technical terminology. Grounding engagement in lived experience can help build broader awareness of the systemic challenges underpinning these risks. By documenting and communicating patient experiences of treatment interruption, hospitalization, and infection-related harm, these groups can strengthen the case for better data and system-level investment in interventions required to safely deliver immunosuppressive therapies, also covering the development of new anti-infectives.
- **Advocate for transparency and equity:** Patient organizations can press for greater transparency in infection reporting with respect to how risks differ by geography and health system capacity. In addition, they are well positioned to advocate for equitable access to diagnostics, anti-infectives, and preventive tools, ensuring that innovations in hematology-oncology also benefit patients in high-burden settings rather than widening disparities. They can also help hold stakeholders accountable for how infection risks are measured, reported, and addressed across clinical trials and routine care. This means pushing for more granular, patient-relevant data, such as treatment interruptions, hospitalizations, and quality-of-life impacts, so infection is recognized not only as a clinical complication but as a determinant of outcomes and access. By highlighting differences in patient experience across regions and care settings, patient organizations can help ensure that gaps in infrastructure, diagnostics, and infection management are visible and addressed, supporting more equitable and context-appropriate care.

In a low-impact AMR scenario, these combined actions reduce inefficiency and strengthen trust. In the more moderate- and high-impact scenarios, they become essential measures to protect patients, trial viability, health system capacity, and market sustainability. Real-world research will be a critical enabler of this shift, transforming infection from a poorly characterized risk into a measurable and manageable determinant of outcomes and value.

Without coordinated action, therapies developed in low-resistance environments risk failing, clinically or commercially, when deployed at scale in high-burden markets. Coordinated action, by contrast, would help stakeholders ensure that innovation in hematology-oncology remains deliverable, equitable, and resilient by embedding infection risk management as a core component of modern hematological cancer care, rather than treating it as a peripheral consideration.

Figure 8. Summary of recommendations



Coordinated action transforms infection from a poorly characterized risk into a measurable and manageable determinant of outcomes, value, and equitable access

Conclusion

AMR sits at the intersection of clinical safety, patient outcomes, and commercial sustainability in hematology-oncology. While scientific innovation continues to expand therapeutic possibilities, the ability to realize these gains at scale remains fundamentally dependent on effective infection prevention and treatment in increasingly immunocompromised populations.

From a clinical and patient perspective, infections remain among the most frequent and consequential complications of hematological cancer care. Pneumonia, sepsis, and bloodstream infections continue to drive morbidity, treatment interruption, and excess mortality across diseases and treatment classes. For patients, particularly in settings with high resistance prevalence, AMR translates into longer hospitalizations, delayed or discontinued therapy, and widening inequities in access to advanced treatments. These risks are compounded by the fact that AMR, despite its growing impact on outcomes, is largely invisible in the clinical trial evidence base.

At the same time, the findings highlight a growing disconnect between trial conditions and real-world delivery. Phase III trials routinely capture the occurrence of infections but rarely report their microbiological drivers, resistance patterns, or regional variation. As a result, trial datasets understate the scale and nature of infection-related risk in high-burden settings and provide limited insight into how AMR may shape outcomes once therapies are deployed globally.

For life sciences stakeholders, this gap is not merely a scientific limitation: it represents a material strategic risk. As hematology-oncology markets expand rapidly in China, South Asia, Latin America, and other high-growth regions that carry some of the world's highest AMR burdens, development programs grounded primarily in low-resistance settings may fail to anticipate future barriers to treatment delivery. Without deliberately integrating AMR considerations into clinical development, market planning, and supportive care strategy, companies could risk compromising patient safety, undermining trial feasibility, and exposing portfolios to delayed uptake, reduced real-world effectiveness, and adverse revenue impacts.

Critically, the analysis also underscores that AMR is not an external shock beyond industry control, but a risk that can be anticipated and mitigated. Companies that act early by strengthening infection surveillance, incorporating AMR-informed trial design, expanding evidence generation in high-burden regions, and investing in infection prevention and supportive care, can simultaneously improve patient outcomes and secure competitive advantage. In an increasingly crowded and globalized hematology market, the ability to demonstrate that therapies are deliverable, resilient, and safe in high AMR settings will become a source of differentiation rather than a regulatory afterthought.

For national authorities, these findings reinforce the need to treat cancer control and AMR as interconnected challenges. Without improved diagnostics, surveillance, data integration, and access to anti-infectives, rising resistance threatens to erode hard-won gains in cancer survival, particularly in LMICs. For patient organizations, there is a parallel imperative to elevate infection risk and treatment disruption as central patient experience issues, ensuring that equity and safety remain visible in both policy and development decisions.

In sum, AMR has evolved from a background clinical concern into a defining constraint and potential disruptor of hematology-oncology innovation and market growth. Addressing it will require coordinated action across public and private actors. Those who fail to adapt could widen the gap between therapeutic promise and real-world impact. Those who lead now will be better positioned to protect patients, future proof portfolios, and sustain value in a world where the proper management of infection risk is fundamental to success.

Study limitations

The literature review was limited by variability in study design, infection definitions, and AMR reporting standards. Data from LMICs was under-represented, potentially biasing findings toward high-income settings. Additionally, few studies directly linked colonization with resistant organisms to subsequent infection.

This trial analysis was constrained by several factors. First, the dataset comprised only 27 trials, which limited statistical power. Some correlations that did not reach significance might have done so in a larger sample. Second, the analysis relied solely on publicly-reported data. Infection outcomes were extracted from data available in trial publications or registries, which may under-represent the true burden of infections and obscure microbiological detail. As a result, findings should be interpreted with caution, acknowledging both the restricted dataset size and the limitations of reporting practices.

Treatment non-completion was defined as failure to complete the assigned regimen for any reason. It is possible that the regimens evaluated may have differed in intended treatment duration, with some administered for a fixed course and others continued until disease progression. Therefore, the reasons for non-completion may be due to study design. However, among patients who developed an infection, systematic differences are not anticipated in treatment discontinuation due to disease progression that would materially affect the interpretation of these findings.

Finally, this paper is focused on bacterial infections. This reflects the predominant role of bacterial pathogens, mainly multidrug-resistant Gram-negative organisms, in driving serious infections and mortality in hematological cancer care. It is recognized, however, that invasive fungal infections and antifungal resistance are significant and growing concerns in this profoundly immunosuppressed population, as reflected in both the trial data and patient experiences described in the paper, and represent an important area for dedicated future analysis.

Clarifications

In this analysis, treatments were grouped by predominant mechanism of immune effect rather than by target specificity alone. Monoclonal antibodies were considered separately from other targeted agents, reflecting their relatively selective impact on humoral immunity through antibody-mediated effector mechanisms, in contrast to the broader intracellular pathway modulation characteristic of small-molecule targeted agents and immunomodulatory drugs.

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Daniel Mora-Brito's work explores current and emerging trends within the realms of global health security, health system strengthening, and equitable access to healthcare, with a focus on LMICs. Daniel has vast experience in the multilateral sector, having occupied advisory positions in the Global Fund to Fight AIDS, Tuberculosis and Malaria, the United Nations Population Fund, and the Organization of American States. He also served a host of civil society organizations, overseeing multi-stakeholder programs at the Pan American Development Foundation and the Global Business Coalition for Health. His expertise covers areas such as health policy and financing, international development operations, institutional reform, and the design and implementation of public-private partnerships. Daniel holds graduate degrees in public management and social policy and development from the Universidad Metropolitana in Caracas, Venezuela, and the University of Texas at Austin, United States, respectively, with training in health policy and economics at the London School of Economics and Political Science.



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